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Coloration of Fundus Lesions in Bilateral Diffuse Uveal Melanocytic Proliferation

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Purpose: To report differences in the coloration of fundus lesions between Asian and Caucasian patients with bilateral diffuse uveal melanocytic proliferation (BDUMP).

Cases: This syndrome was detected in 2 Japanese patients, 69 and 73 years old, with lung cancer who visited our department complaining of visual disturbances. The coloration of the fundus lesions was investigated in these 2 patients.

Results: The fundus lesions in the first patient appeared gray or grayish-brown in color at the first visit. Six months later, the fundus appeared as a mixture of white to dark-brown lesions. The fundus in the second patient exhibited a mixture of white, gray, and dark-brown lesions from the first visit.

Conclusions: The fundus lesions in these BDUMP patients appeared gray or grayish-brown in color at the early stage of the disease, probably because of the abundance of melanin pigments in the uveal melanocytes. At the advanced stage, the fundus exhibited a mixture of dark-brown lesions due to melanin deposits and white, depigmented lesions caused by atrophy and/or necrosis of the melanocytes. **Jpn J Ophthalmol 2003;47:612–615**

Key Words: Bilateral diffuse uveal melanocytic proliferation, coloration of fundus lesions, paraneoplastic syndrome, uveal melanocytes.

Introduction

Bilateral diffuse uveal melanocytic proliferation (BDUMP) is a rare paraneoplastic syndrome presenting with proliferative changes in the uveal melanocytes of both eyes.[1–7] Gass et al[3] summarized the clinical features of BDUMP as: (1) multiple, round or oval, subtle, red patches at the level of the retinal pigment epithelium in the posterior fundus; (2) a striking pattern of multifocal areas of early hyperfluorescence corresponding with these patches; (3) development of multiple, slightly elevated, pigmented and nonpigmented uveal melanocytic tumors, as well as evidence of diffuse thickening of the uveal tract; (4) exudative retinal detachment; and (5) rapid progression of cataracts.

According to a review by Chahud et al[7] in 2001, only 22 cases of BDUMP have been reported in the English literature, including 1 Japanese case.[2] Since then, another Japanese case of BDUMP has been reported in the Japanese literature.[6] We report 2 additional Japanese cases of BDUMP, with emphasis on the difference in the coloration of the fundus lesions between Asian and Caucasian patients.

Case Reports

Case 1

A 69-year-old Japanese man visited our department in January 1998 complaining of visual disturbances. He had been diagnosed as having lung cancer in February 1995 and had undergone lobectomy and chemotherapy. However, cerebral and bilateral intrapulmonary metastases were found 9 and 33 months (November 1997), respectively, after the initial therapy. The corrected visual acuity

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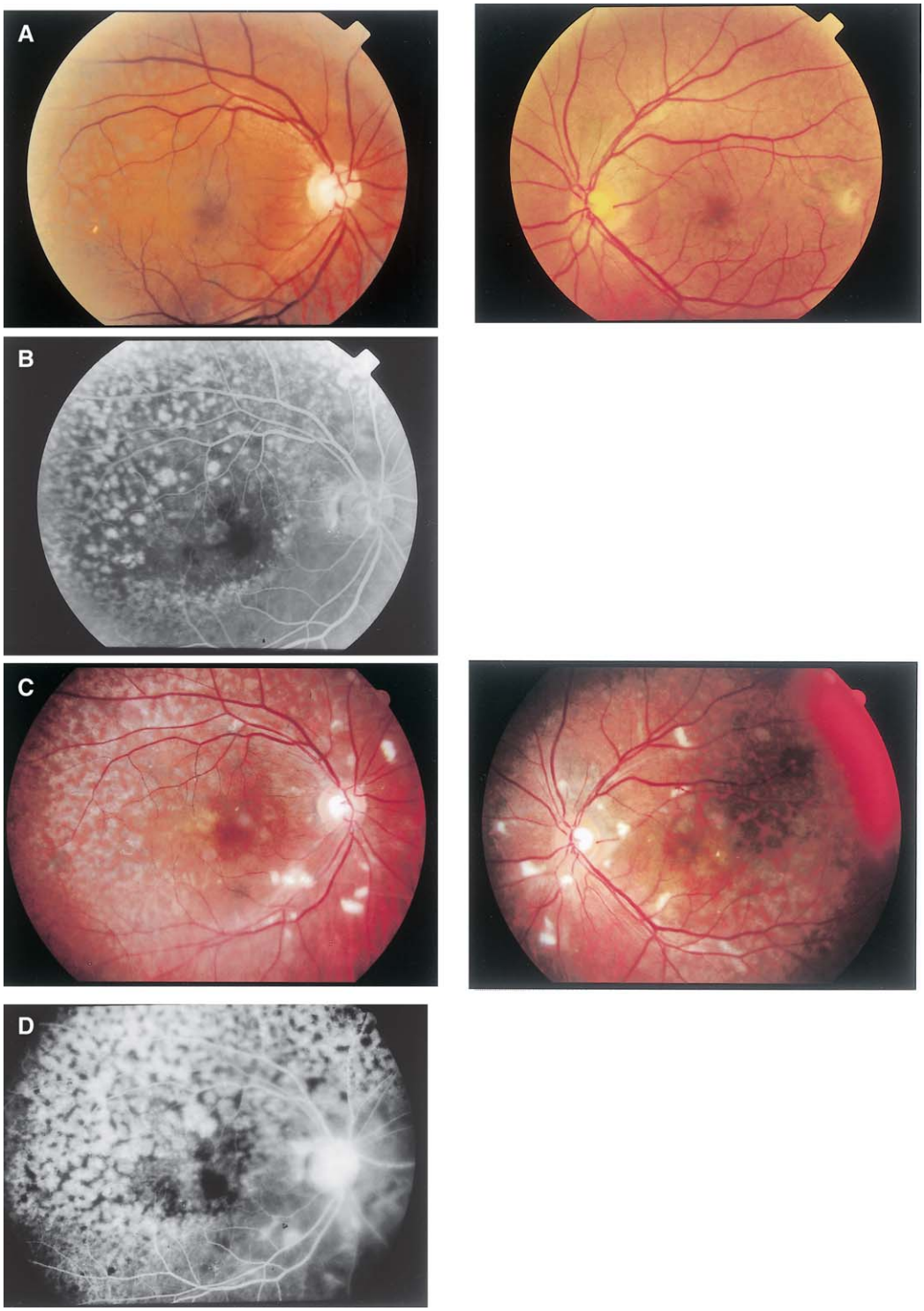

Figure 1. (**A**) Case 1. Fundus photography on the first visit of a 69-year-old Japanese man found to have bilateral diffuse uveal melanocytic proliferation (BDUMP). Gray or grayish-brown lesions are noted at the level of the retinal pigment epithelium in the posterior fundus. There are localized serous retinal detachments in both eyes, each of which is about 1 disc diameter in size, in an area nasal, superior, and temporal to the macula, although they are not clear in the figure. White retinal opacity is seen corresponding to a detachment in the left eye. Left: right eye, right: left eye. (**B**) Case 1. Fluorescein angiography of the right eye on the first visit. Spotty or patchy hyperfluorescence due to window defect can be seen. Multiple fluorescein leakage points correspond to the serous retinal detachments. (There were similar findings in the left eye.) (**C**) Case 1. Fundus photography 9 months after the first visit. Several of the fundus lesions have fused and multiple soft exudates are noted. The coloration of the fundus lesions has changed from white to dark brown. Left: right eye, right: left eye. (**D**) Case 1. Fluorescein angiography of the right eye 9 months after the first visit. Hyperfluorescence due to window defects associated with the widespread retinal pigment epithelium damage is seen corresponding to the lesions. Obstructions in the retinal capillary bed are noted corresponding to the soft exudates. Granular staining was also noted in the retinal vein. (There were similar findings in the left eye.)

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on the first visit was 0.8 in the right eye and 0.5 in the left eye. Mild cataracts were noted in both eyes.

Gray or grayish-brown patches were found in the fundus, and there were focal serous retinal detachments, each of which was about 1 disc diameter in size. The lesions were located nasal, superior, and temporal to the macula (Figure 1A). Fluorescein angiography revealed hyperfluorescence due to window defects associated with the retinal pigment epithelium damage that corresponded with the pigmented patches. Multiple fluorescein leakage points were also detected, although they did not always appear at all of the retinal pigment epithelium damage sites (Figure 1B). The cataracts progressed thereafter and the corrected visual acuity decreased to 0.09 in the right eye and 0.4 in the left eye. Cataract surgery was performed in June 1998 resulting in a postoperative corrected visual acuity of 0.8 in the right eye and 0.9 in the left eye.

Compared with the findings on the first visit, fundus examination in October 1998 revealed that some of the fundus lesions had fused, and multiple soft exudates were present (Figure 1C). The coloration of the fundus lesions became a mixture of white, gray, and dark brown. The soft exudates occurred in the sites anatomically different from those of BDUMP, suggesting that there was no causal relation between these two lesions. The mechanism of the soft exudate production was unclear, but some preexisting systemic factors, such as disseminated intravascular coagulation or anemia, may have played a role. The visual acuity remained fair because the fovea was not affected by the lesions.

Fluorescein angiography showed hyperfluorescence due to the window defects associated with widespread retinal pigment epithelium damage corresponding to the lesions. Obstructions in the retinal capillary bed, corresponding to the soft exudates, were noted. In the late phase, granular staining was observed in the retinal vein (Figure 1D). This abnormal finding in the retinal vein has not been described in the previous reports on BDUMP, suggesting that, as mentioned with the soft exudates, some factors that were independent of the development of BDUMP may have played a role in this venous change through an unknown mechanism.

The patient's general condition deteriorated and he died 1 month after the last ophthalmic examination.

Case 2

A 73-year-old Japanese man visited our department in September 1999 complaining of visual disturbances. Although he was diagnosed as having lung cancer with bone metastases in January 1999, no treatment had been performed at his request. On the first visit, the corrected visual acuity was 0.3 in the right eye and 0.2 in the left eye. Mild cataracts were noted in both eyes. Fundus examination on the first visit (Figure 2A) revealed an extensive lesion that appeared to have formed from a fusion of smaller lesions. The coloration of the lesions was a mixture of white, gray, and dark brown at the level of the retinal pigment epithelium, including the macular area. Fluorescein angiography showed hyperfluorescence due to window defects corresponding to the lesions (Figure 2B). The patient did not return to our department for follow-up because his general condition deteriorated.

Discussion

BDUMP is a paraneoplastic syndrome that affects uveal melanocytes.[1–7] Although the etiology of this syndrome remains unknown, a number of researchers have suggested there is a humoral factor in the development of

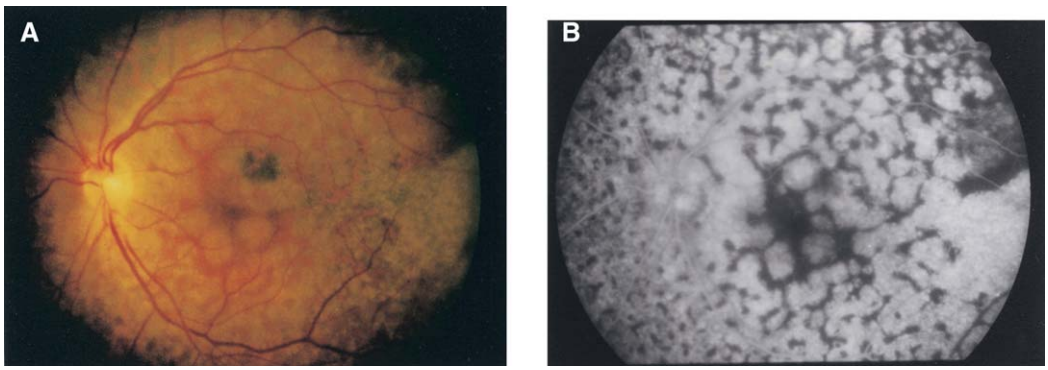

Figure 2. Left eye of case 2, a 73-year-old Japanese man. (Similar BDUMP findings were observed in the right eye.) (**A**) Funduscopy on the first visit. An extensive, fused lesion with a white or grayish-brown coloration is noted at the level of the retinal pigment epithelium including the macular area. (**B**) Fluorescein angiography on the first visit. Hyperfluorescence due to window defect is noted in the large area corresponding to the fundus lesion.

BDUMP.[1,3,5,6] This factor reacts against uveal melanocytes pathologically, resulting in a benign proliferation of the uveal melanocytes.[1,3,4,6]

The coloration of the patch lesions in our cases was different from the lesions previously reported in Europe and America; the lesions were white to dark brown in our cases versus red, orange, pink, or yellow-orange in the Caucasian cases, except for 1 case[3] with brunette fundi. In a report of a Japanese BDUMP case, Tsukahara et al[2] described the fundus lesions as ''atrophic patches'' or ''white patches.'' After stating that the coloration of BDUMP lesions was usually yellow-orange, Makino et al[6] reported that the fundus lesions of their case consisted of a mixture of orange and dark-brown patches. However, the fundus photograph of their case showed a lesion with a gray to dark-brown coloration.

We suggest that the difference in the coloration of fundus lesions between Caucasians and Asians is caused by the difference in the amount of melanin pigments in the melanocytes between the two groups of patients. The dark-gray color of the lesion in a case with brunette fundi supports our hypothesis.

As shown in case 1, the fundus lesions had a dark-brown coloration due to abundant melanin pigments at an early stage, and then exhibited a white coloration due to a partial depigmentation of the lesions at the late stage. Thus, with a long follow-up period, fundus lesions in Asian cases of BDUMP should have changes in the coloration. We believe that such changes in coloration are due to atrophy and/or necrosis of the proliferating melanocytes caused by the compression of the proliferating melanocytes, and to circulatory disturbances in the choroid resulting from the compression by the proliferating melanocytes.

We conclude that there are coloration differences in the fundus lesions in patients with BDUMP that are due to the amount of melanin pigment in the choroid. If this hypothesis is correct, this coloration difference should be present in other highly pigmented eyes.

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