A case of bilateral diffuse uveal melanocytic proliferation with secondary angle closure caused by ciliary body thickening

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ABSTRACT

Purpose: To describe a case of bilateral diffuse uveal melanocytic proliferation (BDUMP) with secondary angle closure caused by ciliary body thickening accompanied by intraocular pressure (IOP) elevation after mydriasis.

Observations: A 55-year-old woman with a history of ovarian cancer had blurred vision in both eyes. Fundus examination revealed multiple patchy lesions in both eyes and a nevus-like elevated lesion in the right eye. Anterior segment optical coherence tomography (AS-OCT) and ultrasound biomicroscopy (UBM) demonstrated angle closure resulting from ciliary body thickening. After mydriasis, the IOP was elevated in both eyes. Instillation of a miotic drug successfully reversed the IOP to normal levels.

Conclusions and Importance: BDUMP caused secondary angle closure in both eyes, presumably due to thickening of the entire ciliary body. AS-OCT and UBM were advantageous for analyzing the morphology of the anterior eye segment in BDUMP. Clinicians should be aware of the possibility of angle closure during the management of patients with BDUMP.

1. Introduction

Bilateral diffuse uveal melanocytic proliferation (BDUMP) is a rare paraneoplastic syndrome that causes progressive loss of visual function in both eyes. Major primary malignant tumors that cause BDUMP are urogenital cancers (e.g., ovarian cancer) in women (69%) and lung cancer in men (52%); the systemic prognoses are usually poor. The five cardinal signs of BDUMP are (1) multifocal, faintly visible, round or oval, red, subretinal patches; (2) associated striking pattern of hyperfluorescence during the early phases of fluorescein angiography (FA); (3) development of multiple, slightly elevated, pigmented and non-pigmented uveal melanocytic tumors, as evidence of diffuse thickening of the uveal tract; (4) exudative retinal detachment; and (5) rapid progression of cataract.

In addition, BDUMP sometimes manifests as iris nodules, iris cysts, ciliary body cysts, diffuse ciliary body thickening, and ciliary body nevus-like lesions, all of which can cause secondary angle closure. However, the mechanisms of angle closure in BDUMP are yet to be elucidated. Here, we describe a case of BDUMP with secondary angle closure resulting from ciliary body thickening using anterior segment optical coherence tomography (AS-OCT) and ultrasound biomicroscopy (UBM).

2. Case report

A 55-year-old Japanese woman was diagnosed with clear cell adenocarcinoma of the ovary with cervical lymph node metastasis. She underwent abdominal hysterectomy and bilateral adnexectomy. She had blurred vision in both eyes (OU) during postoperative chemotherapy (paclitaxel and carboplatin). At presentation, her visual acuity was 20/16 in the right eye (OD) and 20/25 in the left eye (OS). The intraocular pressure (IOP) was 13 mmHg in both eyes. Only mild cataracts were observed. The anterior chambers were clear but shallow, with very narrow angles (Van Herick grade 1) in the OU. When observed with a gonioscope, the patient’s trabecular meshwork in both eyes was covered by the iris and could not be observed even with compression gonioscopy. AS-OCT (SS-1000 CASIA, Tomey, Aichi, Japan) was used to quantitatively analyze the...
anterior segment of the eyes in this patient. The central anterior chamber depths (ACD) were 1.793 mm and 1.762 mm in OD and OS, respectively (Fig. 1A and B), whereas the axial lengths were normal (23.40 mm and 23.24 mm in OD and OS, respectively). The iris in this patient was relatively planar centrally, while the peripheral iris root angled forward (Fig. 1A-F). The iris shape mirrored a plateau iris configuration rather than iris bombe. UBM (UD-8000, 60 MHz, Tomey, Aichi, Japan) revealed structures not observable by AS-OCT. Cysts behind the peripheral iris induced compression of the peripheral angle (Fig. 1C-F, arrows), as previously described as plateau-like iris configuration or pseudo plateau iris. The thick ciliary body (Fig. 1C-F, asterisks) caused its anterior displacement, which was presumably another mechanism of mechanical closure of the peripheral angle. Measurement of the angle parameters, as previously described on UBM images using ImageJ 1.53a (National Institutes of Health, Bethesda, Maryland, USA), further confirmed thickening of the ciliary body (Table 1). The parameters were measured in the superior, nasal, inferior, and temporal quadrants and averaged for each eye (Table 1). Circumferential scans (Fig. 1G and H) clearly showed the ciliary processes (not flattened, i.e. without ciliolenticular block). No suprachoroidal space was observed by UBM.

Phenylephrine (5%, Kowa, Aichi, Japan), which can be counteracted by pilocarpine, was instilled once to examine the posterior portions of the eyes. The right eye showed two pigmented choroidal masses, and both eyes showed multiple gray-white patches in the temporal area of the posterior fundus (Fig. 2A and B). Fundus autofluorescence (Heidelberg Spectralis HRA2, Heidelberg Engineering, Heidelberg, Germany) showed hypofluorescence corresponding to patchy lesions surrounded by hyperfluorescent areas (Fig. 2C and D). OCT revealed a choroidal mass in the OD and subretinal fluid (SRF) in the OU. The subfoveal choroidal thicknesses were 407 and 478 μm in OD and OS, respectively, indicating diffuse choroidal thickening (Fig. 2E and F). FA showed hyperfluorescence from the early phase, corresponding to multiple patchy lesions (Fig. 3A and B). Indocyanine green angiography (IA) clearly showed choroidal vascular structures corresponding to patchy lesions (Fig. 3C and D). The nevus-like elevated lesions were hypofluorescent during the early and late phases (Fig. 3E-H).

Two hours after mydriasis, IOP rose to 26 mmHg in OD and 38 mmHg in OS without symptoms. Oral carbonic anhydrase inhibitor (acetazolamide 250 mg) and intensive 1% pilocarpine instillation lowered IOP (12 mmHg in OD and 13 mmHg in OS) within 90 min. Invasive treatment was not performed, and prophylactic instillation of 2% pilocarpine and 0.1% betamethasone was started because of the patient’s poor general condition. Although UBM observation was not performed because of the poor general condition during the follow-up, ACD measured by AS-OCT slightly increased a month after starting instillations (1.861 mm in OD and 1.852 mm in OS). Moreover, the IOP remained normal for five months thereafter, until the patient died of ovarian cancer.

3. Discussion

The present case showed four of the five cardinal signs of BDUMP, except for rapid cataract progression, and was diagnosed as BDUMP during treatment for ovarian cancer. In addition to its characteristic fundus findings, BDUMP manifests as changes in the anterior segment of the eye, such as iris nodules, iris cysts, ciliary body cysts, diffuse ciliary body thickening, and ciliary body nevus-like lesions. The present case also showed iris cysts and ciliary body thickening (Fig. 1). Furthermore, the patient had a shallow anterior chamber and narrow

![Fig. 1. Anterior segment optical coherence tomography (AS-OCT) and ultrasound biomicroscopy (UBM) in the patient with BDUMP.](image-url)
UBM is more informative than AS-OCT for evaluating the morphology of the ciliary body. In summary, our patient had a thicker ciliary body than normal subjects reported in previous studies.\(^{14,16-18}\) While ciliary bodies are reported to be thinner posteriorly,\(^{14,16-18}\) the ciliary body in the present case was thick even posteriorly (i.e., CBT2000 in Table 1). In comparison with previous reports on normal eyes,\(^{17,18}\) our patient had smaller trabecular ciliary process distance and trabecular ciliary angle and larger anterior placement of the ciliary body (Table 1). These results suggest presence of diffuse thickening and anterior displacement of the ciliary body in the present case of BDUMP. The uveal tract in patients with BDUMP thickens due to proliferation and infiltration by melanocytes.\(^{3}\) We opine that ciliary body thickening in all circumferences induced angle closure in the present case by similar mechanisms as in cases with ring melanoma of the ciliary body,\(^{19-21}\) which induced anterior displacement of the peripheral ciliary body. Hence, we hypothesize that the enlarged and thus anteriorly displaced ciliary body, together with the cysts, caused mechanical closure of the peripheral angle in the present case of BDUMP.

The pathogenesis of BDUMP is yet to be elucidated. Gass et al. speculated that hormones and stimulants secreted by malignant tumors cause BDUMP.\(^{3}\) In vitro, the IgG fraction of patients with BDUMP selectively stimulated cell proliferation of melanocytes,\(^{22}\) which has some effects on the entire uveal tract, resulting in diffuse uveal thickening.\(^{3,7}\) Our patient also had diffuse thickening both in the ciliary body and posterior choroid, as demonstrated by UBM and OCT, respectively. Since BDUMP affects the anterior uvea, observation of the anterior eye segment by AS-OCT and UBM may provide supportive information when...
diagnosing BDUMP.

BDUMP is associated with malignancy. Therefore, treatment of the primary malignancy is fundamental and likely to improve visual symptoms and ocular findings caused by BDUMP. An article reported that treatment against primary malignancy improved visual symptoms. However, the mean survival time after the onset of symptoms of BDUMP is 15.7 months, and few studies have reported the results of long-term treatment. In the present case, although surgery and postoperative chemotherapy were initiated for ovarian cancer, the visual symptoms did not improve.

Other treatments such as plasmapheresis, oral steroids, and ocular steroid injections have been reported. The responses to these treatments vary on a case-by-case basis, but several reports suggest that plasmapheresis may improve visual acuity and serous retinal detachment in patients with BDUMP. Oral steroid treatment resolved serous retinal detachment in a patient with rare concurrent manifestation of BDUMP and cancer-associated retinopathy. However, the effectiveness of oral steroids remains uncertain. In another patient, periocular injection of triamcinolone acetonide reduced SRF. Since our patient’s general condition was poor, plasmapheresis or oral steroid treatment was unsuitable. Instead, the patient was treated with pilocarpine and steroid instillation to prevent IOP elevation owing to secondary angle closure. Topical steroid therapy may be cost-effective, in comparison with plasmapheresis, for patients with BDUMP, although further studies are required to assess the therapeutic effects of steroids on the choroid and the methods of administration.

4. Conclusions

In the present paper, we report a case of BDUMP with secondary angle closure induced by ciliary body thickening. BDUMP causes thickening of the entire ciliary body and anterior displacement of the ciliary body, which may subsequently lead to angle closure. Attentive observation and analysis of the anterior eye segment, with the help of AS-OCT and UBM, provided insight into the mechanisms of secondary angle closure in BDUMP. Clinicians should be aware of the possibility of angle closure during the management of patients with BDUMP.

Patient consent

The consent prescribed by this journal for publication of the case report was not obtained, but the consent form prescribed by our hospital was obtained. This report does not contain any personal information that could lead to the identification of the patient.

Ethics approval

This study adhered to the tenets of the Declaration of Helsinki. The Research Ethics Committee of Niigata University Hospital waived the requirement for ethics approval for the case report.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Fig. 3. Fluorescein angiography (FA) and indocyanine green angiography (IA) in the patient with BDUMP. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

FA showed hyperfluorescence from the early phase, corresponding to multiple depigmented patchy lesions. Hyperfluorescence was prominent in the temporal area of the posterior fundus (A, right eye; B, left eye). IA clearly showed choroidal vascular structures corresponding to patchy lesions (C: right eye, D: left eye). The nevus-like elevated lesions in the right eye were hypofluorescent (yellow arrows; E, early phase; F, late phase around the upper arcade vessels; G, early phase; H, late phase around the lower arcade vessels).
Declaration of competing interest

None.

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