Clinical Brief

Mitochondrial Neuro-gastrointestinal Encephalopathy Syndrome

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ABSTRACT

Mitochondrial neurogastrointestinal encephalomyopathy is a rare disorder affecting the pediatric age group with a heterogenous multisystem involvement. We happen to manage a young child with symptoms of constipation since infancy alongwith cachexia, seizures and peripheral neuropathy. The child later went into encephalopathy preterminally. This clinical syndrome fitted very well with mitochondrial neurogastrointestinal encephalomyopathy. The child had elevated lactate levels and electron microscopy of the rectal biopsy was suggestive of a mitochondrial disorder To the best of our knowledge there is no case report of this syndrome from India and since this presents with diagnostic difficulties so is being reported.
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Mitochondrial neurogastrointestinal encephalomyopathy (MNGIE) syndrome is a rare disorder that presents in childhood; however, marked delay in diagnosis is common. Mitochondrial disorders present with unrelated multisystemic involvement. gastrointestinal and central nervous system are involved. Due to bizarre symptomatology the diagnosis of this disease is often delayed. The authors happen to manage a young child with MNGIE syndrome. His symptomatology started in early infancy with unresponsive constipation associated with severe cachexia, peripheral neuropathy and neurological involvement in the form of seizures and encephalopathy. This being a very rare disorder, difficult to diagnose clinically; prompted us to document it.

CASE REPORT

A 12-year-male child presented with complaints of constipation since infancy, seizures for the last 4 years and vomiting for the last 3 years. Although the child had passed stools in the first 24 hours of birth, the child had constipation from infancy. He used to pass hard, pellet like stools every third or fourth day after some enema or medication. Occasionally the child used to develop abdominal distension, vague dull aching abdominal pain but never had obstipation. The child also had encopresis. Around four years ago the child had generalized myoclonic seizures with frothing lasting for less than 5 minutes. The child had similar episodes of seizures over the next few years and was put on carbamazepine prophylaxis. The child also complained of tingling and numbness in the legs and on examination there was minimal sensory loss from the feet.

The child also had vomiting for the past three years which was nonprojectile, used to occur some time after food, contained undigested food.

He was the first product of a nonconsanguineous marriage. His mother had been suffering from seizures, however she had not been investigated but was on anticonvulsants. He was developmentally normal.

On examination the child was emaciated and stunted with a weight of 17 Kg and height 131cm. The child had pallor and on perabdomen examination, the child had mild abdominal distension and tenderness. There was no organomegaly, however, hard fecal masses could be palpated in the region of the sigmoid colon, descending colon and the transverse colon. Per-rectal examination confirmed hard fecal matter in rectum and ruled out any local pathology. The bowel sounds were sluggish, and there were no visible loops and peristalsis. The rest of the systemic examination was normal.

The investigations revealed hemoglobin of 10g/dl, the total leucocyte count was 8600/cmm and the platelets were 1.7 lacs/cmm. The serum sodium levels were in the range of 121 to 129meq/l and the serum potassium level

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was 4.7meq/l. The liver and renal function tests were normal. The total serum proteins were 7.2g/dl with an albumin fraction of 3.8g/dl. The child had a serum calcium level of 9.1 and random blood sugar level was 96mg/dl. The eye examination was normal. The abdominal X-ray revealed dilated colon and impacted fecal matter and there was evidence of air fluid levels. The ultrasound done revealed no organomegaly, lymphadenopathy or calcification. Barium meal follow through revealed dilated ileum with normal cecum and ileocecal valve alongwith massive dilatation of the transverse, descending and sigmoid colon. A barium enema was done which showed dilated sigmoid, descending and transverse colon and very little barium could go up. The CT scan of the brain did not show the classical changes of leukoencephalopathy.

A full thickness rectal biopsy revealed the presence of ganglion cell ruling out Hirschsprung's disease. The electron microscopic examination demonstrated grossly abnormal mitochondria suggesting it to be a mitochondrial disorder.

The child was managed very aggressively for the constipation, however, the hard fecal masses persisted inspite of enemas, oral laxatives and suppositories. The enemas given used to trickle without any fecal matter.

The child also had peripheral sensory loss suggesting peripheral neuropathy. The child had two seizures during the stay in ward and there was no concomitant hypoglycemia or hypocalcemia. The child was on carbamazepine; however, the child had persistently low sodium levels inspite of sodium correction which could have caused the seizures.

The arterial blood gas analysis came out to be normal. The concomitant serum lactate levels were raised suggesting the possibility of mitochondrial disorder. The cerebrospinal fluid levels of lactate could not be done because of the hemodynamic instability in the child. The child's sensorium deteriorated progressively, child went into Grade IV encephalopathy with seizures and succumbed to the illness.

DISCUSSION

Mitochondrial encephalomyopathies are clinically and genetically heterogeneous because mitochondria are the products of 2 genomes: mitochondrial DNA (mtDNA) and nuclear DNA (nDNA). Mitochondrial neurogastrointestinal encephalomyopathy (MNGIE) is a genetic disorder and is defined clinically by severe gastrointestinal dysmotility; cachexia; ptosis, ophthalmoparesis, or both; peripheral neuropathy; and leukoencephalopathy. Skeletal muscle biopsies of patients have revealed abnormalities of mtDNA. The disease is caused by mutations in the thymidine phosphorylase (TP) gene.[1]

Our index patient had intestinal pseudo-obstruction, cahexia, peripheral neuropathy and some mitochondrial disorder of the brain however, we could not document any leukoencephalopathy. The eye examination was normal. The MNGIE syndrome is a rare disorder that presents in childhood; however, marked delay in diagnosis is common.[2] The same was exemplified in the present case also as the diagnosis of the disorder was not made until the preterminal stages.

Although this is a mitochondrial disorder but an autosomal recessive inheritance has been inferred to in the past because of (1) the high recurrence rate among siblings, (2) the lack of affected parents and progeny and (3) the relatively high rate of consanguinity.[3,4] A chromosomal locus for MNGIE has now been located to 22q13.32-qter, distal to D22S1161, with a maximum two-point LOD score of 6.80 at locus D22S526.[5]

It is worthwhile to note that in mitochondrial disorders, all the mitochondria are inherited from the mother.[6] The mother of present patient also had repeated seizures and was on treatment but had not been properly investigated for the cause.

Management of these heterogeneous disorders includes the empiric supplementation with various "mitochondrial cocktails," supportive therapies and avoidance of drugs and conditions known to have a detrimental effect on the respiratory chain.[6] The prognosis of the disease is not very good and few patients have survived beyond the fourth decade.

CONCLUSION

The MNGIE syndrome is a rare disorder and there is often a delay in the diagnosis of this rare disorder. Clinicians need to be aware of this rare clinical situation in a setting of pseudo obstruction and neurological abnormalities in order to manage effectively.

Contributors : AW collected the data, reviewed the literature and prepared the manuscript. BRT supervised the manuscript and helped in the review of literature. KV reviewed the histopathological and electron microscopy.

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