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Case Report

Multimodal Imaging Findings in Bilateral Diffuse Uveal Melanocytic Proliferation (BDUMP)

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Abstract

Purpose: To present a case of bilateral diffuse uveal melanocytic proliferation (BDUMP), which is a rare paraneoplastic syndrome that causes progressive visual loss in patients with an underlying malignancy.

Case Report: A 59-year-old female patient presented with bilateral visual loss, which had started three months earlier. She had a history of treated ovarian cancer a year before. Fundus examination showed multiple red-orange subretinal patches with irregular and elevated pigmented tumors in both eyes, scattered over the fundus. Multimodal imaging was also consistent with BDUMP. She was referred to a clinical oncologist and underwent screening for systemic metastasis, which revealed multiple foci of secondary malignancies.

Conclusion: Ophthalmologists should be aware of this extremely rare condition. Although there is currently no effective treatment for ocular symptoms, the patient should be promptly referred to an oncologist for systemic screening and potential treatment of the primary site malignancy.

Keywords: Bilateral Diffuse Uveal Melanocytic Proliferation; Paraneoplastic Syndrome; Melanocytes; Malignancy; Ocular Oncology; Ovarian Cancer

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INTRODUCTION

Bilateral diffuse uveal melanocytic proliferation (BDUMP) is considered a rare paraneoplastic syndrome, usually occurring in patients with systemic carcinomas. The condition is characterized by rapidly progressive, painless, bilateral visual loss, uveal melanocytic tumors, rapid cataract formation, and exudative retinal detachment.[1] It is considered a hallmark of poor systemic prognosis.

We report a case of a 59-year-old female patient who was admitted to our ophthalmology hospital for visual loss, which had started three months earlier. She underwent systemic and ophthalmic evaluation and was diagnosed with BDUMP.

CASE PRESENTATION

A 59-year-old female patient sought assistance at our ophthalmology hospital for bilateral painless visual loss that had started three months earlier. She denied redness, tearing, conjunctival swelling, or any ocular secretions. She had a history of ovarian cancer, for which she had completed chemotherapy about a year before. She was under the care of a clinical oncologist, without any reported complications or metastasis. Past family and personal ocular history were unremarkable.

Upon ophthalmological evaluation, her best corrected visual acuity was 20/30 in both eyes. Biomicroscopy revealed incipient cataract in both eyes, without inflammation. Intraocular pressure was normal. Upon dilated fundus examination, multiple red-orange subretinal patches and irregular, elevated pigmented tumors were found scattered over the fundus in both eyes [Figure 1].

Fundus autofluorescence (FAF) revealed islands of decreased autofluorescence bordered by areas of hyperautofluorescence in a “giraffe” or “leopard” pattern [Figure 2]. Fluorescein angiography (FA) showed areas of hypofluorescence corresponding to the topography of the pigmented tumors, bordered by areas of window defects [Figure 3].

Optical coherence tomography (OCT) showed disrupted retinal segments, some areas of increased thickness of retinal pigmented epithelium (RPE) adjacent to areas of focal RPE loss, and subretinal fluid [Figure 4]. High-frequency B-scan ultrasonography showed scattered and focally elevated nevi-like lesions, exudative detachments, and diffuse choroidal thickening in both eyes [Figure 5]. Ultrasound biomicroscopy (UBM) showed bilateral focal areas of ciliary body thickening and multiple unequally sized ciliary and iris cysts [Figure 6].

Given these findings and the patient’s history of ovarian cancer, BDUMP was our initial diagnosis. She was referred to her clinical oncologist for systemic metastasis screening, which revealed metastases in pelvic, inguinal, and retroperitoneal lymph nodes, as well as the abdominal wall.

The patient returned to our office four months later. This time, her visual acuity was 20/400 in both eyes, with slit-lamp examination revealing advanced subcapsular cataract. We also noticed that she had developed hyperpigmentation in the tongue and oral cavity [Figure 7] as well as nail hyperpigmentation [Figure 8]. She is currently treated for systemic metastasis with chemotherapy and is waiting for cataract extraction.

DISCUSSION

Paraneoplastic syndromes are uncommon systemic disorders marked by impaired tissue function at a site distant from the original tumor, without direct tumor spread.[1] They result mainly from aberrant production of hormones and/or growth factors, or from an immune-driven cross-reaction between neoplastic antigens and healthy tissues.[1]

BDUMP is a rare condition marked by bilateral painless visual loss, and can precede the diagnosis of the primary cancer by several months to years. Initially described by Machemer,[2] it is considered a rare condition, with approximately 100 cases reported to date.[3] However, this number has risen in recent decades, largely due to improved cancer survival rates and increased awareness of the syndrome.

This condition is more prevalent in women (61%), with a mean age of onset at 65 years. In this group, BDUMP is most commonly associated with urogenital cancers. A recent review has shown that 71% of female patients with BDUMP had urogenital carcinoma, with ovarian cancer accounting for 26% of cases.[4] Among male patients, >50% had a history of lung carcinoma. Other malignancies previously associated with BDUMP include B-cell lymphoma, as well as carcinomas of the colon, urinary bladder, pancreas, breast, esophagus, colorectum, and kidney. In some cases, the primary tumor remains unidentified.[5] A previous review[4] found that in most patients (48%), the primary tumor was diagnosed either at the same time as or after

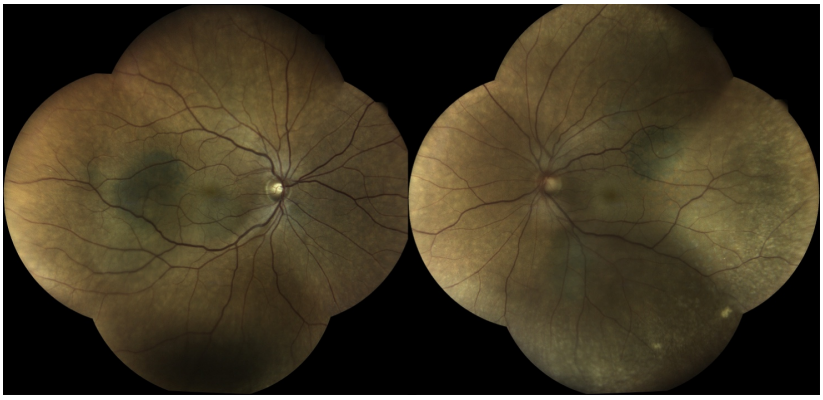

Figure 1. Fundus image showing multiple irregular, elevated, and pigmented choroidal tumors alongside red-orange nummular patches of RPE atrophy.

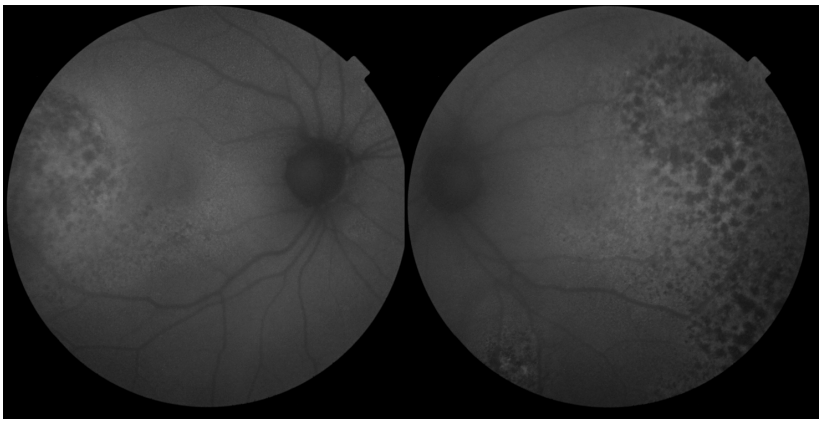

Figure 2. Fundus autofluorescence showing the typical giraffe pattern.

BDUMP, while in 44% of patients, it was identified beforehand. In some instances, the site of the primary cancer was not specified.

Gass[6] described the five cardinal signs of BDUMP: multiple oval and faint orange-red subretinal patches; hyperfluorescence of these patches in the early phases of FA; multiple slightly elevated pigmented and nonpigmented uveal melanocytic tumors along with diffuse thickening of the uveal tract; exudative retinal detachment; and rapid cataract formation.

The diagnosis is based on clinical findings and multimodal evaluation. As previously described, FA reveals a reticular pattern of hypofluorescence surrounded by areas of hyperfluorescence. FAF shows hypoautofluorescence within the nummular patches, with hyperautofluorescence in intervening regions. OCT usually reveals areas of RPE loss and RPE thickening, associated with subretinal fluid. More recently, bacillary layer detachment has been associated with this condition.[7] High-frequency B-scan ultrasonography and UBM findings are less commonly reported in patients with this condition. However, both examinations can aid in diagnosing this paraneoplastic syndrome. Posterior B-scan usually shows a diffuse choroidal thickening and lesions resembling choroidal nevi. Besides, UBM can help identify iris and ciliary body cysts—which can also be present in patients with BDUMP—as well as ciliary body thickening. It also allows the physician to investigate angle closure secondary to this condition. Differential diagnosis includes choroidal metastasis, choroidal melanoma, multiple choroidal nevi, and congenital hypertrophy of the RPE.

The pathogenesis remains unclear, although various hypotheses have been proposed. Some studies suggest that the condition may be related to the secretion of melanocytic growth factor by tumor cells, which is subsequently released into the systemic circulation. Additionally, up to 26% of patients with BDUMP exhibit extraocular hyperpigmentation in mucous membranes and skin, as observed in our patient. Some other

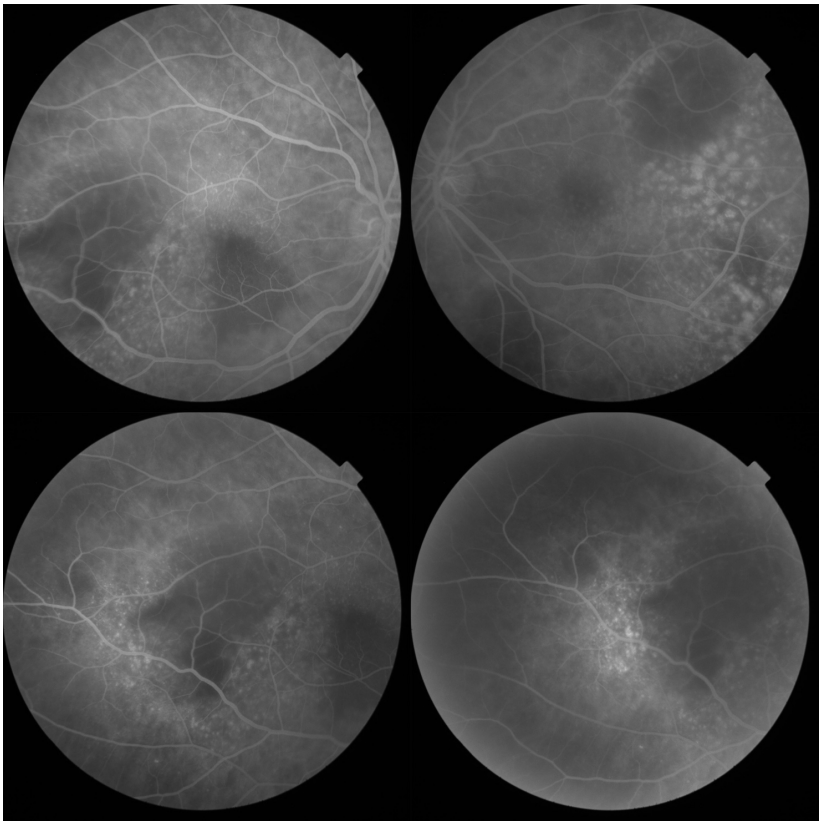

Figure 3. Fluorescein angiography demonstrating hypofluorescent areas corresponding to melanocytic choroidal tumors, surrounded by regions of window defect.

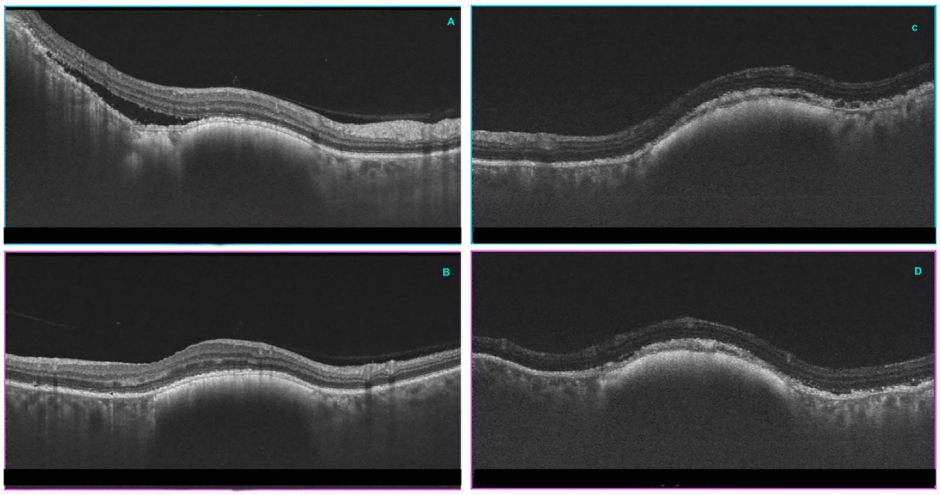

Figure 4. OCT illustrating increased choroidal thickeness, subretinal fluid, disruption of outer retinal layers, and alternating areas of RPE thickening and loss, both in the right (A & B) and left (C & D) eyes.

studies associate this condition with the production of IgG anti-retinal antibodies, such as CMEP (cultured melanocyte elongation and proliferation) factor, while others believe that toxic mechanisms could be responsible.[8]

To date, there is no available treatment for BDUMP. When evaluating a patient with suspected BDUMP, a comprehensive multidisciplinary evaluation must be performed to screen for primary and metastatic cancers, given the condition's strong association with poor prognosis. The mean

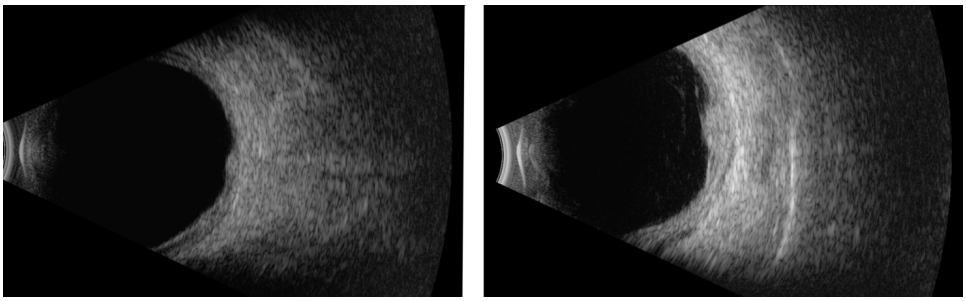

Figure 5. High-frequency B-scan ultrasonography (10 MHz) showing choroidal nevi-like lesions and diffuse choroidal thickening.

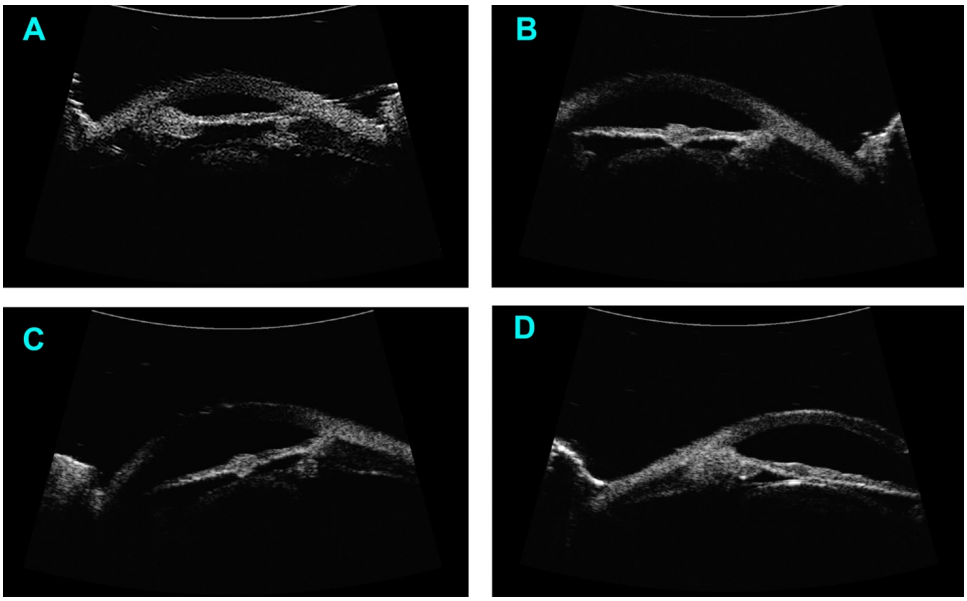

Figure 6. Ultrasound biomicroscopy (40 MHz) revealing focal ciliary body thickening with sectorial angle closure in the right eye (A & B). In the left eye, a homogeneous hyperechoic nodular lesion is observed in the iris (C & D). No evidence of scleral invasion is noted.

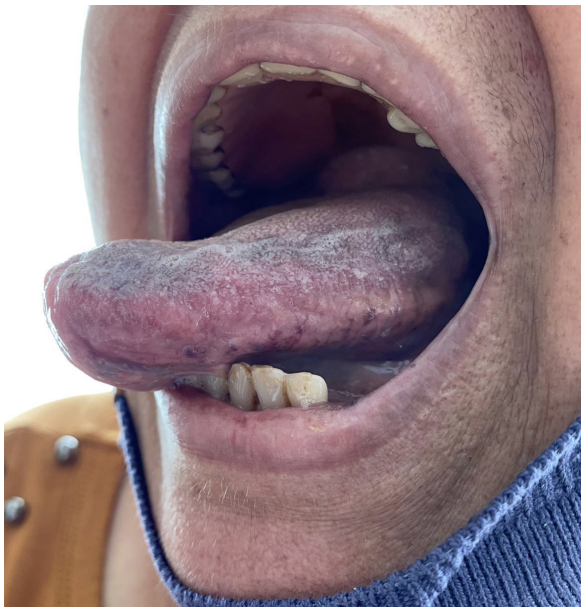

Figure 7. Hyperpigmentation of the patient's tongue.

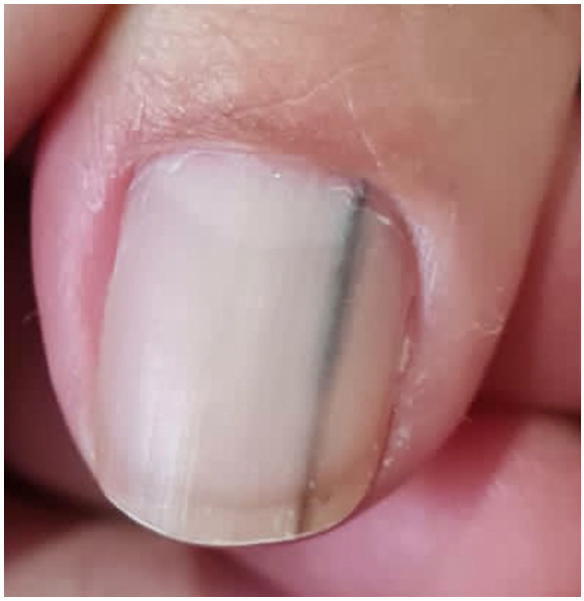

Figure 8. Nail hyperpigmentation.

life expectancy after diagnosis is 15.7 months,[4] primarily due to the burden of the underlying cancer. Visual impairment is often severe, resulting from retinal detachments and/or RPE destruction, and cataract formation. Temporary improvement in visual acuity can occasionally be achieved with phacoemulsification and intraocular lens implantation, as these patients often develop subcapsular cataracts. Additionally, treating the primary tumor is essential when its origin is known and treatment is feasible.

Other treatment options previously described include brachytherapy, steroid administration (systemic, topical, or intravitreal implants), and subretinal fluid drainage. Yet these approaches have yielded only transient or ineffective results. Plasma exchange and plasmapheresis have demonstrated efficacy in some cases.[10, 11] More recently, the combination of intravitreal anti-VEGF and photodynamic therapy has proven effective in reducing treatment-resistant exudate in patients with BDUMP.[12]

In summary, BDUMP is an extremely rare condition that should be considered in the differential diagnosis of pigmented lesions on fundoscopy. This case report underscores the necessity of a comprehensive ophthalmic assessment and extensive screening for primary and metastatic neoplasia in suspected cases. Given the complexity of BDUMP, a multidisciplinary approach is crucial for optimal management. Treatment remains challenging, as visual deterioration typically progresses rapidly and is irreversible. Patients must be informed about the poor prognosis, the limitations of currently available therapeutic options, and the potential burden of underlying systemic malignancy.

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Conflicts of Interest

None.

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