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Dedicated to
Professor Bajram Preza
on the Occasion of
His 100th Birthday Anniversary

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INTRODUCTORY NOTE

With the impressive number of medical publications available, it is an uneasy job to introduce another new journal. Nonetheless, the actual collection of *Neurological Papers* compiled and published from the fellows and the seniors of the Service of Neurology in Tirana, has a strong historical background.

This work traces back with the *Psychoneurological Works*, a compilation of the founders of Albanian neurology and psychiatry, with the collection starting in 1959 and counting more than twelve issues. Approximately half of those contributions were neurological manuscripts: reviews, historical notes, case reports. Among the contributors were the founders of these medical disciplines in Albania: Hiqmet Dibra, Mit Vokopola, Bajram Preza, Xhavit Gjata and Ulvi Vehbiu; just to mention only some of the authors of the first issue. Many others would follow, raising the number of the published papers and their quality, while sharing a life-long knowledge and experience.

However, what is impressive, is the striking majority of case reports being published in the *Neurological Papers*; a global phenomenology in the community of medical publications. Neurology holds a share of 26% of all case reports published from *Lancet* in the period 2003-2008; ranking first on the list from all medical specialties, and probably remaining such thereafter [1]. As a matter of fact, neurological patients hold particularities that make situations and occurrences strange and unexpected. If the reader wants to overcome the *Baader-Meinhof* phenomenon, i.e. impression that something happens more frequently than it actually does, he/she might strive to go through the fifteen case reports published here: the clinicians' findings have shifted considerably during the Covid-19 pandemics [2, 3]. There are several articles dedicated to neurological conditions related to, or whose appearance is suspected following this viral infection.

What is unusual and what is not? For the time being, there is an important – maybe hyperinflated – bulk of medical publications. Things were different, let's say, one hundred years before. William Osler, the renowned Canadian physician, stated:

> *…Always note and record the unusual…Publish it…Such communications are always of value* [4, 5].

The present collection relies mainly, in case descriptions and rarities. The wide application and availability of imaging has rendered documentation easier than previously. There is abundant presence of images related to all cases, as well as a literature review in all of these. Infarct of Percheron artery, Lafora disease, Olivopontocerebellar atrophy, phenylketonuria or IgG4-related pachymeningitis – just to mention a few – will count among conditions needing a second glance, and with a cogent rationale of writing.

While revisiting 400 case histories of Galen of Pergamum, sources will surprisingly uncover that one tenth of these were dedicated to neurological and psychiatric disorders [6]. Centuries before the famous physician focused as well in symptoms associated with fever and epidemics. For a collection of neurological papers written during the Covid-19 pandemics, whose end is still uncertain, it seems that history is completing a full circle.

The actual publication opens with *two review* articles. The first deals with *Cognitive Disorders in Multiple Sclerosis*; the second is dedicated to *Basilar Artery Occlusion*, with the current recommendations on its diagnosis and management. Based on a thorough and updated reference reviewing, these papers cover highly important issues to the everyday neurological practice and treatment dilemmas.

Authors have made all attempts to produce an updated and correct bibliographical database in all articles; treatment suggestions however should be considered from the clinician case by case and in a personalized approach, since medicine is an evolving discipline.

Of course, this collection is to be seen as non-exhaustive both from the casuistic point of view, as well as from the methodological approach. Authors' dilemmas remain probably the same in all publications. In the preface of one their numerous editions of *Dialectic of Enlightenment,* the renowned authors wrote:

> *This restraint has made the book a piece of documentation; we hope that it is also more…* [7].

With all these possible restraints in mind, we also hope that the present collection of neurological papers, is more than a simple documentation.

Jera Kruja
Gentian Vyshka

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COGNITIVE DISORDERS IN MULTIPLE SCLEROSIS

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Introduction

Multiple sclerosis is a chronic, neurodegenerative disease characterized by autoimmune inflammatory demyelination of the central nervous system that affects various functions and is clinically characterized by exacerbations, relapses, and progressive disability over time [(1)].

The disease may initially present with focal neurological signs (less often) or evolve into (more often) a continuous progressive decline in neurological functioning, usually affecting motor skills, sphincters and cognition.

Cognitive disorders are a group of neurological symptoms, from the most disabling and disturbing to patients with multiple sclerosis (MS), negatively affecting social and emotional functioning, employment status and general quality of life [(2)]. They include attention, information processing speed, verbal and non-verbal memory, learning and language, executive functions [(3)].

Common cognitive symptoms include deficits in complex attention, speed of information processing, executive functioning, short- and long-term verbal and visual memory, and verbal fluency. These deficits negatively affect many aspects of daily life, such as the ability to function in the family, participate fully in society and work.

Cognitive impairment may affect 40% to 70% of MS patients, has been reported in all stages and subtypes of the disease, although it is more frequent in the secondary progressive type and is the leading cause of neurological disability in adults. young and middle-aged. The areas that have typically shown the most deficits are: speed of information processing (20-50%), memory (33-65%), attention (12-25%) and executive function (17-19) % [(4)]

The components of cognition affected in multiple sclerosis are:

1. **Information processing speed** Information processing efficiency in MS refers to working memory (storing and manipulating information for a short period of time) and information processing speed. Both can be damaged in MS and can interact with each other. MS patients typically show problems in complex tasks that

require rapid information processing. In particular, when tasks involve significant working memory, distractibility, or require rapid visual scanning MS patients tend to have difficulty

2. **Memory** In MS, the changes occur mainly in explicit (declarative) memory, which are related to the deliberate recall and recovery of personal experiences and knowledge of the world. In general , there is the storage of implicit (non-declarative) memory, in which previous experiences facilitate the execution of a task, without a conscious perception of it. Episodic memory is more affected in MS [5] . In this way, the most frequent complaints during the consultation are related to difficulties in remembering conversations, meetings and details of work tasks.

3. **Attention** The most affected components of attention are: selective attention, sustained attention, altered and divided attention. In contrast , the level of vigilance and focused attention are components that are not often impaired. Changes in attention level have been associated with difficulties in both working memory and processing speed. Most tests that assess components of attention also take into account speed of information processing and working memory [6] .

4. **Executive** Functions Executive functions encompass a variety of different abilities including cognitive flexibility, concept formation, verbal abstraction, problem solving, inhibitory control, planning, and verbal fluency, and MS patients have been shown to exhibit difficulties in most of these domains. executive.

5. **Language and Intelligence** Verbal communication (expression and understanding) is often preserved, except for the occasional difficulty in naming. If there is a problem in verbal comprehension, these seem to be more related to difficulties in information processing or working memory.

6. **Visuo-Spatial Functions The** main differences are related to face recognition and angle matching. Although visual disturbances such as optic neuritis can exert a negative influence on perceptual processing , perceptual deficits have been observed regardless of the existence of primary visual impairment in up to 25% of patients [7] .

7. **Social Cognition** The individual's ability to understand their own and others' minds and feelings in order to respond appropriately to the person's social environment. It is the way we perceive the social world. It is one of the 6 main cognitive functional areas. MS is associated with impaired social cognition , and has an impact on the quality of life and social relationships [8] . Difficulty recognizing facial emotions in MS patients, especially elderly patients.

Materials and Methods

The main objective of the study was to determine the cognitive disorders in patients with MS and compare it with the normal population, how demographic and health factors have influenced the different spheres of cognition. For this, 57 patients with MS were taken in a prospective study at the Neurology Service of QSUT , Tirana and the same number of healthy controls who were matched according to age, gender and educational level. Both groups were subjected to an approved test to test cognitive disorders in patients with Multiple Sclerosis such as BRNB-T, which has a sensitivity of 71% and a specificity of 94% for the identification of cognitive impairments in the different areas explored and summarizes these tests. : SRT (LTS and CLTR), SPART (IR and DR), SDMT, PASAT and WLG. It takes 30-45 minutes. The demographic data taken in the study were: age, gender and educational level. While the disease data that influenced the cognitive functions taken in the study were: EDSS, medication, age of the disease and clinical form of MS. Beck's test was used to exclude those patients with major depressive disorders.

Results

The study included patients with an average duration of the disease of 80.2 (±71.5) months, which varied between 4-288 months. With an average EDSS of 1.9 (±1.6) Kurtzke points and varies between 1 and 6.5 Kurtzke points. The predominant clinical form is RRMS in 42 patients or 73.7% of patients, followed by SPMS in 13 patients in 22.8% and PPMS in 2 patients or 8.5% of them. 52 out of 57 patients are on medication and respectively 40 or 70.2% are on Interferon , 12 or 21.1% are on Fingolimod and 5 or 8.8% are without Multiple Sclerosis modifying medication.

I Impact of Demographic Factors on Cognitive Function in Both Study Groups (MS Patients and Healthy Controls)

1. **Age**
2. **Educational level**
3. **Gender**

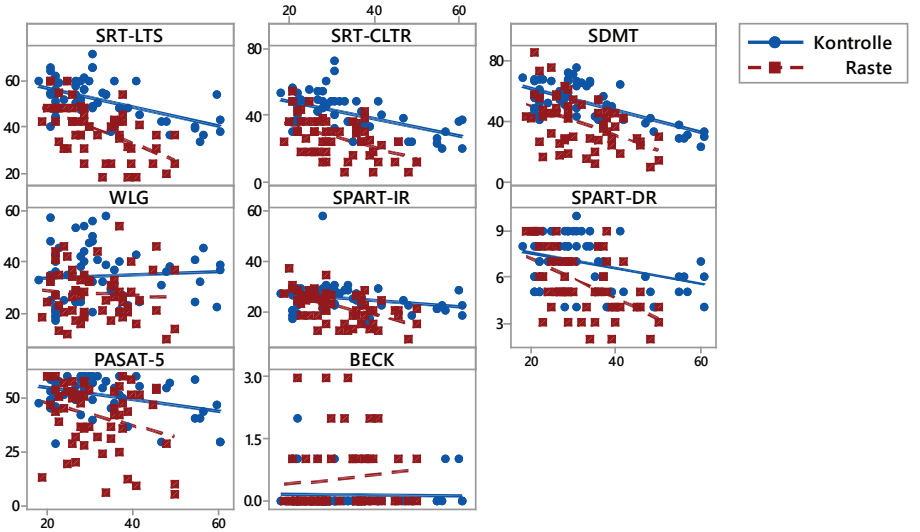
1. Age

In our sample, the average age (32.17 ± 15), which is a little younger compared to that obtained in the study in the Italian (41.5 ± 9.8) and Dutch (45.8) [9] population . It is known that age is one of the demographic factors that affects test results.

In our study consistent with others [10] increasing age is associated with poorer performance on all battery tests except the WLG verbal fluency test.

The effect of age has also been observed in the SPART (IR and DR) and SDMT [11], revealing that the older the patient's age, the greater difficulty in information processing and visuospatial memory was observed.

A marked age-related decline in performance is observed in the SRT tests (LTS and CLTR), and slightly less in the PASAT 5.0 in both study groups (patient and control).



Our study includes young patients and proves once again that impairment of information processing speed and long-term and short-term visual memory occurs from a young age. Without neglecting long-term and short-term verbal memory that is significantly damaged in both groups over the years. What becomes less impaired over the years is verbal fluency, which, both in patients with multiple sclerosis and in healthy controls, has no clinically apparent impairment. Sustained attention is slightly less impaired over the years, in patients it is more impaired and the decline is visible, while in healthy controls attention is less impaired over the years.

2. Education

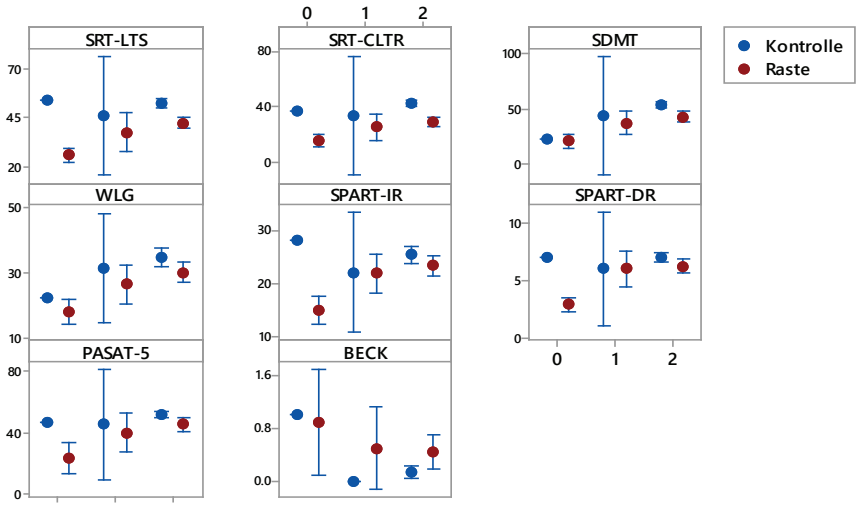
Regarding the level of education, compared to other studies [12], we have found a high level of education, more than secondary education and below 8th grade, both in patients and in controls. Showing that the higher the level of education of the individual (patient or control), the better the cognitive performance. This was observed in all cognitive tests in patients and controls.

The PASAT-5.0 test is one of the tests that patients with higher education have almost similar to controls as in other world studies, probably because these patients of mostly young age groups are professionally active and cognitively trained.

Also, the SDMT, SPART-IR and SPART-DR test in patients with higher education does not show a very big difference in the performance of cognitive tests. This shows that, just like in the world studies and in our study, the speed of information processing and visual-spatial memory in educated patients over 12 years old, in our study population mainly young, there are no big differences between patients and healthy controls. So these cognitive areas are less damaged by the disease if the patient is educated.

An uneducated individual performs as well as an ill person on the SDMT, indicating that information processing speed is also impaired in healthy controls if they are uneducated.

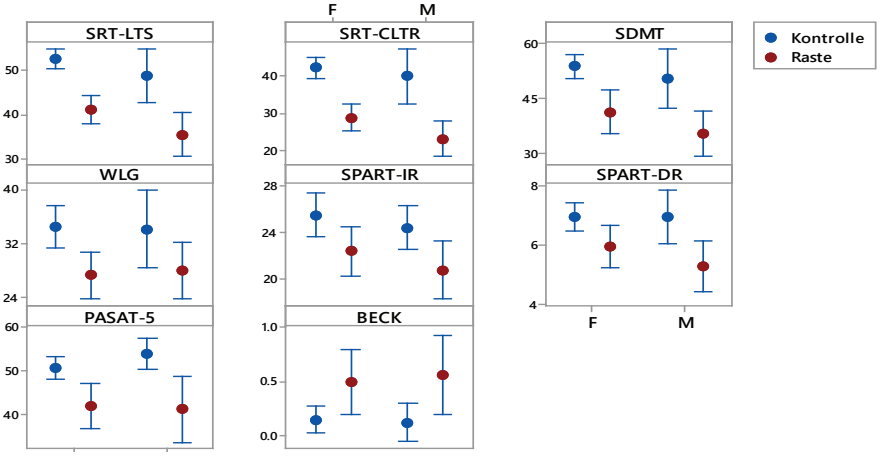
Thus, education affects cognitive performance in patients with MS, not to be significantly different from controls.



3. Gender

In our study we found that females perform slightly better than males (in both study groups, patient and controls) in the SRT (LTS and CLTR), SDMT, SPART-IR tests.

So women have better verbal/non-verbal memory and information processing speed than men. Whereas men perform better on the PASAT 5.0 tests, which shows that they have better sustained attention than women.



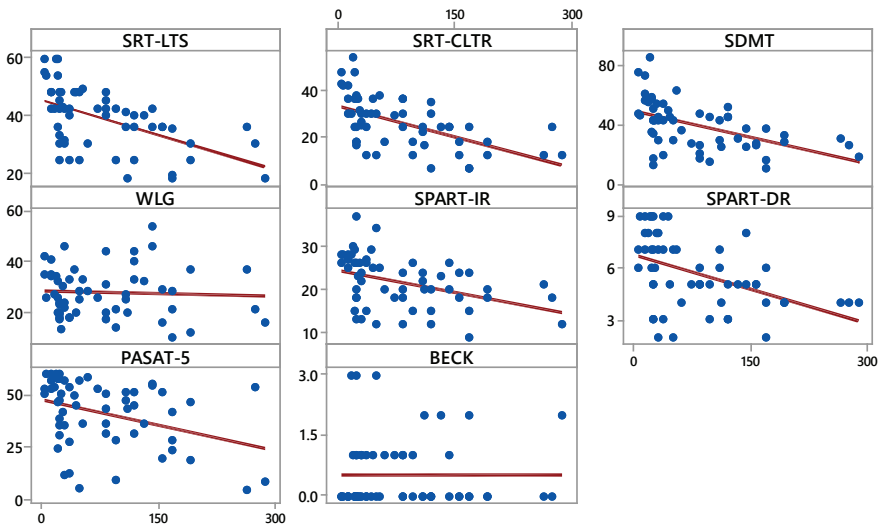
II As far as the factors of the disease are concerned, the cognitive disorders studied in patients with MS are seen to affect:

1. **Duration of illness**
2. **EDSS**
3. **Clinical form**
4. **Maintenance medicine**

1. In our study, the average duration of the disease is 80.2 (±71.5) months, with an interval between 4 and 288 months. It is seen that in patients with multiple sclerosis, over the years from the moment of diagnosis of the disease, all cognitive functions begin to decline.

There is a greater decline in verbal short-term and long-term memory (SRT-LTS and SRT-CLTR) and non-verbal (visual) long-term (SPART-DR), information processing speed (SDMT) and attention (PASAT 5.0).

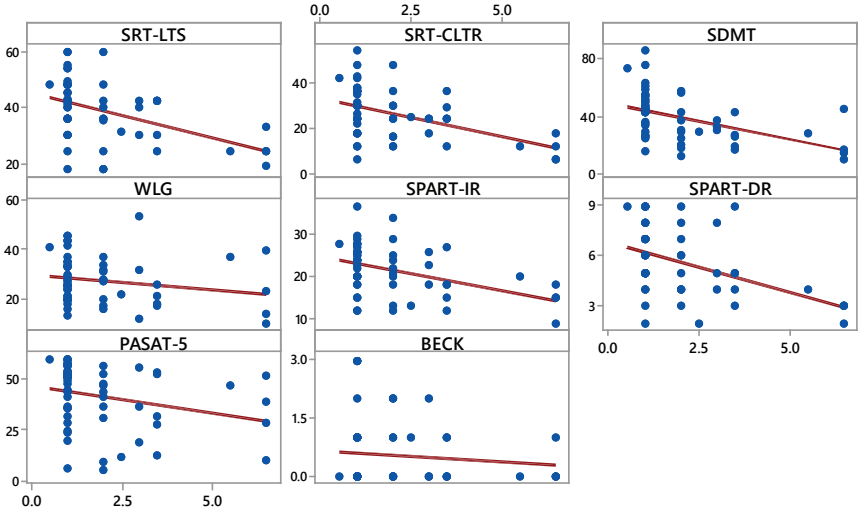
Easier decline with age of the disease has short-term visual memory (SPART-IR). There is no very pronounced influence , with the age of the disease, verbal fluency (WLG).



2.EDSS or Kurtzke's Expanded Disability Scale, which evaluates all functional systems and shows the patient's physical condition, it is important to make the correlation with cognitive disorders. The average EDSS of our study is 1.9 with a miss interval of 1 and 6.5

points according to Kurtzke. High EDSS scores are an independent predictor of cognitive impairment. In particular, the involvement of the cerebellar functional system turns out to have a major role in impairing the speed of information processing and verbal fluency [14].

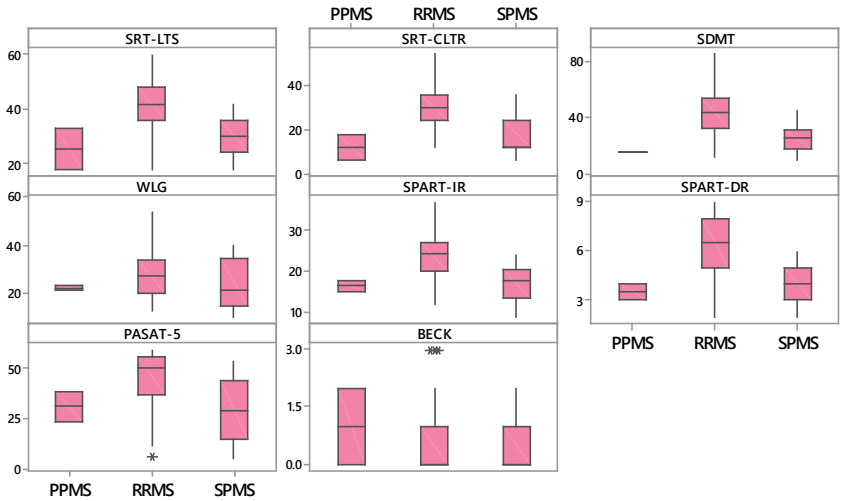
What is important in the study is that physical disability measured by the Kurtzke EDSS test correlates with cognitive disability. Expressed through test results, this shows that the higher the EDSS, the lower the SRT (LTS and CLTR), SDMT, SPART (IR and DR), PASAT scores. So WLG is the one that is less affected even when EDSS increases over time during the course of the disease.



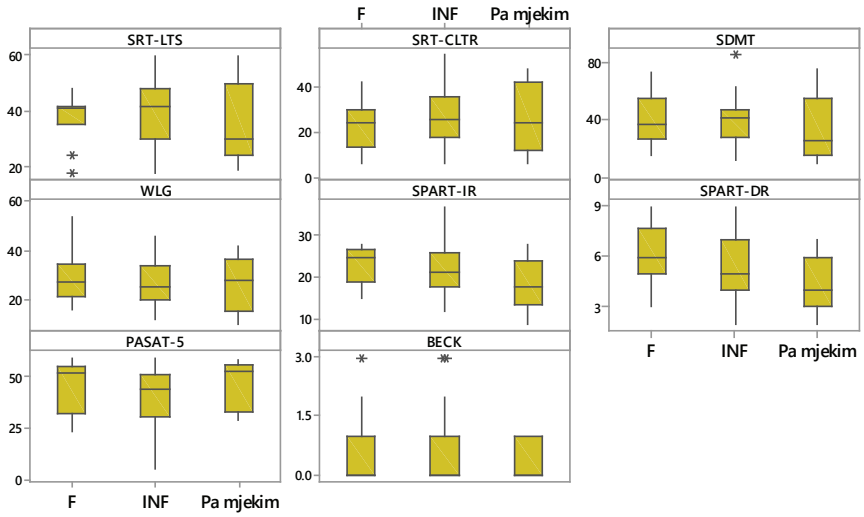
3. The clinical form of the disease and the connection with the cognitive function is important.

Cognitive impairment is present in all subtypes of the disease, however it appears to be more severe in patients with SPMS and PPMS, thought to be due to extensive neurodegeneration and cortical involvement. The same results in our study, where with the clinical form SPMS and PPMS perform with lower results than those with RRMS.

In patients with the clinical form of PPMS, cognitive disorders are more frequent and more pronounced on tests exploring delayed verbal recall, executive functions, and verbal episodic memory compared to RRMS. The same thing happens in this study, where it can be seen that in the clinical form of PPMS, there is a more pronounced impact on these components than in RRMS.



4. Being or not on maintenance medication for multiple sclerosis , has not been a variable that has been concluded as influencing the results of cognitive tests. Even the type of medication in our patients taken in the study (INF or Fingolimod) is seen to have no impact on cognitive function.



Conclusions

Cognitive impairment is one of the areas that has been continuously investigated in MS, not only from the point of view of early diagnosis but also of starting treatment efficiently. Early detection of cognitive impairment is particularly important in MS, as this is a chronic progressive disease that begins at a young age. In addition to early treatment with disease-modifying medications, MS patients with cognitive deficits certainly benefit from other therapeutic strategies, rehabilitation, compensatory measures, and lifestyle adjustments to manage those disabling symptoms. Such studies help to compare cognitive adjustments in other MS populations in the world and in the normal population to take measures in the early detection and prevention of potential factors that cause cognitive decline.

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BASILAR ARTERY OCCLUSION. CURRENT RECOMMENDATIONS ON DIAGNOSIS AND MANAGEMENT: A LITERATURE REVIEW

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Abstract

Basilar artery occlusion (BAO) causes serious neurological presentation because of the important structures perfused by this artery. Different clinical presentation is seen, varying from the level of occlusion. High clinical suspicion and imaging studies like computed tomography (CT), CT angiography (CTA) and MRI aid in diagnosis. Admission to stroke unit as soon as possible is of utmost importance and revascularization therapy is the treatment of choice. Recanalization of the basilar artery can be accomplished either by systemic intravenous thrombolysis (IVT), intra-arterial thrombolysis (IAT) or endovascular thrombectomy (EVT). Poor outcomes remain in BAO despite revascularization therapies, demonstrating the important differences to anterior circulation anatomy. Time to door or time to groin, good collateral circulation, initial NIHSS score <15, and distal BAO remain the most important prognostic factors to good clinical outcomes.

Key-words*: basilar artery occlusion, endovascular thrombectomy*

Anatomic and clinical remarks

The basilar artery (BA) is formed by two vertebral arteries (left and right) and it supplies important and critical areas of the brain and brainstem. Anatomically, it is further divided into three arbitrary segments[1]:

- Proximal: from the vertebral artery (VA) to anterior inferior cerebellar arteries (AICA)
- Middle: from AICA to the origin of superior cerebellar arteries (SCA)
- Distal: from SCA to the terminal posterior cerebral arteries (PCA).

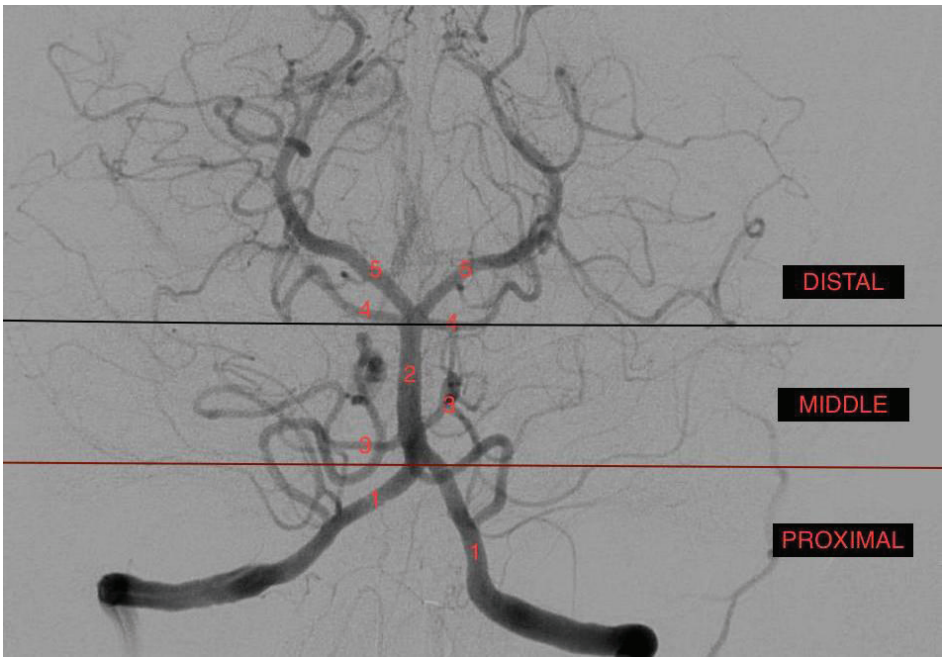

Figure. 1. Digital Subtraction Angiography (DSA) showing the posterior circulation. (1) Vertebral Artery, both left and right; (2) Basilar Artery, arising from the two vertebral arteries; (3) Anterior Inferior cerebellar Arteries (AICA); (4) Superior Cerebellar Arteries (SCA); (5) Posterior Cerebellar Arteries (PCA). The horizontal lines divide the basilar artery in the three arbitrary segments, as described above: Proximal – below the red line, Middle – between the red and black horizontal lines, Distal – above the black line.

Basilar artery occlusion (BAO) usually arises due to local thrombosis that is superimposed on a preexisting atherosclerotic plaque mainly in the lower or middle third of the basilar artery, but it can also arise due to occlusion of both vertebral arteries, or occlusion of a single vertebral artery (when the occluded artery is the only one of adequate size).

Basilar artery occlusion involves a large number of bilateral structures like the corticospinal and corticobulbar tracts; cerebellum, middle and superior cerebellar peduncles; medial and lateral lemnisci; spinothalamic tracts; medial longitudinal fasciculi; pontine nuclei; vestibular and cochlear nuclei; descending hypothalamospinal sympathetic fibers; and CN III-VIII. As a result, the complete syndrome comprises bilateral long tract signs (both sensory and motor) with variable cerebellar, cranial nerve, and other segmental abnormalities of the brainstem[2].

When there is embolism, the clot usually lodges at the terminal bifurcation of the basilar ("top-of-the-basilar syndrome" as detailed by Caplan 1980) results in infarction of the reticular activating system in the midbrain, presenting clinically as coma. Other features such as transient loss of consciousness, oculomotor disturbances, hemianopia, bilateral ptosis, and pupillary enlargement with preserved reaction to light may also be present[3].

On the other hand, occlusion of the midbasilar artery, gives rise to the locked-in syndrome, in which the patient is mute and quadriplegic (due to damage of descending motor pathway) but conscious (sparing of the reticular activating system is sparred)[2]. Horizontal eye movements are damaged but vertical eye movements and ability to elevate the eyelids are intact. The pupils are small and reactive to light. In case of inadequate perfusion to the distal basilar artery territory by the posterior communicating arteries, midbasilar disease may also present with coma[2].

Evaluation and radiologic imaging

Despite clear anatomical remarks and respective clinical syndromes, depending on the level of the basilar occlusion, the clinical diagnosis remains vague in basilar artery occlusion so imaging studies aid in making a diagnosis. Patients presenting with the beforementioned brainstem symptoms should be rapidly evaluated by stroke neurologists, neuroradiologists and endovascular teams, and an urgent imaging confirmation with computed tomography (CT) scan of the head followed by CT angiography (CTA) of head and neck, and/or magnetic resonance imaging (MRI).

CT is usually the first imaging study performed because of its cost-effectiveness, easily readability and high sensitivity of ruling out hemorrhagic lesions within early minutes or hours. A hyperdense basilar artery may be present on the CT scan, however, CT has a low sensitivity for early ischemia and even more so in the brainstem, cerebellum, and posterior circulation[4]. A high index of clinical suspicion is needed to make a diagnosis of stroke in the posterior circulation. Additional evaluation with CT angiography may visualize a filling defect within the basilar artery[5]. MRI is more sensitive than CT to identify early posterior fossa ischemia or infarction. Diffusion Weighted Imaging (DWI) sequence can show an acute brainstem or cerebellar infarct within seconds of the arterial occlusion[6]. Magnetic resonance angiogram (MRA) is a great non-invasive diagnostic approach to show the vascular occlusion. Another important tool, often regarded as the gold standard in visualizing the arterial occlusion is the digital subtraction angiography (DSA). DSA is used not only to depict the vascular obstruction before treatment, but also to ensure successful endovascular treatment and revascularization. The **thrombolysis in cerebral infarction (TICI)** grading system was first described in 2003 as a tool to determine the response of thrombolytic therapy in ischemic stroke. Nowadays, it is widely used in neurointerventional radiology for evaluation of post endovascular revascularization. Its main goal is to determine procedural success and predict the prognosis [7]. TICI score has undergone changes during the years (Table 1), with the most recent adding of TICI 2c [8]. TICI 2c and TICI 3 are considered successful endovascular revascularization nowadays. TICI

2b even though very likely exhibit a clinical outcome similar to TICI 2c and TICI 3, remains a suboptimal therapeutic goal [9].

Despite its limitations compared to MRI, CT is still the first diagnostic test performed in most emergency centers all over the world because of its readability and its costs. It is very important to enhance the fact that despite the modality chosen, the whole process should not delay transfer to a stroke unit and recanalization therapy.

TICI score	Original TICI criteria	Modified TICI criteria
TICI 0	No perfusion beyond the occlusion	SAME
TICI 1	Minimal perfusion	Penetration past the initial obstruction with minimal filling of the normal territory but not perfusion.
TICI 2a	Only partial filling (less than two-thirds) of the entire vascular territory is visualized	Some perfusion, with distal branch filling <50% of territory visualized
TICI 2b	Complete filling of all of the expected vascular territory is visualized but the filling is slower than normal	Substantial perfusion, with distal branch filling >50% of territory visualized
TICI 2c	-	Near-complete perfusion; Slow flow in few distal cortical vessels/presence of small distal emboli
TICI 3	Complete perfusion with normal filling of all distal branches	SAME

Table. 1. **TICI score. Original TICI score and the modified TICI score used nowadays with the adding of TICI 2c.**

Consensus on management and current data from clinical trials

As discussed above, acute BAO is a potentially life-threatening condition. All patients should be admitted to a stroke unit as soon as possible, because it has now been well established that time is brain and recanalization therapy has a limited time window and prognosis

is time-dependent. Recanalization of the basilar artery can be accomplished either by systemic intravenous thrombolysis (IVT), intra-arterial thrombolysis (IAT) within 4.5 hours, or mechanical endovascular thrombectomy (EVT). Recanalization is successful in more than half of BAO patients treated with IAT or IVT. There is no well defined treatment window for basilar thrombosis, but just like large vessel occlusion (LVO) of anterior circulation, it is much longer than what it used to be (6 to 8 hours). The commonly accepted time window is up to 24 hours.[10] In special cases, if the patient is having symptoms and minimal stroke on brain MRI it is reasonable to consider EVT up to 2-3 days.[11]

For patients with BAO who do not receive reperfusion treatment mortality rates in the 3-month post-stroke period vary between 40 and 86%.[12] Mortality rates remain high despite introduction of reperfusion therapies such as IVT and IAT.[13,14]

Acute stroke management recommendations changed in 2015 after the five studies (MR CLEAN, REVASCAT, ESCAPE, SWIFT PRIME, EXTEND IA) regarding LVO in the anterior circulation, with EVT becoming the standard treatment.[15,16,17] In contrast, only a few registry studies, single-and multicentre studies, meta-analysis and randomized clinical trials (RCTs) have been published on EVT of BAO.[18-32] Most of the RCTs point out the fact that differences in vascular anatomy between the anterior and posterior circulation may influence treatment response to revascularization therapy. Extrapolation of successful results from RCTs of the anterior circulation may not reflect the real success rate in the posterior circulation.[33] Because of the collateral flow, and possible therapeutic effect on both ends of the thrombus, IVT for BAO may be more effective compared to anterior circulation.[33]

Park et al. studied collaterals in BAO and concluded that good collateral circulation and distal BAO are independent predictors of clinical outcome after endovascular treatment.[34]

Subsequent therapy for secondary prevention doesn't differ from anterior circulation stroke and it focuses on treating underlying causes and modifying risk factors.

MRCLEAN - Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands

REVASCAT - Endovascular Revascularization with Solitaire Device versus Best Medical Therapy in Anterior Circulation Stroke within 8 h

ESCAPE - Endovascular Treatment for Small Core and Proximal Occlusion Ischemic Stroke

SWIFT PRIME - Solitaire™ FR as Primary Treatment for Acute Ischemic Stroke

EXTEND IA - Extending the Time for Thrombolysis in Emergency Neurological Deficits with Intra-Arterial Therapy

Conclusions

Poor outcomes remain in BAO despite revascularization therapies, demonstrating the important differences to anterior circulation anatomy. Despite that, revascularization therapy remains the treatment of choice in BAO and imaging studies, especially MRI are very helpful in deciding to undergo EVT in patients that present relatively late. Time-window for EVT remains up to 24h in most cases but in patients with good collaterals which haven't yet deteriorated clinically it can be considered even after 24h. IVT and IAT seem to be more successful in good clinical outcomes compared with anterior circulation, but because of the vague presentation and probable mild clinical symptoms in the first hours, most patients present beyond the time-window of IVT and IAT so EVT remains the only option to be considered. Time to door or time to groin, good collateral circulation, initial NIHSS score <15, and distal BAO remain the most important prognostic factors to good clinical outcomes. TICI 2c or TICI 3 is now the new standard in defining successful revascularization. Further analyses and RCTs to study factors affecting outcome in BAO are warranted.

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LEPTOMENINGEAL CARCINOMATOSIS FROM LUNG ADENOCARCINOMA, PRESENTING AS REFRACTORY HEADACHE

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Introduction

Leptomeningeal carcinomatosis(LC) is the dissemination of malignant cells from the primary tumor sites to leptomeningeal layers of central nervous system.. It has been found in about 5–8% of people with solid tumors and is usually terminal. If left untreated, it has median survival to4–6 weeks [1] and if it is treated median survival is about 2–4 months. [2, 3] Some new opportunities for therapies have recently become available. [3, 4] Leptomeningeal metastasis is divided into three categories based on the origin of the primary tumor: 1) solid tumor 2) hematological malignancy and 3) primary central nervous system tumo. [5,6] Treatment of leptomeningeal metastasis is based on factors including histologyof tumor, prognosis, age of patient and the state of systemic diseases. [7] Treatment options include radiatiotherapy, systemic chemotherapy ,use of targeted agents, intrathecal therapy, and immunotherapy.

In this report, we present a case of LC from lung adenocarcinoma.

Case description

A 57-year-old woman presented with severe headache and neck pain for nearly 3 weeks. She was treated with antiinflamatory medications t but without any benefit. On presentation, she appeared to be a healthy woman with significant headache. Her medical history was only significant for hypertension and thyroidectomy due to hyperthyroidism. She was a non-smoker and she didn't use alcohol or any drugs. Her heart and lung examination was normal. Her abdomen was non-tender and non-distended, with normal bowel sound and no palpable organomegaly Her blood pressure was 130/78 mm Hg, heart rate 50 bpm, respiratory rate 18/min, temperature $36,8^0$ C and oxygen saturation 96% on room air. On physical examination, she had difficulty in active and passive movements of her head and

neck. She had nuchal rigidity and a negative Kernig's sign. . Her neurological examination did not reveal any cranial nerve deficit, or motor or sensory impairment.

Her Cranial MRI was suggestive of increased leptomeningeal enhancement.

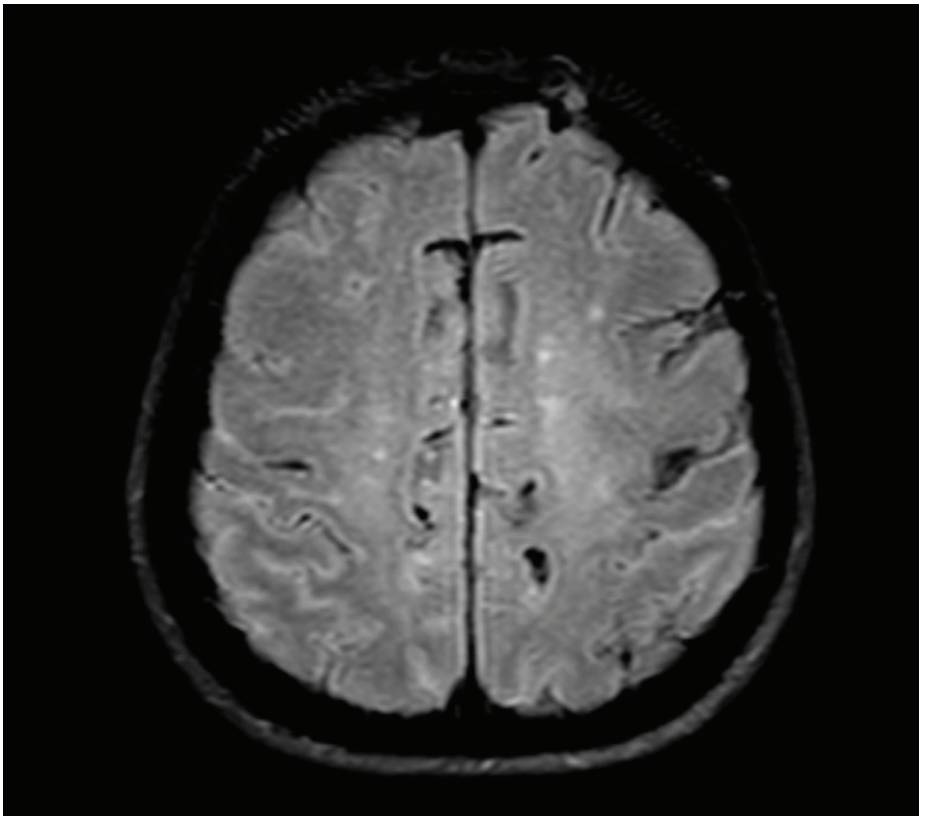

Fig 1. In this figure is showed leptomeningeal enhancement in parietal lobe,in Flair sequence.

Cerebrospinal fluid (CSF) analysis showed 17 cells /mm^3 (leukocyte and large undifferentiated cells). Glucose CSF : 25 mg/dl. Protein CSF 39 mg/dL.

The total body computed tomography showed tumoral mass in the right lung, without other local and abdominal lesions or lymphadenopathy. A transthoracic needle biopsy was performed and the pathological report was suggestive of adenocarcinoma grade 2.

She is being treated with intrathecal methotrexate every 3 weeks and she died after 6 months.

Discussion

Headache is the most common presenting sign found in 39% of patient[8.9]Clinical manifestations are due to meningeal irritation, ischemia secondary to tumour infiltration at blood vessels,hydrocephalus involvement of posterior fossa ,involvement of spinal cord.

The guidelines by National Comprehensive Cancer Network (NCCN) suggest any one of the following diagnostic criteria for diagnosis: CSF showing atypical cells (cells with anaplastic features), neuroimagery features consistent with meningitis carcinomatosis regardless of clinical findings or clinical features suggestive of CM with abnormal CSF analysis (high white blood cell count, elevated protein and low glucose) in a known case of malignancy. MRI scan er may be normal and does not exclude the possibility of CM. However, in patients having a typical clinical presentation, an abnormal MRI scan alone is sufficient to approve the diagnosis. CSF analysis show high opening pressure (>200 cm of H_2O), low glucose level, elevated protein level, and malignant cells .

Treatment of leptomeningeal metastasis is based on factors including histologyof tumor, prognosis, age of patient and the state of systemic diseases. [7] Treatment options include radiatiotherapy, systemic chemotherapy ,use of targeted agents, intrathecal therapy, and immunotherapy.

If left untreated, it has median survival to 4–6 weeks [1] and if it is treated median survival is about 2–4 months. [2, 3]

Conclusion

Pulmonary adenocarcinoma is one of the causes of Leptomeningeal metastasis and the first clinical signs may be those that come as a result of neurological complications from infiltration.Severe headache may be the only presenting sign.

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RARE PRESENTATION OF MYELITIS AS NEUROLOGICAL INVOLVEMENT OF PRIMARY VARICELLA ZOSTER VIRUS INFECTION IN AN IMMUNOCOMPETENT ADULT HOST.

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Abstract

Transverse myelitis due to primary or secondary VZV infection in adults is very rare in immunocompetent hosts and can be serious if left untreated. In this condition, an immediate diagnosis and treatment are required.

We represent a case of an 18-year-old female patient who was admitted to the ER exhibiting acute onset of difficulty walking, sensory alterations of lower limbs, and urinary hesitancy. The patient had a prior recent history of VZV primary infection and there were noticed crusted skin lesions appeared in the head, face, and trunk. On laboratory evaluations, VZV IgM and IgG resulted positive for both immunoglobulins in peripheral blood serum. Spinal MRI shows a T2-weighting hyper signal on the T5-T6 level. Clinical features were resolved within 5 days after intravenous corticotherapy and acyclovir. The case states the importance of prompt diagnosis and treatment of VZV myelitis as a rare and serious medical condition.

Key-words: *Varicella Zoster Virus, Transverse Myelitis, Early diagnosis and treatment*

Introduction

Varicella-zoster virus (VZV) is a herpes virus that causes chickenpox (known as primary infection) and herpes zoster (known as secondary infection or reactivation of latent virus).[1] Transverse myelitis (TM) is a syndrome characterized by acute or subacute spinal cord dysfunction that clinically presents with impairment of motor, sensory and autonomic functions below the level of the lesion. Etiologies for TM can be classified as parainfectious, paraneoplastic, drug/toxin-induced, systemic autoimmune disorders, and acquired demyelinating diseases like multiple sclerosis (MS) or neuromyelitis Optica (NMO)[2]. Transverse myelitis due to primary VZV infection or reactivation of latent virus (known as Herpes Zoster) in adults is very rare in immunocompetent patients and can be serious if left untreated. We report a case of an 18 old female patient with primary VZV infection that debuted with motor and sensory impairment of lower limbs and autonomic dysfunction as well on the 12th day of primary VZV infection.

Case presentation

We report a case of an 18-year-old female patient who was admitted to the ER of UHC "Mother Teresa" exhibiting acute onset of difficulty walking for 2 days, sensory alterations of lower limbs, and urinary hesitancy in the continuum. The patient had a prior 12 days history of primary VZV infection and there were noticed secondary crusted skin lesions appeared in the head, face, and trunk (Fig.1). Upon neurological examination, she was found to have: Inferior spastic paraparesis valued as 2/5 in motor function test; T5-T6 sensory levels and distal dysesthesia of lower limbs; bilateral Babinski sign; Urinary retention. She was hospitalized in Neurology Department. Serologic tests for VZV IgM and IgG resulted in positive for both immunoglobulins. CSF biochemistry analysis resulted in normal. The T2-weighting sequence in MRI showed medullar hyper signal on the T5-T6 level (Fig.2). During hospitalization, treatment with a high dose of acyclovir and Methyl Prednisolone was administered. At the end of the treatment, the clinical features mentioned above were significantly resolved in 5 days.

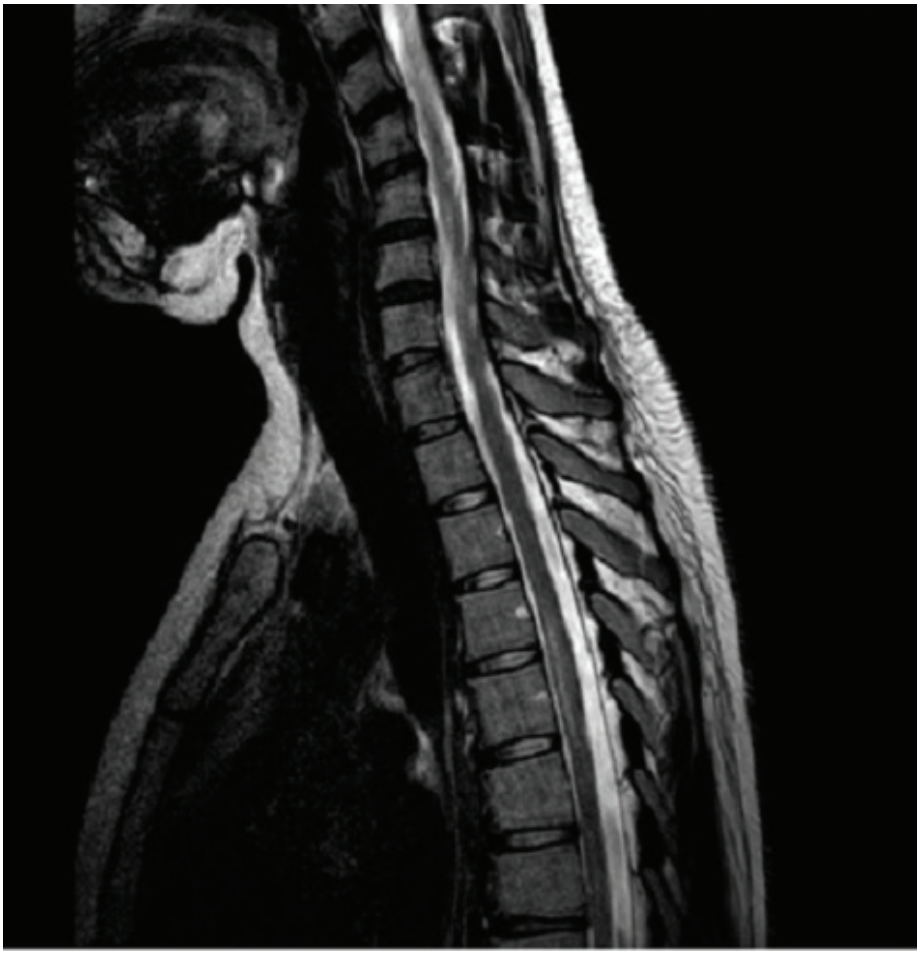

Fig. 1. T2-weighting MRI, hyper signal in T5-T6

Discussions and recommendations

Varicella Zoster Virus is a DNA virus that is a member of the herpesvirus group. Transverse myelitis due to primary VZV infection or reactivation of latent virus (known as Herpes Zoster) in adults is very rare in immunocompetent patients and can be serious if left untreated. In general, about 25%-50% of TM cases are caused by viral infections, including herpes virus or poliovirus[3]. Transverse myelitis in primary VZV infection is not common. Literature indicates that all the levels of the spinal cords can be affected. As a rare condition, prompt, accurate evaluations in diagnosis and treatment are decisive in providing a good prognosis and minimizing complications. Some studies support this conclusion. On the other hand, there is a study that shows that the administration of therapy prolongs symptomatic improvement.[4]

Ongoing studies are needed, so we can clarify the importance of symptomatic and etiologic early treatment during the clinical history of VZV causing Transverse Myelitis. In this way, we can have a better approach to managing similar conditions.

Conclusions

Myelitis due to Varicella Zoster Virus is a rare serious condition among immunocompetent patients. Clinical features, imaging evaluations, and laboratory findings are essentials in diagnosing transverse myelitis due to VZV. Though symptomatic and etiologic therapy respectively corticotherapy and Acyclovir must be administered as fast as diagnosed. Prompt, accurate evaluations in diagnosis and treatment are decisive in providing a good prognosis for this condition.

ARTERY OF PERCHERON INFARCT, A CASE REPORT

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Abstract

Artery of Percheron (AOP) is rare vascular pattern of thalamic blood supply. Occlusion of this artery, usually provides bilateral thalamic infarcts with or without midbrain selection, and presents with a variety of clinical signs such as altered mental status, confusion, memory impairment, coma, generalized weakness, dysarthria, oculomotor impairment. Here we describe the case of a 52-year-old male who presented in emergency department with lethargy, memory impairment, ocular movement disturbance and motor deficit. An AOP infarction with midbrain involvement was suspected and magnetic resonance imaging (MRI) confirmed the diagnosis. The sleep-wake cycle was impaired and didn't recover despite long hospitalization. High clinical suspicion is needed in the presenting hours because emergency imaging with computed tomography (CT) and CT angiography (CTA) are usually inconclusive.

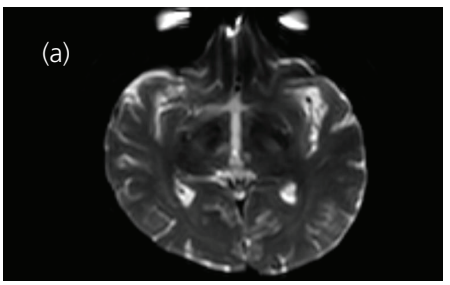
Key words: *Artery of Percheron, bilateral thalamic infarct*

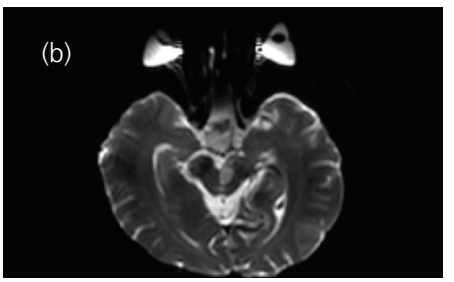
Introduction

The artery of Percheron (AOP) is a rare vascular variant in which a single dominant thalamic perforating artery arises from the P-1 segment of the posterior cerebral artery and bifurcates to supply both paramedian thalami. Occlusion of the AOP differs from other arteries in the cerebral vasculature because it is the only case when occlusion of a single artery affects bilateral structures. Clinical manifestation varies due to the range of neurological functions encompassed by the thalamus. An AOP infarct may present with altered mental status (even coma in certain cases), transient or episodic loss of consciousness (LOC), memory impairment, psychosis, speech impairment (aphasia or dysarthria), and oculomotor dysfunction. Clinical diagnosis of AOP infarct remains difficult, differently from predictable more common neurological syndromes like the middle cerebral artery.[1]

Case Report

We report the case of a 52-year-old male who presented in the emergency department in a confused state and retrograde amnesia, twelve hours after the beginning of symptoms. Slurred speech was present and the patient was unable to walk due to generalized weakness. Neurological exam revealed right facial droop, right hemiparesis with muscle strength 4/5 on both limbs. Left palpebral ptosis, internal and external ophthalmoplegia with preserved movement on lateral gaze, were also present suggesting Weber syndrome. Computedtomography (CT) and CT angiography (CTA) performed on admission revealed no ischemic changes or vascular lesions. Non-contrast magnetic resonance imaging (MRI) of the brain was performed 24h after hospitalization and showed signal restriction in both thalami, right greater than left [Figure 1a] and left mesencephalon [Figure 1b], on axial diffusion-weighted images (DWI), consistent with acute infarct. The apparent diffusion coefficient (ADC) map confirmed the restricted diffusion [Figure 1c].





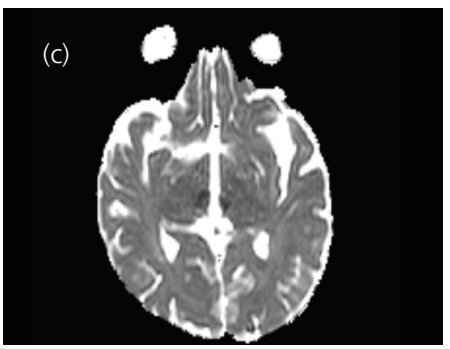


Fig. 1. (a) MRI, DWI showing signal restriction in bilateral thalami;

(b) DWI showing signal restriction in left midbrain, concerning for Weber syndrome;

(c) ADC confirming the DWI findings in bilateral thalami showed in (a) are of an ischemic nature.

An embolic cause of stroke was suspected and transthoracic echocardiography demonstrated left atrial enlargement and impairment of left ventricular function. EKG revealed no abnormalities, but 48hours-Holter monitoring confirmed the presence of paroxysmal atrial fibrillation. The patient was hospitalized for 30 days and during his stay some of the initial symptoms regressed but his sleep wake cycle was impaired, and he could only stay awake for 4-5 hours a day. He was discharged on novel oral anticoagulant (NOAC), rivaroxaban 20mg/daily.

Discussion

The thalamus is a bilateral, oval-shaped structure located deep into the grey matter. Some of the thalamus functions include emotions, memory, alertness, sleep-wake cycle, and sensorimotor control. Intralaminar nuclei of the thalamus may project into the brainstem ascending reticular activating system or cerebellum, hence an infarct presents with altered mental status or even coma and cerebellar signs, respectively. There is a difference between involvement of mediodorsal and anterior nuclei which usually present with memory impairment, aphasia, dysarthria, and psychosis, and the involvement of rostral midbrain which mostly presents with frontal eye field defects1. The vascular variability and the complicated anatomical structure of the thalamus are responsible for the diversity of the clinical symptoms in thalamic infarctions; moreover, these clinical features may involve the midbrain because of the vascular overlap. Paramedian thalamic infarction associated with midbrain infarction due to occlusion of AOP is difficult to diagnose clinically due to the variability involvement of thalamus and midbrain, because of ambiguous and overlapping clinical presentations2. Clinical features vary widely as reported in the literature, from mild symptoms such as dizziness and confusion to more severe signs like coma. The presentation may also include more classic signs of a stroke or focal lesion, as in the case of aphasia, dysarthria, and oculomotor impairment. CT typically shows no abnormalities in acute AOP infarction. CTA also tends to be normal, as occlusions in such small caliber arteries are usually not distinguishable. In contrast, MRI is usually diagnostic. A retrospective study of 18 cases of AOP stroke showed that 100% of cases were detected with MRI imaging, versus only 50% by CT scan, confirming once again the higher sensitivity of MRI in brainstem and posterior fossa infarctions3.

Conclusion

AOP infarction provides a clinical challenge for neurologist. The complexity of symptoms, non-revealing CT and CTA, result in delays in diagnosis. High clinical suspicion and MRI are required to confirm the diagnosis. DWI is the sequence of choice to diagnose AOP infarcts. Embolic cause should always be considered in these distal small arteries and elongated monitoring may be needed to confirm paroxysmal atrial fibrillation.

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LAFORA DISEASE AND FAST PROGRESSION IN A 16 YEAR OLD PATIENT: A CASE REPORT

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Introduction

Lafora disease is a rare autosomal recessive, severe form of progressive myoclonus epilepsy. Studies over pathogenesis of this disease show that it is caused by mutations in EPM2A or NHLRC1, responsible for encoding laforin (a dual-specificity protein phosphatase) and malin, (an E3-ubiquitin ligase), respectively, which lead to hyperphosphorylated glycogen that precipitates and accumulates into polyglucosan deposits called Lafora bodies. Besides the brain they are also seen in liver, skin, and sweat glands[1,2].

Case report

We report a case of a 16 years old female whose onset of the disease was at 8 years of age with atonic seizures during daytime while she was at school. She first started treatment with Valproic Acid but with no result in seizures management. She was referred to have quit school 6 months ago because of difficulties in learning, judging, concentrating and socializing. During this period she has also become agitated, confused, depressive, and during the latest two weeks her condition further deteriorated to difficulty walking, loss of coordination, impaired executive functions and an exacerbation of the frequency of seizures was shown. Several types of epileptic seizures are demonstrated: atonic seizures with sudden fall and loss of consciousness; myoclonic seizures with brief, jerking of right limbs, head and eyes deviation to the right; sensory Jacksonian seizures with involvement of the right arm; occipital seizures with temporary blindness. Neurological examination revealed: apathy, dysarthria, bilateral mydriasis with pupils 6 mm with light reflex present bilaterally, severe ataxia, and continuous exaggerated involuntary myoclonic movements of right limbs. She is currently on triple therapy with Anti-Epileptic Drugs (AED) with Valproic Acid (2500mg/day), Levetiracetam (2500mg/day) and Clobazam (40mg/day) but no improvement is seen.

Head CT scan and MRI showed no abnormality. EEG showed: bilateral intermittent slow spike waves, persisting during hyperventilation as well, and diffuse sharp spike waves and fast polyspikes enhanced by photic stimulation.

Genetic testing (CentoXome Trio) revealed: homozygous likely pathogenic variant in the EPM2A gene, consistent with the diagnosis of autosomal recessive progressive myoclonic epilepsy type 2A (Lafora).

Discussions

Lafora disease is a rare autosomal recessive disease and its prevalence is reported to be 4/million. Death occurs within 10 years of disease onset. While laforin and malin function as an interacting complex in which malin is recruited by laforin to glycogen molecules that are forming long glucose chains, when a mutation of malin or laforin occurs, these glucose chains extract water and form double helices resulting to precipitation of these molecules and accumulation of Lafora bodies[3]. The phenotype of the disease is not reported the same in all cases and the correlation between genotype and phenotype has not always been simple because of the considerable heterogenicity of the EPM2A genes, where 90 pathogenic variants are known till now[4]. Moreover, the disease survival and complications vary between different countries and health systems. The typical onset of the disease is on the early adolescence and it progress till death which mostly occurs at the first decade of onset, however, studies have shown that some modifier genes other than EPM2A can modulate the course of the disease in patients[5]. Diagnosis is made by considering the patient`s history and clinical presentation, EEG findings, biopsy and genetic testing. Brain MRI seems to be unremarkable because no specific changes are noticed.

The ultimate challenge of Lafora disease is definitely the treatment. AED and vagal nerve stimulation seem to lower the frequency of seizures by reducing the neuronal glucose availability for glycogen and Lafora bodies synthesis. Metformin is also prescribed and is reported to slightly reduce the number of Lafora bodies resulting in less seizures[6,7]. Future perspectives of the treatment strategies

tend to implement gene therapy such as virus vectors to deliver a functional laforin or malin gene, degradation of Lafora bodies by delivering alpha-amylase, and reduction of glycogen syntesis[8,9].

Conclusion

Lafora is a rare disease which unfortunately leads to deterioration and fatal ending after several years of symptoms` onset.

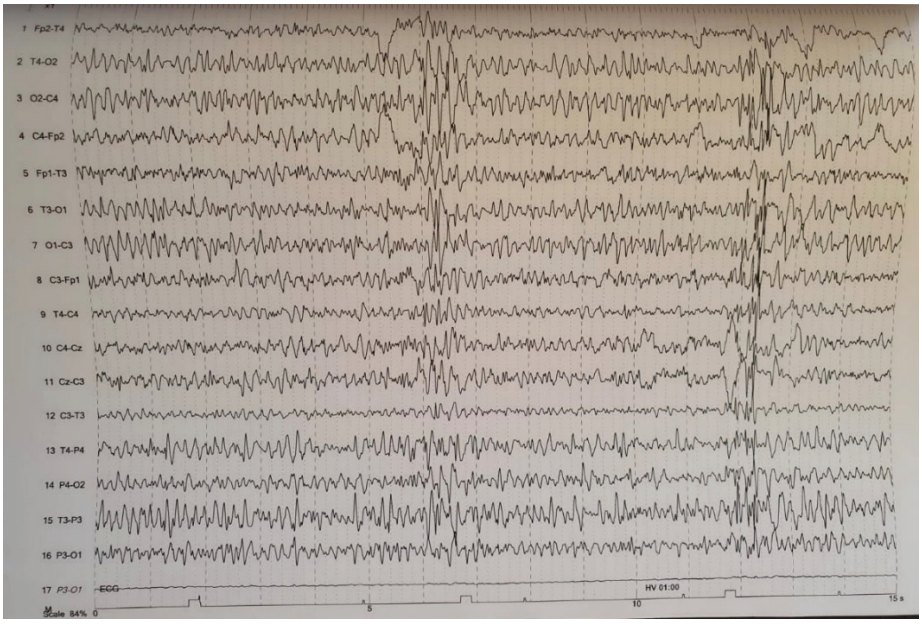

Figure 1: EEG findings of the patient

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HYPERTROPHIC PACHYMENINGITIS, IGG4-RELATED: CASE REPORT

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Introduction

The IgG4, related disease is a systemic disease recently characterized as an inflammatory condition. The involvement of the central nervous system is rare and may be isolated or associated with other organs. Commonly, it involves the hypophysis, presenting hypophyses as the main manifestation, but it can also affect the dura mater, presenting as IgG4 related hypertrophic pachymeningitis.[1] Neurological manifestations occur because of mass effect, typically due to vascular or nervous structures compression, resulting in functional deficits according to the anatomical site of the lesion. The main histopathological features are dense lymphoplasmacytic infiltrate, fibrosis arranged, at least focally, in a storiform pattern, and obliterative phlebitis, associated with increased numbers of IgG4+ plasma cells or an increased IgG4/IgG ratio in tissue.[2-3] In this disease, the serum IgG4 levels are usually increased (about in 70% of patients).[2] We are reporting a case of a 20-year-old male patient who presented with paresthesia of both hands that then spread to the lower extremities. As the months passed, the patient began to lose strength in the four sides and had difficulty maintaining the correct posture.

The immunophenotypic profile of the lesion associated with imaging exams and patient's clinical condition enabled the diagnosis of IgG4-related hypertrophic pachymeningitis.

Case report

We are presenting a case of a 20-year-old male patient with the onset of symptoms with paresthesia of both hands, which then spread through the lower extremities. As the months passed, the patient began to lose strength in the four extremities and had difficulty maintaining the correct posture. The patient came to the neurology clinic 6 months after the onset of the symptoms. Then the patient underwent a head and cervical MRI, where hyposignal of the medulla oblongata up to C7 level of the spinal cord was visible, which indicated a secondary medullary suffering from extrinsic compression because of a significant leptomeningeal thickening. There was also an intense

contrast enhancement of the lesion. Due to the deterioration of the clinic the patient is consulted by a neurosurgeon and a decompressive laminectomy was performed. In the operative procedure, meningeal fragments were taken, which were negative for tuberculosis. Also, directly after the surgery, a lumbar puncture was performed where hypoglycorrhachia, hyperproteinorrachia and the presence of 48 cells/mmc with lymphocytic predominance were detected. During the recovery time (at this time the patient had started 75 milligram prednisolone per day) the patient clinical condition improved. During the stay in the hospital, with the reduction of the dose of prednisolone the patient suffered a deterioration of the clinical condition due to a deterioration of motor strength, especially in the superior extremities. At this time the patient performed another head and neck surgery (a second decompressive laminectomy from C1 to C7) and a high dose of dexamethasone (8mg 2 IV) was started. At this time meningeal fragments were taken, where histological and immunohistochemical study, was made. The histological study of the lesion showed a marked lymphoplasmacytic inflammatory process with storiform fibrosis and obliterative phlebitis and the immunohistochemical study showed a predominance of IgG4+ plasma cells, with about 40 IgG4+ plasma cells per high-power field. Serum IgG4 levels were within the normal range. The immunophenotypic profile of the lesion associated with imaging exams and patient's clinical condition enabled the diagnosis of IgG4-related. The patient also underwent a total body PET-TC to detect systemic involvement of the disease, which resulted negative. The patient started therapy again, with prednisolone 60mg/day and methotrexate 2.5 mg /day. Currently, the patient is using only methotrexate 2.5 mg/day and he is in good clinical condition.

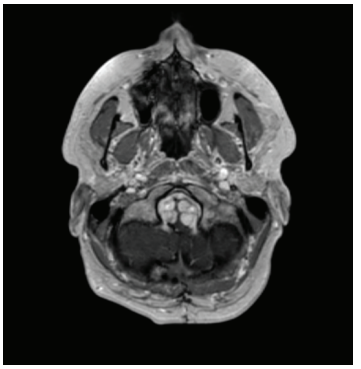

Fig 1. Axial T1 intense contrast enhancement of the lesion.

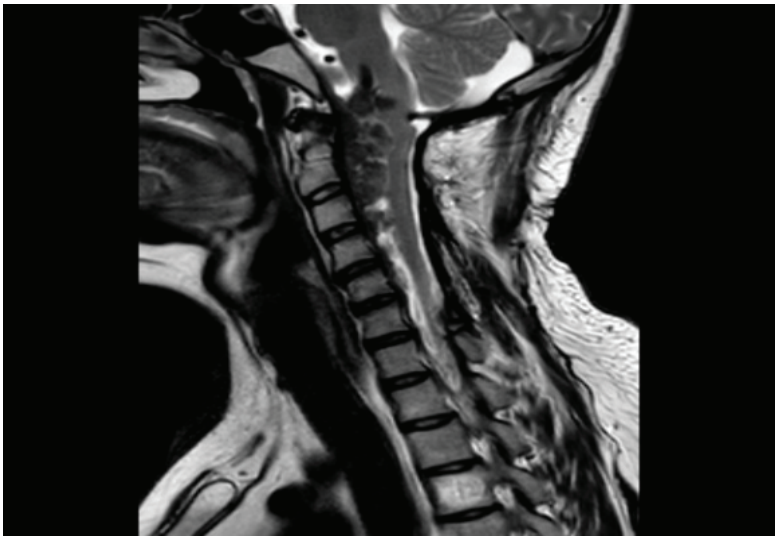

Fig 2. Sagital T2 Hypointens lesion in the anterior aspect of the spinal canal that extend up to the level of C7.

Discussion

IgG4-RD has been described as a multisystemic, lymphoproliferative and fibro-inflammatory disease that is characterized as a polyclonal IgG4 infiltration, leading to storiform fibrosis and oblitering phlebitis.[4] . The involvement of the central nervous system is rare. When it happens, it is more common in the pituitary gland and the dura mater. Serum IgG4 levels are elevated in 70% of patients .But in our patients IgG4 level was normal. Serum IgG4 are not very significant because we can find them increased in case of allergies, infections or in some types of cancerous diseases.[5] The differential diagnoses include intracranial hypotension, subdural empyema, , leptomeningeal carcinomatosi or other causes of pachymeningitis such as tuberculosis[3]. The disease has a good response to corticosteroid therapy . Despite its effectiveness in most cases, recurrence rates are high when there is a dose reduction or treatment interruption. Rituximab, mycophenolate mofetil, methotrexate and cyclophosphamide are used to treatment maintenance after glucocorticoids therapy. In some cases, decompressive laminectomy is needed[34].

Conclusion

The IgG4, related disease is a systemic disease recently characterized as an inflammatory condition. The involvement of the central nervous system is rare and may be isolated or associated with other organs. The immunophenotypic profile of the lesion associated with imaging exams and patient's clinical condition enabled the diagnosis of IgG4-related hypertrophic pachymeningitis.

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NON-TRAUMATIC CONVEXITY SUBARACHNOID HEMORRHAGE (CSAH) IN CEREBRAL AMYLOID ANGIOPATHY

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Introduction

Convexity subarachnoid hemorrhage (cSAH) is a type of spontaneous, non-traumatic, and non-aneurysmal SAH characterized by blood collections in one or more cortical sulci in the convexities of the brain[1]. Cerebral amyloid angiopathy (CAA) usually manifests as cerebral hemorrhage (in 2% of cases), non-traumatic convexity subarachnoid hemorrhage (in 38-74% of cases) in normotensive patients older than 60 years of age[2]. CAA is characterized by the deposition of beta- amyloid in the walls of the cortical and leptomeningeal vessels. Hemorrhages associated with CAA manifest as multiple, lobar and widespread in white matter, basal ganglia and brain stem. We report the case of a 66-year-old patient with non-traumatic subarachnoid hemorrhage, probably from amyloid angiopathy.

Non-traumatic convex subarachnoid hemorrhages (cSAH) are seen in only 5-6% of cases of SAH. Many possible etiologies for cSAH are described, but a series of studies suggest that CAA is probably the main cause of cSAH in patients over 60 years old (however, in familiar cases younger age is reported), in which other vascular abnormalities are not confirmed by imaging.

Case report

we present a case of a 66-year-old patient who came to Emergency Department of "Mother Teresa" University Medical Center after two episodes of loss of consciousness, eyes fixation and tonic-clonic seizures. The first episode lasted 5 minutes and was followed by post-ictal confusion lasting about 1 hour. The second episode occurred in the morning of the following day, with 24 hours distance from the first one and was presented clinically the same but he did not regain consciousness. Upon objective neurological examination, spastic tetraparesis was revealed, he appeared somnolent, opened his eyes

only to painful stimulus and did not follow commands. The patient was known to be suffering from Parkinson Disease for 17 years, under treatment and at the time of presentation stage IV Hoehn and Yahr. A head CT scan was performed and it revealed: evident hyperdense lesions in the bilateral cerebellar sulci, in the bilateral occipital horns, and bilateral temporal sulci, ex vacuo dilation of the ventricles and cerebral cortical atrophy. No vascular abnormalities were seen in supra-aortic CT Angiography.

Discussion

Cerebral amyloid angiopathy (CAA) is a disease characterized by the pathologic deposition of amyloid-beta within cortical and leptomeningeal vessels, causing loss of integrity and fragility of these vessels, leading in most cases to intracerebral hemorrhage (ICH).

Besides the physical examination and patient`s history, it is crucial to know the imaging diagnostic criteria of CAA which include: presence of cortical hemorrhagic lesions in MRI including lobar ICH, strictly cortical CMBs, and/or cSS without the presence of deeper hemorrhages in patients older than 55 years of age.[3] Studies have shown that atrial fibrillation is a concomitant comorbidity of most patients suffering CAA, therefore the diagnosis of CAA and understanding patients individual risk for ICH plays an important role since AF needs anticoagulation, but in the other hand it increases risk for ICH. A good diagnostic algorithm should be made in order to decide the risk-benefit ratio for anticoagulant medication.

CAA presents as a cerebrovascular disease as well as a neurodegenerative disease such as dementia. Even though the impact of it is well known, the molecular mechanisms that cause disease progression are not totally clear. Till now, genetic therapy to enhance expression of target molecules has been successful, however continuing research for other treatment options such as NMDA receptor antagonists and B Amyloid clearance is ongoing.[4] What we can do at the moment is managing comorbidities such as cardiovascular diseases in order to reduce risk of ICH in CAA.[5]

Conclusion

CAA can be a lifethreatening condition due to ICH and among different localizations of hemorrhage, SAH is the most common and sometimes it can be the first presentation of the disease. Such cases should be continuously followed by CT scan or MRI because it can progress to recurrent SAH and/or spinal hemorrhage.

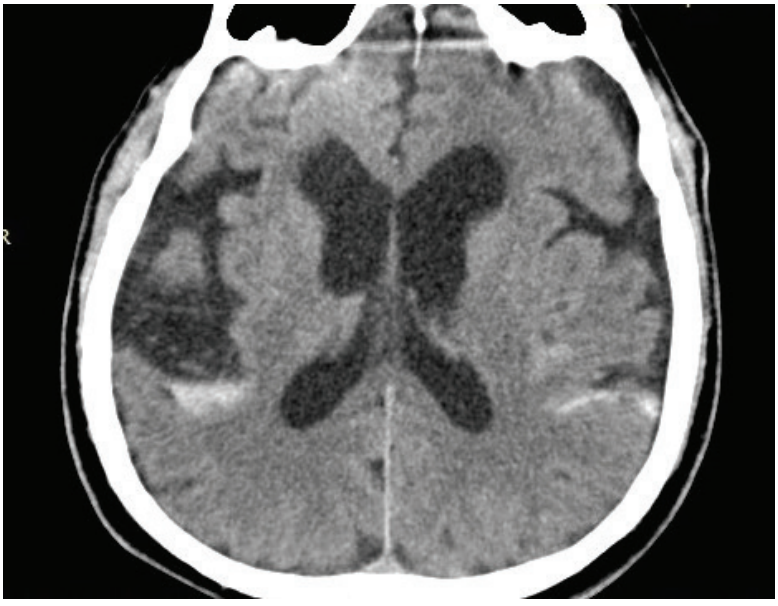

Figure 1: CT scan showing hyperintensity in bitemporal sulci

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SPINAL DURAL ARTERIOVENOUS FISTULA MIMICKING LONGITUDINALLY EXTENSIVE TRANSVERSE MYELITIS

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Background

Spinal dural arteriovenous fistula (SDAF) is a rare condition, that predominantly affects the thoracolumbar spine. Clinical manifestations are nonspecific and can be misattributed to other causes of myelopathy resulting in delayed treatment. We describe a case of a patient with rapid progression of the symptoms within five days, from sensory disturbances to complete inability to move the inferior limbs.

Case report

A 66-year-old male patient was admitted to the Neurology Department complaining of an inability to walk, numbness of the inferior extremities, and voiding difficulty. The symptoms began one month before admission with low back pain, ascending paresthesia, and tingling sensation followed 5 days later by rapidly progressing weakness in the lower limbs. He was under treatment for mild hypertension and benign prostatic hypertrophy. The patient underwent a lumbar spinal Magnetic Resonance Imaging (MRI), which revealed a disc herniation at the L5-S1 level and a hemangioma of the first lumbar vertebra. The pain and the sensory symptoms were attributed to this finding and physiotherapy was recommended to him by his neurologist. Urinary retention was misrelated to prostatic hypertrophy and catheterization of the urinary bladder was performed. As the patient continued to be bedridden, another spinal MRI was ordered showing a T2-weighted hyperintense lesion extending from the T10 level to the conus medullaris. Longitudinally extensive transverse myelitis was suspected and the patient was hospitalized for further investigations.

Upon neurologic examination, inferior paraplegia with absent ankle and knee reflexes was evident. All modalities of sensation were decreased below the L1 dermatome. Cranial nerve and upper extremities examination showed no abnormality. General examination demonstrated ecchymotic and edematous lower extremities. Nerve conduction studies, sedimentation, hepatitis markers, human immunodeficiency virus, and B12 vitamin test results were normal. Doppler ultrasound exam indicated bilateral deep venous thrombosis of the lower limbs.

Contrast-enhanced spinal MRI pointed out spinal cord edema and peri-medullar hypertrophic vessels from inferior thoracic levels, indicating the presence of a dural fistula with spinal venous congestion. The diagnosis was confirmed by spinal angiography. The patient underwent surgical treatment with an improvement of the neurologic status in the follow-up 2 months later.

Discussion

SDAVF is characterized by abnormal communication between a dural artery and the spinal medulla venous system, leading to spinal venous hypertension and congestion. This results in clinical manifestations, which include sensory disturbances, sphincter dysfunction, and decreased muscle strength. SDAVF is a rare cause of myelopathy and occurs most often in middle-aged men. The initial symptoms are nonspecific and the patients can be misdiagnosed with peripheral neuropathy, inflammatory myelitis, spinal neoplasms, and degenerative spinal disease. Spinal angiography is the gold standard for diagnosis. Treatment consists of endovascular embolization or surgical ligation of the fistula.

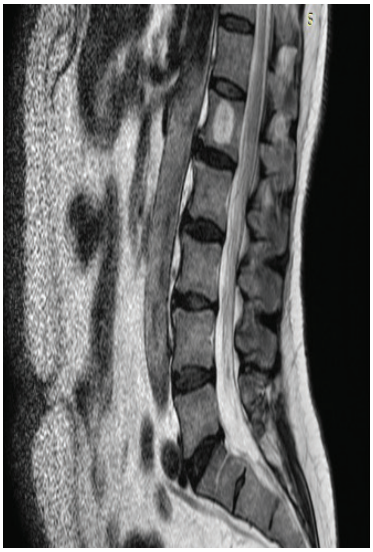

Fig 1. Lumbar MRI showing hemangioma of L1-vertebra and degenerative disc disease

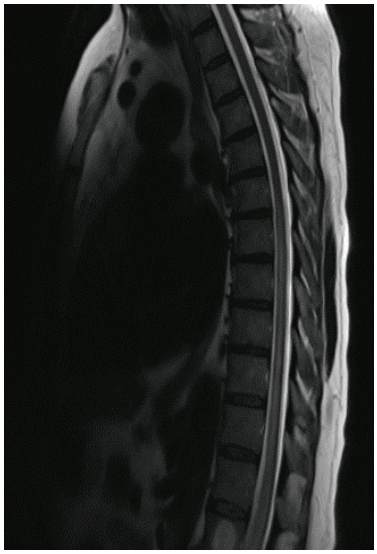

Fig 2. T2-tse sagital MRI

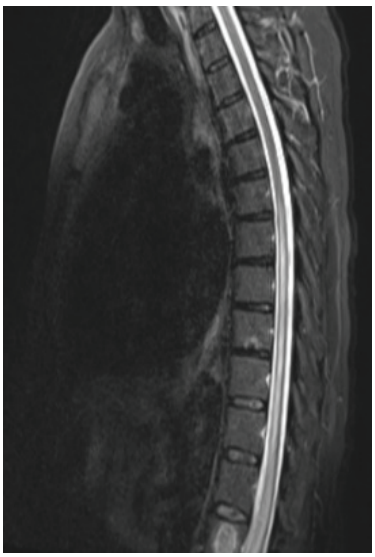

Fig 3. T2-tirm sagital MRI :medullary hyperintense lesion consistent with medullary edema

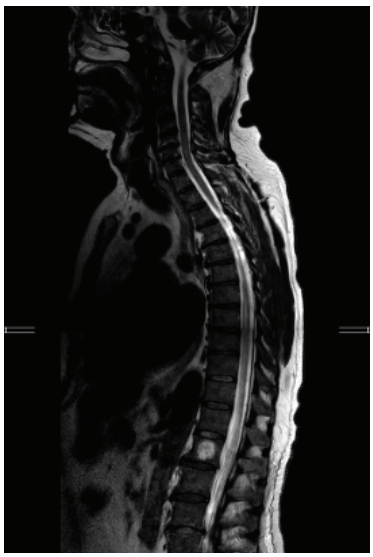

Fig 4. T2-tse sagital MRI + kiv

Conclusion

In patients with symptoms of myelitis, dural fistulas should be keeped in mind in the differential diagnosis. Early diagnosis and treatment is essential to prevent severe disabilities.

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SPORADIC OLIVOPONTOCEREBELLAR ATROPHY (OPCA): A CASE REPORT

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Introduction

Olivopontocerebellar atrophy (OPCA) is a neurodegenerative syndrome that is most often characterized by progressive cerebellar ataxia,slurring of speech,disphagia and dysphonia.Other possible neurologic findings include hypertonia,hyperreflexia,rigidity,abnormal eye movements and neck dystonic posture. A diagnosis of olivopontocerebellar atrophy may be based on the presence of the above signs and symptoms, an evaluation of the family history, imaging studies and some laboratory tests. On Magnetic Resonance there is atrophy of the brainstem and cerebellum as well as hyperintensities on T2, especially in pons which is called the hot cross bun sign. There is significant controversy and confusion in the medical literature because of its association with two groups of disorders, specifically multiple system atrophy (MSA) and spinocerebellar ataxia (SCA). This disorder is slowly progressive with death occurring approximately 20 years after onset.

Case report

We report the case of a 54-year-old male who presented at our clinic with inability to walk and frequent falls since the age of 25. Five years ago he developed dysarthria,dysphagia and subsequently presented with progressive neurologic signs and symptoms,including urinary incontinence,fatigue,trouble with sleep,muscle spasms, worsening gait disturbance and dementia. There was nothing special in the patient's family history and past medical history .His routine laboratory investigations were all normal. A routine MRI of the brain was performed which showed cerebellar atrophy,prominent widening of the CSF spaces in the posterior fossa, and reduction in the size of the pons- "hot cross bun sign"- suggestive with a diagnosis of OPCA. Mini mental status examination (MMSE) test result was 24/30.

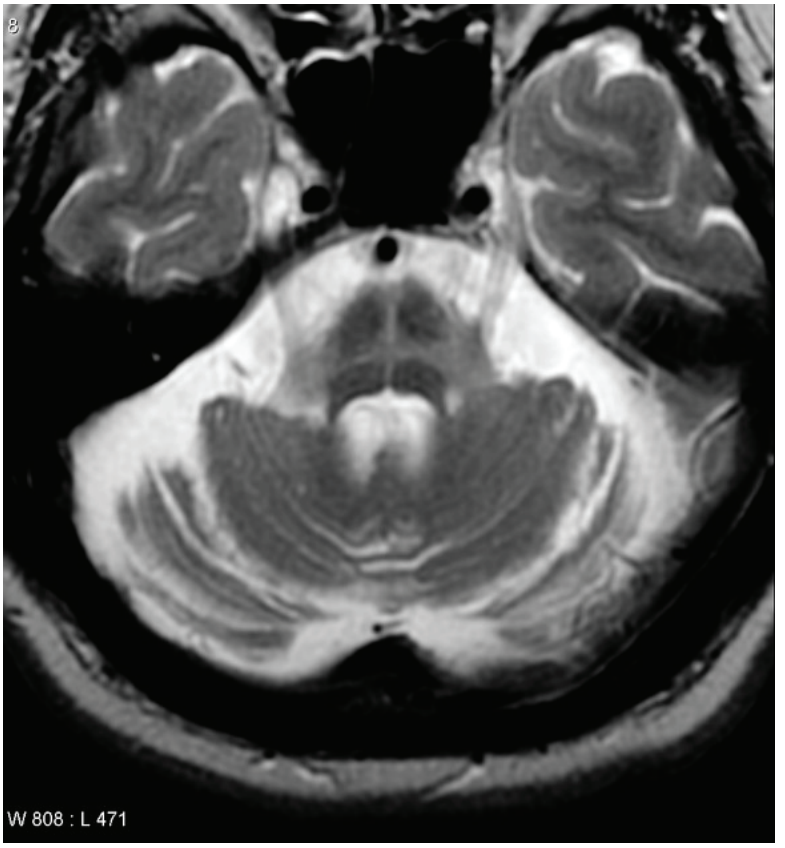

Figure1-1. MRI of the patient with the typical Hot cross bun sign. (Hot cross bun sign refers to the MRI appearance of the pons when T2 hyperintensity forms a cross on axial images, representing selective degeneration of transverse pontocerebellar tracts and median pontine raphe nuclei.

Conclusion

Diagnosis of olivopontocerebellar atrophy is often challenging and a correlation of both physical and radiologic findings is required. MRI of the brain remains the gold standard in diagnosing olivopontocerebellar atrophy and distinguishing OPCA from other neurological diseases and helps in determining several subtypes of OPCA. This article aims to present this rare case to assist clinicians by reviewing literature on MSA, and summarizing important features of the condition.

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A CASE OF LUMBAR ARACHNOIDITIS DUE TO SPINAL CORD STENOSIS EXACERBATED BY COVID-19 VACCINATION.

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Introduction

Arachnoiditis is a rare clinical entity, the diagnosis of which can be challenging, but early diagnosis and treatment can significantly improve outcomes and reduce disability.[1] We present the case of a patient with leg weakness and sphincter dysfunction, whose symptoms aggravated after the administration of the Covid-19 vaccine.

Case presentation

We report the case of a 60-year-old woman, who presented with inferior paraparesis, lower back pain, saddle anesthesia, difficulty urinating, and bowel dysfunction. The patient was also being treated for Diabetes Mellitus, Atrial Fibrillation, Hypertension, Rheumatoid Arthritis, and Anemia from Iron deficiency and had a history of spinal infarction at T8-T10 level in 2017, which improved after treatment and extended physiotherapy. She had no history of recent trauma or lumbar surgery and she had not performed any invasive diagnostic tests. One year before hospitalization she presents to our clinic with severe lower back pain that radiated in her left leg, leg weakness, and urinary and bowel dysfunction. An MRI is performed and she was diagnosed with lumbar spinal stenosis and disc herniation in the L2-L3 level. The neurosurgeon decides to treat her with analgesics and physiotherapy with some improvement during the following months. However, her symptoms significantly worsened several months later, after the administration of the Covid-19 adenovirus vector vaccine. The patient now was unable to walk and gradually worsened and become bedridden by the time she presented in our clinic again. Another MRI is performed during hospitalization and the patient resulted with lumbar spinal stenosis and disc herniation in the level L2-L3 with inflammation and subsequent fibrosis of the arachnoid mater and progressing to nerve root adhesions, clumping, and destruction of the subarachnoid space in this level suggestive of arachnoiditis. After proper diagnosis, the patient was started on a three-day course of Methylprednisolone 1,0 g with visible

improvement of her paraparesis. The patient starts walking with bilateral support and is discharged with Prednisone 50 mg/day with gradual tapering and physiotherapy.

Discussion

Arachnoiditis has been attributed to intervertebral disease, spinal cord diagnostic procedures and surgery, trauma, subarachnoidal hemorrhage, and infectious causes.[1,2] Diagnosis of arachnoiditis is based on clinical presentation and symptoms, and imaging, with the chosen modality being spine MRI.[1,2,8,9] Treatment of arachnoiditis includes pain relief, glucocorticoids, immunotherapy, and spinal cord stimulation.[6,1] Our patient showed significant improvement with high-dose corticoids, so other interventions were considered unnecessary. After excluding other causes, we concluded that our patient had arachnoiditis caused by spinal cord stenosis secondary to intervertebral disease, which was aggravated by active immunization via an adenovirus vector vaccine against Covid-19. This may be suggestive of the effect of Covid-19 vaccination on the Nervous System, potentially causing increased inflammation or aggravation of previous neurological disorders. [4,5]

Fig. A. Sagittal T2-weighted images showing thickened, clumped, and displaced lumbar nerve roots with altered T2 signal intensity and lumbar spinal canal stenosis at L2/L3.

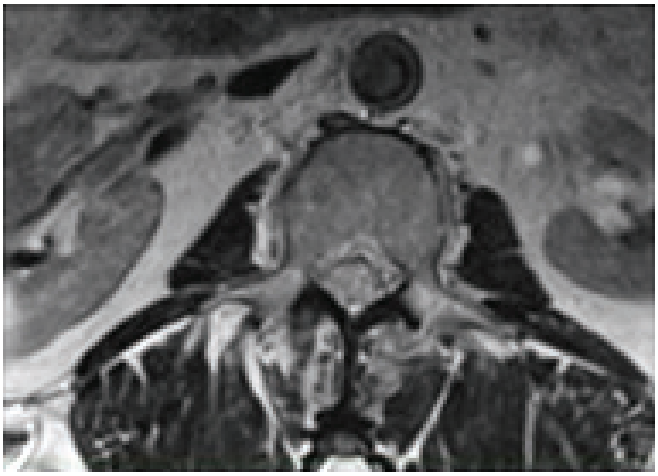

Fig. B. Axial T2-weighted images showing thickened, clumped, and displaced lumbar nerve roots with surrounding inflammation with altered T2 signal intensity and lumbar spinal canal stenosis at L2/L3

Conclusions

Lumbar arachnoiditis is a rare neurological disorder whose proper diagnosis and treatment may change patient outcomes.[1] This case is added to the cases published in the literature that may associate Covid-19 vaccination with increased inflammation in the Nervous System or aggravation of existing neurological diseases.[4,5]

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VITAMIN B12 DEFICIENCY: A GREAT MIMICKER

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Background

Vitamin B12 deficiency can present with a wide spectrum of symptoms that mimic other neurologic, psychiatric, or hematologic diseases. Neurologic complications include cognitive disturbances, neuropathy, gait disorders, autonomic dysfunction, and clinical deterioration of preexisting neurologic conditions. Here we present a series of five cases of cobalamin deficiency, whose presentation initially suggested another neurologic disease. We highlight the fundamental principle of medicine to always rule out reversible causes for any neurologic condition and the importance of measuring vitamin B12 levels as part of the workup.

Case reports

Case 1: A 68-year-old male patient presented with a 10-day history of progressive inferior paraparesis, fatigue, generalized muscular weakness, and vertigo. His past medical history was relevant for hypertension, great amounts of alcohol consumption for a long time, and deep venous thrombosis, for which he had discontinued treatment with anticoagulants. On examination, a flaccid inferior paraparesis without any sensory symptoms was evident. Deep tendon reflexes were absent. Nerve conduction studies revealed an axonal type of motor neuropathy. An alcohol-related polyneuropathy versus an acute inflammatory polyneuropathy was suspected. Laboratory examinations showed a slightly increased mean corpuscular volume (MCV) and a slight leukopenia. Liver, renal, and thyroid function tests, serum electrolytes, calcium, phosphorus, tumor markers, and blood glucose levels were within normal ranges. The vitamin B12 level was 109 pg/mL.

Case 2: A 43-year-old man presented to the ER with acute worsening difficulty walking, vertigo, ataxia, and paresthesia in both arms and legs. His history was significant for 10 years of alcohol abuse. His brain MRI was normal, and his spine MRI showed an increased signal in the cervical posterior columns. Given the acute presentation, a

spinal infarct was suspected. On further questioning, he reported that he began feeling numbness and pain in both inferior extremities 7 months ago, after an abdominal hernia surgery. Laboratory findings were significant for a vitamin B12 level of 50.1 pg/mL and macrocytic anemia.

Case 3: A 53-year-old female patient presented as an outpatient referred by the neurosurgeon with cervical pain and progressive worsening of numbness and weakness in the upper and lower limbs for one year. She was suspected to have a spinal disc herniation with cervical myelopathy, and she was referred to a neurosurgeon. Neurologic examination was notable for spastic tetraparesis with bilateral dorsal plantar responses. All sensory modalities were diminished in a "long socks and gloves" pattern. Her past medical history included Hashimoto's thyroiditis and proton pump inhibitor drug intake. On further questioning, she revealed that she was aware of a low vitamin B12 level (64.35 pg/ml) for 2 months, but the patient had not taken any medication due to fear of a possible allergic reaction. Brain MRI was normal, and lumbar-sacral MRI showed an L5-S1 disc herniation. Fibrogastroscopy examination revealed atrophic gastritis. Laboratory examinations showed macrocytic anemia, low sideremia, normal ferritinemia, and tumor markers.

Case 4: A 62-year-old female with a past medical history of hypertension and diabetes mellitus, presented with a one-month history of difficulty walking, dementia, and visual hallucinations for which she was consulted by a psychiatrist and was started on antipsychotics. Brain MRI showed cortical atrophy, predominantly of the temporal lobe bilaterally. At admission, a spastic inferior paraparesis was evident on examination and she scored 17 points on the MMSE (Mini-Mental State Examination). A rapidly progressive dementia was suspected. Thyroid function and tumor markers were normal. Blood tests revealed anemia without alteration of MCV and low vitamin B12 level.

Case 5: A 22-year-old female was admitted to the Neurology Department with fatigue, progressive worsening of difficulty walking, numbness in the lower limbs, and disequilibrium of 2 months in duration. She reported a history of intermittent treatment

with folic acid and corticosteroids for hemolytic anemia, thought to be on an autoimmune basis. Neurologic examination was significant for sensory ataxia, absent deep reflexes, and a broad-based gait. The spine MRI was normal. Vitamin B12 level was 50.06pg/mL (228-1515pg/ml).

Discussion

Vitamin B12 is essential in DNA synthesis, red blood cell development, and neurologic functions. B12 deficiency presents with hematological, gastrointestinal, and neuropsychiatric manifestations [1, 2]. Neuropsychiatric symptoms and signs such as paresthesia and limb weakness, ataxia, memory loss, hallucinations, personality or mood changes, and loss of vision, are difficult to be attributed to B12 deficiency, especially when they happen without a hematological or gastrointestinal context and in the absence of anemia [1, 3].

At presentation, patients with B12 deficiency may be misdiagnosed as other neurologic conditions and as a result mistreated [4, 5, 6, 7]. In this case series, we performed B12 measurement as part of the workup in the differential diagnosis of acute peripheral neuropathy, ischemic myelopathy, acute deterioration of mental status, disc herniation, and in patients with a history of anemia of undetermined cause. Some clues in the anamnesis and labs results lead us to consider B12 deficiency as a possible cause: in the first and second cases, the history of alcohol abuse and hematological abnormalities made us think of malnutrition/ malabsorption; in the third and fifth cases the presence of other autoimmune diseases. The cause of deficiency in the third case was thought to be autoimmune atrophic gastritis, though atrophic gastritis due to long-term Omeprazole use was also considered. Antiparietal cell and anti-intrinsic factor antibodies were not taken in any of the cases. There is a correlation between vitamin B12 deficiency and hypothyroidism, so we performed thyroid function tests in all patients [8, 9].

In all five cases, the diagnosis of cobalamin deficiency was based on a low cobalamin level. Testing for methylmalonic acid and homocysteine was not necessary.

Vitamin B12 replacement of 1000 mcg IM daily was started with clinical improvement, but a not total reversal of the symptoms.

Conclusion

Serum vitamin B12 determination should be encouraged as part of standard clinical evaluation in all patients presenting with signs and symptoms of peripheral neuropathy, in the differential diagnosis of myelopathy, even in absence of hematologic manifestations, especially in patients with risk factors. It should be recommended as routine screening among patients with psychiatric symptoms, regardless of their age or previous state of health.

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A RARE CASE OF CARCINOMATOUS MENINGITIS DUE TO NONHODGKIN LYMPHOMA

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Introduction

Carcinomatous meningitis (CM) is a devastating condition where malignant cells, that originate from a primary tumor, migrate to the central nervous system and invade the meninges, both cranial and spinal. Atypical cells, in the progression phase of cancer, find a way of transmission from a primary tumor and spread to a distant site. A variety of cancers are known as the primary source of the leptomeningeal carcinomatosis including breast cancer, lung cancer, melanoma, as well as hematological ones (leukemia and lymphoma) (1),(2). Leptomeningeal metastasis from solid tumors occurs in 5 to 8%, while it happens more frequently in hematological malignancies (5 to 15%), the most prevalent of which is B-cell lymphoma(3).

Case report

We present the case of a 60-year-old Albanian man with a history of Non-Hodgkin Lymphoma, treated previously with chemotherapy, who presented with loss of coordination, severe radiculopathy, and difficulty of speech. The patient was previously seen in the Emergency Department (ED) the last two months with repeated episodes of headache and high levels of blood pressure. The head Computed Tomography (CT) performed resulted normal. Upon neurological examination he was found to have right hemiparesis, Wernicke aphasia, right dysmetria on finger to nose test, bilateral Babinski sign, positive Lasegue sign and positive right Kernig sign. The patient was diagnosed 1 year before with Diffuse Large B-Cell Lymphoma (DLBCL). Laboratory tests were unremarkable. Brain Magnetic Resonance (MR) revealed prepontine and perimesencephalic pathological enhancements after administration of gadolinium, in favor of secondary lesions infiltrating the leptomeninges.

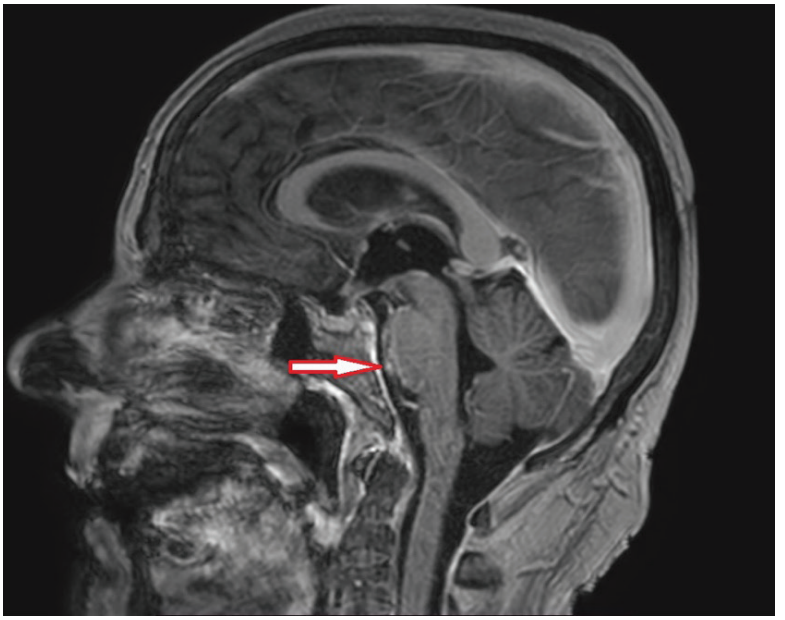

Fig 1: Sagittal view showing the prepontine enhancement.

Discussion

In around 5% of cancer patients, the cerebrospinal fluid (CSF) serves as an entrance point for malignant cells into the leptomeninges. High clinical suspicion is required for an accurate diagnosis of leptomeningeal metastasis (LM)(4)(5). Gadolinium enhanced brain MRI imaging is required to confirm the clinical diagnosis.

Our patient was presented two times in the ED previously, appearing with a normal neurological exam, thus complaining of severe headache and hypertension. The brain enhanced CT was negative for brain parenchymal metastasis, vascular events or hydrocephalus. Due to the fact that a malignancy history was mentioned in his prior anamnesis, it was evident that he should have been furtherly examined with a brain MRI, which has its specific findings in CM such as ependymal, leptomeningeal, and dural enhancement.

Brain MRI with gadolinium enhancement is considered to be better capable of detecting the pathognomonic abnormalities of CM when compared to contrast-enhanced CT (6). Theoretically, to exclude the other possible causes and differentials of the meningeal irritation (which was the main reason of the headache complaint of our patient), a lumbar puncture (LP) should conclude the diagnosis, which should be performed cautiously at least two times, in order to increase the sensitivity of the malignant cells in the CSF (7). Unfortunately, in our patient, the LP wasn´t realized because of the early bad prognosis.

The accurate anamnesis, clinical neurological exam and the further complementary MRI, were enough to name the condition as CM, even without a lumbar puncture. It is important to highlight that the diagnosis of CM must be decided in the broader context of the clinical circumstances, and should not be made only on the basis of the presence of an abnormal-appearing brain imaging. Having a negative CSF result, but the presence of leptomeningeal enhancement on brain and spine MRI, is adequate to make diagnosis of CM, in a breast cancer patient that already shows the signs and symptoms of meningeal irritation. Another completely different situation occurs in a prostate cancer patient, with enhancement of the leptomeninges in MRI. This condition is not enough to name the diagnosis as CM, due to the fact that prostate cancer seldom shows tropism for the leptomeninges (8). In this case, it would be useful to fulfill the examination eventually with a LP.

Conclusions

Our patient was diagnosed with carcinomatous meningitis due to leptomeningeal dissemination of the Non-Hodgkin Lymphoma cancer cells. Clinical evaluation, prior history of malignancy and head MRI confirmed our diagnosis. Non-Hodgkin Lymphoma is a non-frequent cause of Carcinomatous meningitis which should still be considered in the differential diagnosis. Despite early initiation of aggressive treatment, the prognosis remains fatal.

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ACUTE TRANVERSE MYELITIS FOLLOWING COVID-19 INFECTION

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Introduction

Acute transverse myelitis (ATM) or long extensive transverse myelitis (LETM) were found to be associated with COVID-19, along with other neurologic complications like confusion, delirium, headache, ageusia, anosmia, stroke, and in rare cases, seizures and epilepsy [1]. We describe a case of acute transverse myelitis following COVID-19 infection. It is critical to consider SARS-CoV-2 infection as a potential trigger of postinfectious myelitis in cases presented with spastic paraplegia with urinary retention and a positive test for COVID-19 when other viral or autoimmune etiological factors are ruled out.

Case presentation

A 49-year-old woman was admitted to our hospital with progressive weakness of the lower limbs that rapidly progressed to acute spastic paraplegia with urinary retention following the typical respiratory symptoms of COVID-19 infection. The neurological examination revealed hypoesthesia below the Th4 level with a spastic paraplegia and urinary retention. There was a positive plantar extensor reflex bilaterally. Cognition and cranial nerves were unaffected. The polymerase chain reaction (PCR) test of the throat swab was positive for SARS-CoV2 roughly 2 weeks prior the hospitalization. Thoracic CT showed mild bilateral ground-glass opacification. Laboratory findings revealed an elevated C-reactive protein but a normal white blood cell count at the time of hospitalization. The patient's and her family's medical histories revealed no signs of neurological disorders, and she had not received any vaccinations before. Cerebrospinal fluid (CSF) analysis showed a slight increase in lymphocytes with lymphocytic pleocytosis and a normal protein level, whereas oligoclonal bands were negative. Further work-up was unremarkable for varicella-zoster virus, anti-Aquaporin-4 antibodies, and myelin oligodendrocyte glycoprotein antibodies. Magnetic resonance imaging (MRI) of the spine was normal at the time of hospitalization, but 6 weeks

post-COVID-19 infection, it revealed a T2 signal hyperintensity of the spinal cord at the cervical levels, suggestive of acute transverse myelitis (Fig. 1 a,b). Initial treatment, because of persisting symptoms and a negative workup for active infection, was done with methylprednisolone at a dose of 500 mg/day for 5 days. During the course of the disease, the patient improved, gaining some strength and power to the limbs with a motor deficit of 2/5 bilaterally in the inferior limbs, according to the Medical Research Council (MRC). The patient was discharged after 2 weeks with moderate spastic paraparesis, hypoesthesia below the Th4 level, and an altered bladder function. She was not able to walk independently. A steroid tapering scheme was also initiated.

Discussion

An increasingly large number of articles have emerged over the past years with evidence regarding various neurological complications of the novel severe acute respiratory syndrome Coronavirus 2 SARS-CoV-2 infection emerging during the COVID-19 pandemic. During the COVID-19 pandemic, the neurologic complications of SARS-CoV-2 infection became increasingly recognized. Transverse myelitis is an autoimmune inflammatory condition of the spinal cord that can be triggered by any virus including SARS-CoV-2. It is reported in the literature that an immune-mediated inflammatory process is the main pathophysiological mechanism of action in the case of acute tranverse myelitis, rather than the direct invasion of the central nervous system by SARS-CoV-2 [2]. Previously, others suggested a direct invasion of the central nervous system by other human Coronaviruses like SARS or MERS [3]. SARS-CoV-2 has been linked to peripheral neuropathy and muscle damage as well [4]. Cases of Guillain-Barré syndrome in association with severe COVID-19 infections were reported [5].

So, there is plenty of evidence to suggest that a caution correlation between COVID-19 and acute tranverse myelitis can be made. So was it in our case, where the acute transverse myelitis occurred shortly after infection with COVID-19 with its signs and symptoms and it was confirmed in the Cervical MRI 6 weeks post infection, after an incubation period. In order to consider SARS-CoV-2 as the causative agent of acute transverse myelitis, no other causes of myelitis could

be identified after an extensive workup. The etiology was attributed to an immunogenic overreaction secondary to infection. This patient improved with corticosteroid therapy. Our case shows that improvement might also occur with moderate steroid treatment, avoiding high doses of steroids because of uncertain effects on the immunogenic elimination of SARS-CoV2.

Conclusion

We aim to increase awareness of such a neurologic complication following COVID-19 although it is unclear whether post-infectious myelitis after COVID-19 behaves differently from other virus infections.

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Figures

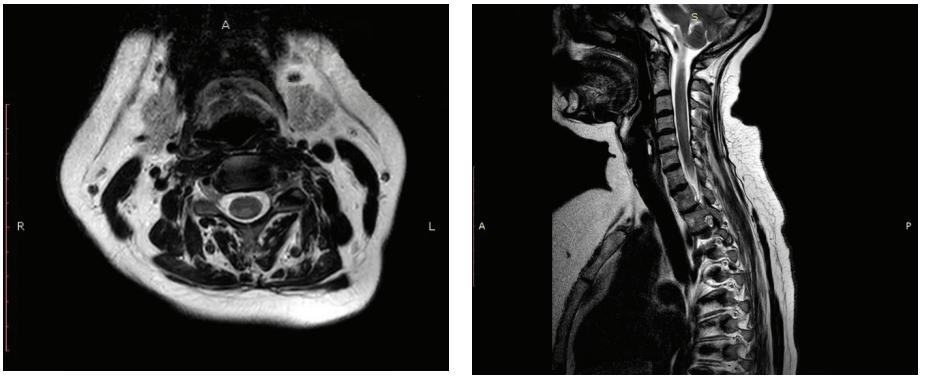

Fig.1(a) Spine MRI 6 weeks post-COVID infection axial and sagittal views at the C2-C4 cervical levels with a T2 hypersignal medullary lesion.

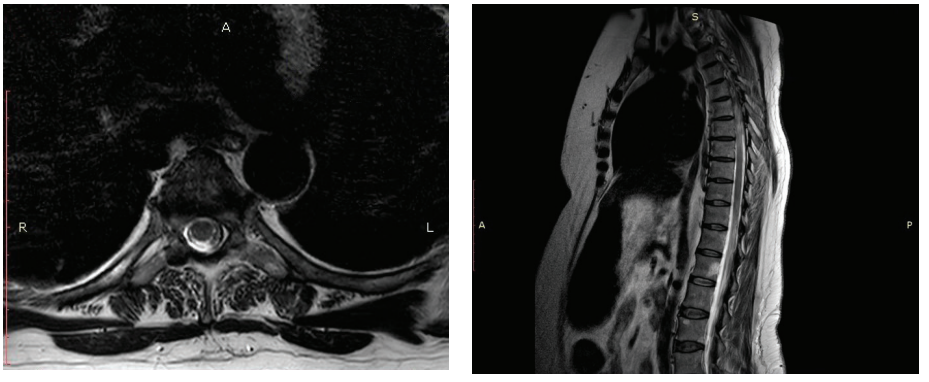

Fig.1 (b) Total spine MRI at the time of the deficit presumed time of incubation with no lesion evident in MRI axial and sagittal views

UREMIC ENCEPHALOPATHY MIMICKING ACUTE BULBAR STROKE WITH PROGRESSION FROM BRADYKINESIA TO CHOREIC MOVEMENTS IN A DIABETIC PATIENT UNDERGOING HEMODIALYSIS.

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Introduction

Uremic encephalopathy (UE) is an uncommon neurologic complication encountered in patients with acute or chronic renal failure. UE can be classified into three types based on the Magnetic Resonance Imaging (MRI) findings: cortical/subcortical, which may develop in any uremic patient; white matter involvement and basal ganglia involvement[1]. Basal ganglia lesions are reported rarely and are manifested by acute or subacute onset of movement disorders such as tremor, myoclonus, chorea and parkinsonism[2, 6]. The mechanism can be explained by the high metabolic requirements of the putamen and its sensitivity to metabolic changes. PET studies have suggested that bilateral lesions of putamen may be caused by long-term glucose utilization failure[3, 6].

We present the case of a patient with end-stage renal disease who developed symmetrical bilateral basal ganglia syndrome manifesting as acute bulbar stroke.

Case presentation

A 42-year-old man of Romany descent presented to the Emergency Room with a 4-days history of sudden onset of generalized weakness, dysphagia, dysarthria, right hemiparesis, and unsteady gait. His past medical history was significant for long-standing uncontrolled diabetes mellitus type 2 on insulin therapy, hypertension, mild anemia, tobacco using, and chronic kidney disease secondary to diabetic nephropathy, for which he has been on regular hemodialysis for the last three years. His family history was irrelevant for any movement or psychiatric disorder. He had no history of a recent infection. Neurological examination showed hypophonia, dysarthria,

dysphagia, mild right-sided hemiparesis, hypomimia, bradykinesia, and a short-steps gait. There was neither rigidity nor tremor or myoclonus. Deep reflexes were decreased and the plantar responses were extensor bilaterally. Brain Computed Tomography demonstrated bilateral symmetric low densities in the basal ganglia. On admission, laboratory investigations demonstrated urea at 66 mg/dl, creatinine at 8.48 mg/dl, and serum glucose level of 20 mg/dl. No other metabolic or electrolyte disturbances were evident. The pre- and post-dialysis serum sodium levels were in the normal range. On further questioning, he reported several episodes of hypoglycemia recently. The acute clinical presentation in a patient with vascular risk factors made us think of a bulbar stroke, so we performed a brain MRI, which revealed bilateral and symmetric hyperintensity of bilateral basal ganglia on T2- and fluid-attenuated inversion recovery, associated with restricted diffusion on diffusion-weighted imaging and reduced apparent diffusion coefficient.

Based on previous medical history, clinical and imaging findings, the patient was diagnosed with bilateral basal ganglia syndrome triggered by hypoglycemia. He was discharged from the hospital 10 days after admission, without significant changes in neurological status.

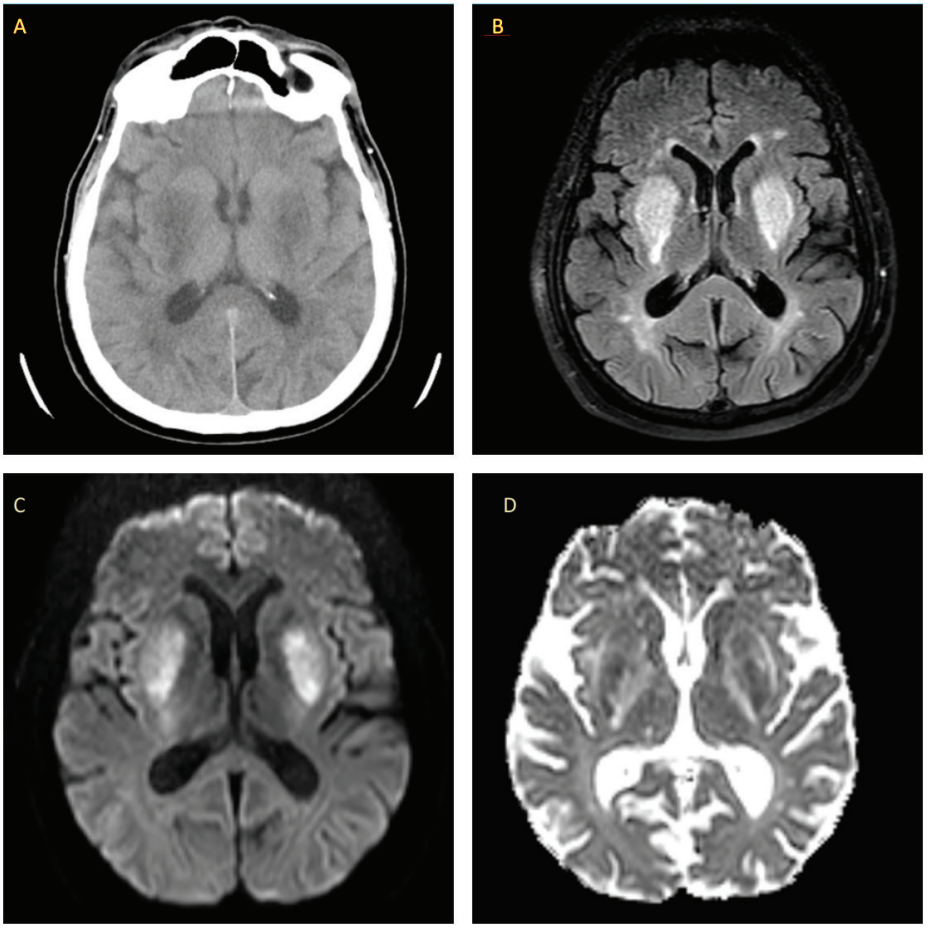
Three months later, the patient presented with generalized choreic movements. He denied any exposure to antipsychotics or antiemetics drugs. The involuntary movements were so severe that he was unable to stay stable during hemodialysis. Also were associated with episodes of hypoglycemia, and were improved with relative increased glucose levels. He was prescribed Haloperidol 1.5 mg per day, divided into three doses. The choreic movements continued and were intensified by hypoglicemic state, especially after the hemodialysis procedure.

Discussion

UE can present with a broad spectrum of neurologic symptoms and signs such as headache, seizures, dysarthria, alterations of consciousness from mild inattention to coma, cognitive disorders, gait abnormalities, and less commonly involuntary movements [1, 5]. The syndrome of bilateral basal ganglia lesions, known as uremic striatopallidal syndrome, is a rare clinic-radiological disorder, characterized by hypo- or hyperkinetic extrapyramidal manifestations in association with bilateral basal ganglia MRI abnormalities [6]. It is a rarely described complication, usually reported in Asian patients with diabetes [2,4]. The pathophysiology remains not fully understood. Uremic neurotoxins, diabetic microangiopathy, and metabolic derangements are thought to play an important role [6]. There have been several case reports of this syndrome in diabetic uremic patients presented with acute onset of chorea or parkinsonism, usually reversible after the intensification of hemodialysis [4, 7]. To our best knowledge, there has been only one case report of acute generalized chorea followed by chronic parkinsonism induced by relative hypoglycemia [8, 9]. Our patient presented initially with symptoms suggestive of an acute bulbar stroke, but also bradykinesia and hipomimia suggestive of parkinsonism, which progressed to generalized choreic movements. The clinical picture persisted despite regular treatment with hemodialysis. Based on clinical progression and alterations of glucose levels, we suggest that severe and frequent hypoglycemia may lead to the persistence of movement disorders.

Conclusion

Glycemic fluctuations can trigger the syndrome of acute basal ganglia lesions in uremia and lead to permanent damage to the brain. Therefore, it is advisable to keep strict glucose control in diabetic uremic patients to prevent this syndrome and its progression.



A. Bilateral symmetric low densities in the basal ganglia on CT scan

B. Bilateral symmetric hyperintensity of bilateral basal ganglia on T2/ FLAIR

C & D. Restricted diffusion on diffusion-weighted imaging and reduced apparent diffusion coefficient.

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ADULT PHENYLKETONURIA IN ADULTHOOD, A CASE REPORT

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Introduction

Phenylketonuria (PKU), is an autosomal recessive condition affecting phenylalanine metabolism with high phenylalanine levels causing neurological dysfunction [1]. Patients with untreated phenylketonuria most often present in the first year of life with developmental delay, seizures, profound mental retardation, behavioral changes and sometimes pyramidal or extrapyramidal dysfunction [2]. Rarely neurologic symptoms develop in adulthood. We report the case of a 24-year-old woman presenting with one year history of imbalance, impaired gait, cognitive impairment and behavioral changes. The medical history, brain MRI, urine analysis and genetic testing lead us to the diagnosis of the patient.

Case report

We report the case of a 24-year-old woman presenting with a one-year history of imbalance, impaired gait, cognitive impairment and behavioral changes.

According to her parents she reached the childhood milestones at appropriate age. She attended school and completed high school, but with poor outcome. From the age of 18 she stays mostly at home and does not have an active social life. She is the youngest of two daughters and her relatives do not have any relatable disease.

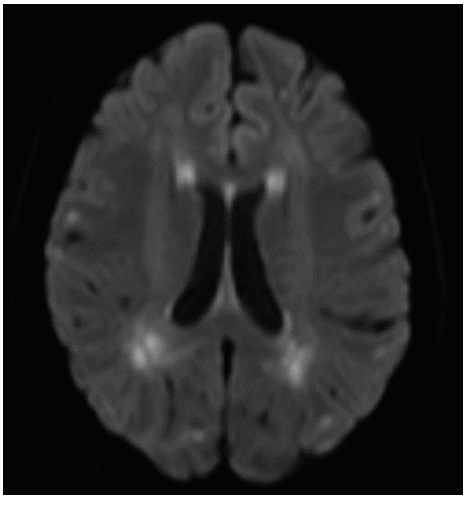
Over the past years she complained of some short episodes of vertigo, which were resolving spontaneously. Mild difficulty in maintaining balance was noticed in the last year. Over the months it progressed to severe gait impairment. Also, short term memory loss and small behavioral changes were reported from her parents. Her favorite hobbies were listening to music and dancing at home. She was quite attached to her parents and needed them around during evaluations.

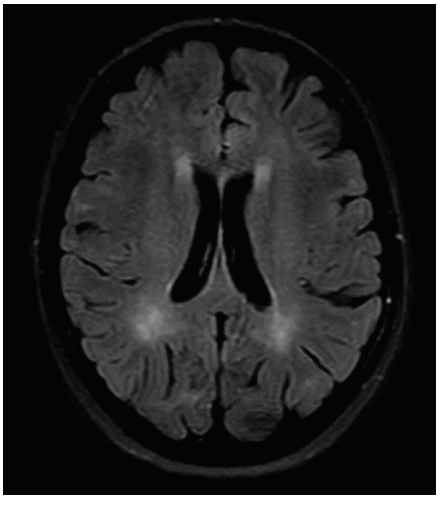
The patient has pale skin, red hair and blue eyes.

Cognitive evaluation showed good orientation in space and time, difficulty recalling objects mentioned to her 5 minutes before and she was not able to do simple mathematical tasks. Language comprehension was intact and she could perform simple and complicated actions.

In the neurologic examination cranial nerves were intact and no motor or sensory deficits were found. She has bilateral Babinski sign and right Hoffman sign. Deep tendon reflexes were brisk in the lower extremities. Romberg sign was negative. Her gait was spastic and ataxic. Tandem walking was impossible. She could make a few steps on her own but for longer distances she needed unilateral support. She had bilateral eyelid twitch.

Cerebral MRI reported of diffuse non-enhancing lesions of the periventricular white matter in both cerebral hemispheres with restricted diffusion (DWI). No pathologic enhancement after intravenous contrast. Images were in favor of a metabolic pathology, with adult onset metachromatic leukodystrophy and adult phenylketonuria as probable diagnoses.





When asked, the patient mentioned that her urine always smelled very heavy.

Abdominal Ultrasound, Full Blood Count, basic blood panel, TSH, FT4, ANA, ENA, MPO, fibrinogen, C3,C4, RF were normal. Urine collected for analysis was reported with heavy odor and in urinalysis a Ketones level of 15mg/dL was reported (normal value <5). The patient was referred to genetic testing for two diagnoses Metachromatic Leukodystrophy and Phenylketonuria based on clinical and imaging data.

In genetic testing two heterozygous variants were found in the PAH gene, which suggest the presence of autosomal recessive Phenylketonuria.

Based in the history, progression of the disease, white matter changes in MRI and especially the genetic testing we diagnosed the patient with Adult-Onset Phenylketonuria.

Discussion

Phenylketonuria is an autosomal recessive disease usually presenting in the first year of life with developmental delay, mental retardation and behavioral changes. There have been reported several PKU cases with normal development or with minor and unspecific symptoms until adulthood [3]. The symptoms of adult-onset PKU vary from dementia, behavioral changes, paraparesis and tetraparesis, parkinsonism ect [3]. MRI shows increased signal in T2 and FLAIR sequences, more often in the occipital and parietal regions, with reduced diffusion in the acutely affected areas. Thanks to newborn screening and prompt treatment, severe symptoms of PKU are rarely seen in developed countries, but still are reported in countries in which screening is not widely available [4].

Conclusions

Although rare, the adult-onset PKU should be taken into consideration in patients with neurologic symptoms and white matter changes, especially changes which suggest hypomyelination rather than demyelination. In some cases, the severe cognitive impairment associated with phenylketonuria can be partially reversed with dietary treatment. Our patient had not received screening tests

for phenylketonuria in infancy. Brain MRI and genetic testing were crucial diagnose this patient. The early identification of the underlying condition may avoid the neurological deterioration and need for any further expensive investigations.

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POST-PARTUM CARDIOMYOPATHY AND STROKE, CASE REPORT

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Abstract

Postpartum cardiomyopathy, also known as peripartum cardiomyopathy (PPCM) is one of the rare causes of stoke in young females. PPCM is defined as new onset heart failure between the last month of pregnancy and 5 months post delivery with no determinable cause. Risk factors include multiparity, advanced maternal age, , pre-eclampsia, chronic hypertension, smoking, alcoholism, malnutrition, and long-term tocolysis.

We describe the case of a 34-year old patient, who was admitted for shortness of breath three months after delivery of her second baby. One week later she presented in the Neurology Emergency Room with acute onset of left hemiparesis and difficulty speaking. The MRI showed a wedged shaped hypodensity involving the gray and white matter of the right anterior temporal and parietal lobe, features suggestive of hemodynamic right sided acute ischemic stroke. This case highlights the importance of multidisipilinary team collaboration in clinical approach for further evaluation and proper treatment of PPCM patients complicated with stroke.

***Keywords*:** peripartum cardiomyopathy, female, stroke, interprofessional team members

Introduction

Postpartum cardiomyopathy (PPCM) is defined as new onset heart failure between the last month of pregnancy and 5 months post delivery with no determinable cause. Postpartum cardiomyopathy is a rare cause of heart failure and stroke in young females. The incidence of PPCM is 1:4000 with higher rates in developing countries.

The diagnostic criteria of this idiopathic cardiomyopathy according to European Society of Cardiology (ESC) include:

1. No other identifiable cause of heart failure.
2. Heart failure develops at the end of pregnancy or within five months after delivery
3. Left ventricular ejection fraction of less than 45%,with or without left ventricular dilatation.

Despite many researches made to establish the exact etiology of PPCM, the exact mechanism of disease still remains unknown. One theory suggests that Prolactin (PRL) has a major effect in the pathogenesis of disease: oxidative stress leads to cleavage of PRL by cathepsin D into abnormal 16 kDa protein,which leads to destruction of intima of blood vessels and damage to the heart. On the other hand, placenta secrets Fms-like tyrosine kinase 1 (Flt 1) that leads to endothelial dysfunction.Some studies suggest that Relaxin-2,a hormone produced by placenta,ovaries and breast decreases vascular resistance and increases cardiac output.For the above effects on blood pressure and cardiac output is one of the hormones which leads to PPCM.

Some nutritional deficiencies before and during pregnancy, multiparity, increased maternal age, chronic hypertension, alcoholism, smoking, pre/eclampsia, viral myocarditis, autoimmunity, vascular dysfunction hemodynamic stresses and genetics are some risk factors which lead to PPCM. However, the exact etiology and pathophysiology is not known and therefore PPCM remains a diagnosis of exclusion.

Patients usually present with progressive dyspnea paroxysmal nocturnal dyspnea , cough, hemoptysis, and in some rare cases with ankle edema . Tachycardia, and elevated jugular venous pressure are common.Some patients present with thromboembolic complications such as deep vein thrombosis, stroke,acute limb ischemia, pulmonary thromboembolism.

Here, we report a rare case of a young female with peripartum cardiomyopathy complicated by stroke.

Case report

A 34- year-old female ex-smoker patient, three months after giving birth to her second child, presented in the Emergency Room after developing a 40-minute episode with slurring of speech, difficulty moving her left half of the body and left hemihypoesthesia.She was hospitalized a week prior in the Pulmonary Department with severe fatigue, palpitation, non-productive cough, low blood pressure (90/50mmHg) and progressive dyspnea with oxygen saturation of 80%. The family history was positive for premature coronary artery disease and premature death. She reported that her mother and her grandmother died round the age of 50 from cardiac disease.

On examination the patient had a temperature of 36.6°C ,heart rate of 123 beats per minute, blood pressure was 90/70 mm Hg , respiratory rate of 22 breaths per minute and oxygen saturation of 93%. There was no peripheral edema. Chest examination and other systems were unremarkable.

On investigation laboratory tests were all normal, except of a high NTproBNP (4973.30). (Details are shown in Table 1.)

On neurological examination, the patient had left-sided upper motor neuron type facial nerve palsy, muscle strengths in the left upper and lower limbs were 4/5 and 5/5 respectively and there was a left Babinski sign.

A computed tomography scan of the head and a computed tomography angiography (CTA) of the supra aortic arteries were performed immediately and were both normal.

The MRI showed a wedged shaped hypodensity involving the gray and white matter of the right anterior temporal and parietal lobe, features suggestive of hemodynamic right sided acute ischemic stroke. [Figure 1]. Electrocardiogram showed sinus tachycardia.

Transthoracic echocardiography (TTE) showed global hypokinesis of the left ventricular wall with an LVEF of 25%, moderate mitral regurgitation and left ventricular dilatation.

A diagnosis of right sided ischemic stroke (hemodynamic) with peripartum cardiomyopathy was formulated. The patient was treated with Aspirin 100 mg daily, Furosemide 20 mg twice a day, Spironolactone 25 mg daily, Metoprolol 12.5 mg daily, and prophylactic low molecular weight heparin (UFH) 4000 units subcutaneously once a day. She was initiated Entresto (Sacubitil/Valsartan) 50 mg daily,under rigorous surveillance of the hemodynamic parameters.At the time of discharge, her speaking improved significantly and there were no motor deficits.The patient was counselled about avoiding subsequent pregnancies. Anticoagulation was started at two weeks following the ischemic stroke to avoid the risk of bleeding, as the infarct was involving more than one-third of the right middle cerebral artery region. Cardiologists support the use of anticoagulation in PPCM if left ventricular ejection fraction is less than 30%.

Table 1. Laboratory parameters on admission.

Parameters	On admission	Reference range (adults)
Hematocrit (%)	48,4	42-52
Hemoglobin (g/dl)	15,0	13-17
White-cell count (per mm3)	9,5	4-10,5
Differential count (%)		
Neutrophils	52,9	40-72
Eosinophils	2,2	<5
Lymphocytes	35,7	25-45
Monocytes	8,99	3-9
Mean corpuscular volume (fL)	85,8	80-100
Prothrombin time (sec)	12,5	11-14
Creatinine (mg/dl)	0,79	0,72-1,25
Sodium (mmol/liter)	138	136-145
Potassium (mmol/liter)	4,2	3,5-5,1
Random blood sugar (mg/dl)	86	74-100
Urea (mg/dl)	32,7	19,1-44,1
Total bilirubin (mg/dl)	0,35	0,3-1,2

CRP (mg/dl)	0,13	< 0,5
Alanine transaminase (IU/L)	45	< 55
Aspartate transaminase (IU/L)	30	5-34
CK(IU/L)	78	30-200
CK-MB Imuno (ng/ml)	2,8	< 5,2
Troponine I (ng/ml)	0,001	< 0,034
NTproBNP	**4973.30**	**< 125**

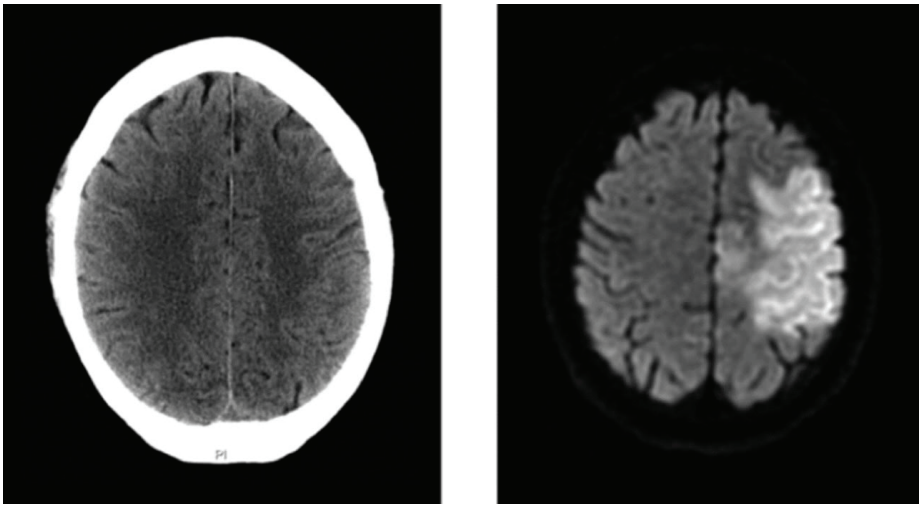

Figure 1. Normal CT scan and Magnetic Resonance (MRI) showing right sided acute ischemic stroke.

Discussion and Recommendations

Peripartum cardiomyopathy is a rare disease of unknown cause that strikes women and is associated with a high mortality rate. Strokes in young adults are uncommon,and the diagnosis is challenging and requires vigilance.

In our patient, the etiology was secondary to hypokinesia of the left ventricle (EF=25%) due to peripartum cardiomyopathy. Maternal age > 30 years,smoking and family history are the risk factors for PPCM in this case. Management of PPCM complicated with stroke requires a

multidisciplinary approach that involves cardiologist, neurologist,obstetrics, psychologist and physiotherapist.

Ongoing studies are needed to help researchers better understand the cause of PPCM and develop new treatments. Health care professionals have tried treatments that alter the immune system, such as intravenous γ-globulin, but they're not proven.More research is needed according the role of Bromocriptine in treatment of PPCM.

Conclusion

PPCM is a rare cause of stroke in post-partum patients and an interprofessional approach is essential in the diagnosis and management.PPCM should be considered as a differential diagnosis in any patient which presents with dyspnea,cough and tachycardia during puerperium.Early diagnosis and therapy prevents the further complications.

Conflict of interest

None declared.

Ethical statement

Authors state that the research was conducted according to ethical standards.

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