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Diagnosis of bilateral diffuse uveal melanocytic proliferation unveils primary gastric adenocarcinoma: a case report

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Abstract

Background: Bilateral diffuse uveal melanocytic proliferation (BDUMP) is an extremely rare paraneoplastic syndrome, with most cases reported as secondary to female urogenital and male lung malignancies. We reported this case of BDUMP patient whose primary malignancy was gastric adenocarcinoma verified with gastroscopy and subsequent pathological test.

Case presentation: A patient complaining blurred vision was suspected of bilateral diffuse uveal melanocytic proliferation (BDUMP), due to bilateral round oval patches at the posterior pole and cardinal signs in retinal angiography. Malignancy screening was suggested, and pathological report from gastroscopy confirmed the primary lesion as gastric adenocarcinoma. The patient chose palliative care due to late stage and unresectable nature of the malignancy.

Conclusions: Identifying BDUMP warrants further investigation of a primary malignancy. Our case provided evidence for the link between gastric adenocarcinoma and BDUMP.

Keywords: BDUMP, Gastric adenocarcinoma, Paraneoplastic syndrome

Background

Bilateral diffuse uveal melanocytic proliferation (BDUMP) is a rare paraneoplastic syndrome (PNS) affecting the eye, with around 60 cases reported [1]. There are five cardinal signs: (1) multiple, round or oval, subtle, patches at the level of the retinal pigmented epithelium (RPE) in the posterior fundus; (2) multifocal areas of early hyper-fluorescence corresponding with these patches; (3) multiple, slightly elevated, pigmented and non-pigmented uveal melanocytic tumors, as well as evidence of diffuse thickening of the uveal tract; (4) exudative retinal detachment; and (5) rapid progression of cataract [2]. It is thought either a substance secreted by the tumor or an antibody stimulated by the tumor, that causes benign proliferation of choroidal melanocytes [1]. Female urogenital (69%) and male lung carcinomas (52%) were reported more often, with sporadic cases including pancreatic, esophageal, breast, hepatocellular, Bartholin gland and renal cell carcinoma and central nervous system lymphoma [1]. Herein, we reported this case of BDUMP patient whose primary malignancy was gastric adenocarcinoma verified with gastroscopy and subsequent pathological test. This report was organized in adherence to CARE guidelines.

Case presentation

A 50-year-old Chinese male presented with bilateral blurred vision for 3 months. Nine months earlier, he experienced pulmonary embolism and lower limb venous thrombosis, and was diagnosed with antiphospholipid

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antibody syndrome (APS). He had lost 10 kilograms in the past 9 months. No other gastric or constitutive symptoms were reported.

On examination, his best corrected visual acuity (BCVA) was 20/200 OU. Anterior chamber was basically normal except for moderate cataract in both eyes. Fundus examination showed bilateral diffuse oval yellow patches in the posterior pole (Fig. 1a and b, top left), corresponding to a classical giraffe sign, namely hypo-fluorescence in autofluorescence (AF, Fig. 1a and b, top middle) and hyper-fluorescence in the early and late phases of fundus fluorescein angiography (FFA, Fig. 1a and b, top right) and indocyanine green angiography (ICGA) (Fig. 1a and b, bottom middle), with late phase pinpoint leakage. Spectral domain optical coherence tomography (SD-OCT, Fig. 1a and b, bottom right) B-scan well-depicted a mosaic pattern of RPE alterations between irregular thickening and atrophy. Blocked fluorescence on ICGA due to choroidal lesions was also noticed (Fig. 1a and b, white arrows). Based on these typical findings, the patient was diagnosed with BDUMP, and malignancy screening was strongly recommended.

Blood tumor markers reported as: CA19–9795.0 U/ml, CA125 3770.0 U/ml, Cyfra 211 57.6 ng/ml, CA242 > 150.000 U/ml, NSE 46.1 ng/ml. ^{18}F- fluorodeoxyglucose (FDG) positron emission tomography–computed tomography (PET/CT) (Fig. 1c) showed an FDG-avid lesion in the gastric antrum (Fig. 1c, big arrow), and multiple hypermetabolic lymph nodes (Fig. 1c, small arrows) were also noted in perigastric, retroperitoneal, mediastinal and left supraclavicular region, suggestive of gastric malignancy with distant lymph node metastasis. Based on these findings, gastroscopy was ordered. Pathological diagnosis (Fig. 1d) reported as poorly differentiated adenocarcinoma. The patient was finally diagnosed with BDUMP and secondary APS due to gastric adenocarcinoma. Systemic chemotherapy was suggested, but after evaluation, the patient's systemic condition was too poor to tolerate any chemotherapy. After consideration, the patient chose palliative care out of the late stage and unresectable nature of the malignancy and economic reasons.

Discussion and conclusions

BDUMP is an extremely rare paraneoplastic syndrome affecting the eye secondary to a primary malignancy, which can be ocular as well as systemic. We reported a case of BDUMP secondary to gastric adenocarcinoma, verified with pathological staining. Gastric adenocarcinoma was rarely reported to be associated with BDUMP. Dolz-Marco et al. [3] reported one delayed onset BDUMP case 17 years after total gastrectomy for gastric adenocarcinoma, with no evidence of primary cancer recurrence or second malignancy. Our case validated the association of gastric adenocarcinoma and BDUMP.

Despite various origins of primary malignancies, the mechanism of BDUMP is considered to be associated with a serum factor in patients' IgG fraction, namely

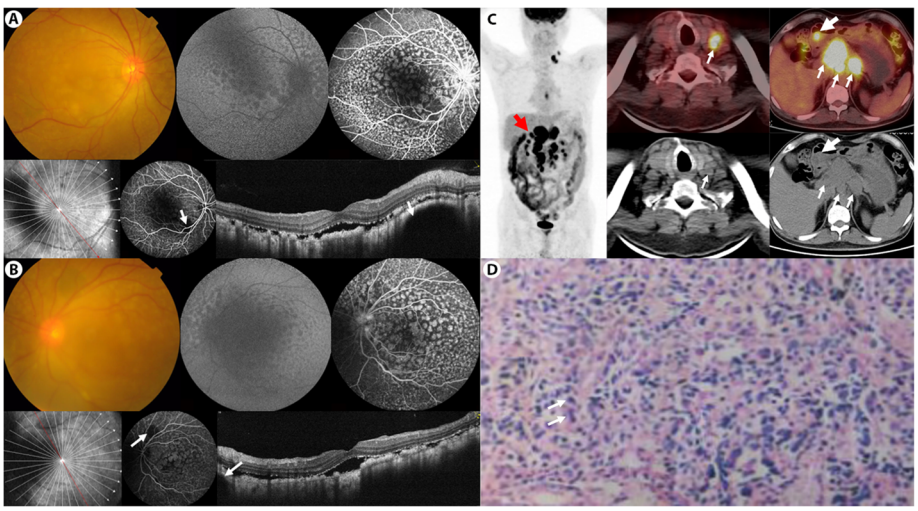

Fig. 1 Multimodal imaging of bilateral diffuse uveal melanocytic proliferation secondary to gastric adenocarcinoma. **a** and **b** Fundus photography (top left) showed bilateral diffuse oval yellow patches in the posterior pole, corresponding to hypo-fluorescence in autofluorescence (top middle) and hyper-fluorescence in the early and late phases of fundus fluorescein angiography (top right) and indocyanine green angiography (ICGA, bottom middle). Notice the choroidal lesions (white arrows) indicating choroidal melanocytic proliferation in ICGA and spectral domain optical coherence tomography (bottom right). **c** ^{18}F-FDG PET/CT showed an FDG-avid lesion in the gastric antrum (big arrow), and multiple hypermetabolic lymph nodes in perigastric, retroperitoneal, mediastinal and left supraclavicular region (small arrows). **d** Haematoxylin-eosin staining of the gastric lesion, confirming gastric adenocarcinoma. The neoplastic cells with most deeply-stained nuclei were diffusely distributed (white arrows), mixed with lymphocytes and epithelium

cultured melanocyte elongation and proliferation (CMEP) factor [4]. Hepatocyte growth factor (HGF) and anti-retinal autoantibodies to α-HGF were also suggested as an alternative etiology [5].

Treatment of BDUMP primarily targets the primary malignancies, including local resection, radiation and systemic chemotherapy. Since systemic factors elicited by primary malignancies is considered involved in the pathogenesis of BDUMP, this could possibly explain the improvement of visual symptoms in some cases after these treatments targeting the malignancy [1]. Plasmapheresis can theoretically remove plasma CMEP, but with variable effectiveness [6]. Intravitreal anti- vascular endothelium growth factor (VEGF) agents were proven effective in some cases with intra-retinal fluid [3]. Other interventions such as ocular radiation, sub-retinal fluid drainage, corticosteroids were generally unsuccessful [6]. The prognosis of BDUMP is extremely poor, with 15.6 months' median survival and in some exceptional cases, 4 to 9 years [7], due to the dissemination of the primary malignancy.

In summary, identifying BDUMP warrants further investigation of a primary malignancy. Our case provided evidence for the link between gastric adenocarcinoma and BDUMP.

Abbreviations

BDUMP: Bilateral diffuse uveal melanocytic proliferation; PNS: Paraneoplastic syndrome; APS: Antiphospholipid antibody syndrome; RPE: Retinal pigmented epithelium; BCVA: Best corrected visual acuity; AF: Autofluorescence; FFA: Fundus fluorescein angiography; ICGA: Indocyanine green angiography; SD-OCT: Spectral domain optical coherence tomography; FDG: Fluorodeoxyglucose; PET/CT: Positron emission tomography–computed tomography; CMEP: Cultured melanocyte elongation and proliferation; HGF: Hepatocyte growth factor; VEGF: Vascular endothelium growth factor

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Authors' contributions

All authors were involved in patient's diagnosis, treatment and care. ML drafted the manuscript and collected all the images. YZ and ZC contributed to manuscript revision. YL and LZ contributed to image evaluation and manuscript revision. RD coordinated and participated in the entire process of drafting and revised the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

Not applicable.

Ethics approval and consent to participate

This study adhered to the tenets of the Declaration of Helsinki. We were informed that no regular ethics approval is regularly needed for case reports from the Peking Union Medical College Hospital Review Board.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The authors declare that they have no competing interests.

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