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Diffuse metastatic melanoma to the retina: a clinicopathologic report

A 54-year-old female was referred to evaluate a peripheral melanotic fundus lesion in the left eye. A month prior, she noticed a temporal field defect in the same eye. Three months before the ocular symptoms, she underwent bowel resection for small intestinal obstruction caused by multiple tumours in the intestinal wall and regional lymph nodes, which are suggestive of hematogenous metastatic disease. Excised masses were pathologically proved to be metastatic melanoma. The patient provided no definite history of a previous primary melanoma; however, she had a curious account of a pigmented lesion appearing in her forearm skin during pregnancy 20 years earlier, for which a biopsy was not performed and that had spontaneously disappeared postpartum. No other relevant ocular or medical history was obtained. On examination, the visual acuity was 20/20 in both eyes. Bilateral anterior segment examination was normal, and intraocular pressure was 16 mm Hg. Funduscopy of the right eye was normal, but the left eye demonstrated a pre-equatorial diffuse pigmented lesion. The lesion extended as a patch between 7- and 11-o'clock meridians, accumulating at the fundus periphery, covering the underlying retina, and extending anterior to ora serrata (Fig. 1A). The surface of the lesion had a velvety friable appearance with few pigmented particles dispersed into vitreous adjacent to the main lesion (Fig. 1B). A single, small, pigmented spot was also observed temporal to the macula adjacent to the inferotemporal arcade. However, on magnified fundus imaging, multiple minute pigmented particles could be detected scattered over the retinal surface (Fig. 1C). Ultrasonography demonstrated a diffuse lesion with medium internal reflectivity, 3 mm in thickness (Fig. 1D). Systemic staging with magnetic resonance imaging showed evidence of a few small liver nodules and 5 brain lesions. The largest brain lesion was associated with hemorrhage, which was subsequently excised through craniotomy and was pathologically proved to be a melanoma. This was followed by full-brain irradiation of the smaller brain lesions, with inclusion of the eyes within the radiation field. The patient continued to notice gradual decline in vision and progressive pain in her left eye. Two months after irradiation, the left eye vision deteriorated to light perception, and intraocular pressure became 50 mm Hg. The anterior chamber contained a dark pseudohypopyon of tumour cells, and ultrasonography confirmed full involvement of the vitreous cavity with dispersed cells. The left eye, becoming blind and painful, was subsequently

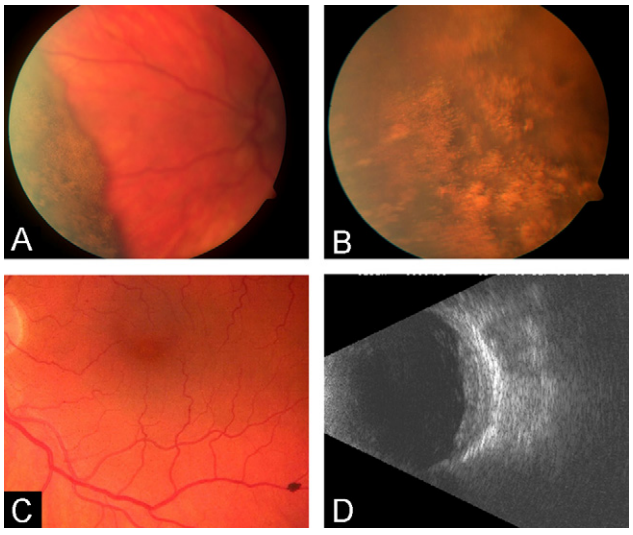

Fig. 1—A, Peripheral diffuse melanoma extending from 7 to 11 o'clock of the left eye. B, Melanoma demonstrates velvety friable surface. C, a single pigmented spot adjacent to the inferotemporal arcade with dispersion of minute pigmented particles over the retinal surface. D, b-scan ultrasonography demonstrates a diffuse lesion with medium internal reflectivity.

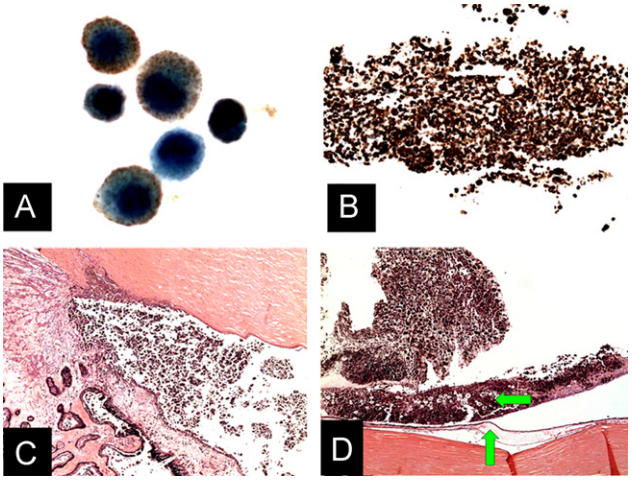

Fig. 2—A, Papanicolaou staining of cells dispersed in vitreous of the enucleated eye shows large, discohesive, pleomorphic cells with high nucleus to cytoplasm ratio and scattered melanin granules within the cytoplasm. B, Cytospin of vitreous shows highly reactive cells to HMB-45 (dark brown) indicative of their melanocytic origin. C, Malignant cells involve anterior chamber angle, obstructing the trabecular meshwork and filling Schlemm canal. D, Melanoma cells stained with HMB-45 are infiltrating the full thickness of the retina (*horizontal arrow*), without infiltration of choroid (*vertical arrow*), or sclera.

enucleated. Two months later, the patient passed away from widespread melanoma metastases.

Histopathology of the enucleated eye showed a large pigmented tumour mainly involving the nasal quadrant of the globe, with extensive dispersion of tumour cells inside the eye. Papanicolaou staining of the dispersed cells in the vitreous showed large discohesive pleomorphic cells with high nucleus to cytoplasm ratio and scattered melanin granules within their cytoplasm (Fig. 2A). Immunohistochemistry of tumour cells was highly reactive to HMB-45, characteristic of melanoma (Fig. 2B). Malignant cells involved the anterior chamber angle, obstructing the trabecular meshwork and filling Schlemm's canal (Fig. 2C). Melanoma cells could be detected infiltrating the retina without involvement of the uvea or sclera in the examined sections (Fig. 2D).

Intraocular metastases from cutaneous melanoma represent less than 4% of all metastases to the eye, whereas uvea is involved in 75% of cases and retina in 20%.[1–4] Cutaneous melanoma metastatic to the retina has been reported to have variable presentations, such as a unifocal pigmented retinal mass related to a major blood vessel, or as multiple preretinal patches, usually related to the major vascular arcades.[3,5–7] It has been postulated that melanoma metastases reach the surface of the retina through the walls of retinal vessels.[3,7] Retinal metastases of cutaneous melanoma commonly involve adjacent intraocular structures and produce seeding of melanoma cells into the vitreous. Vitreous melanoma metastases could be extensive and may occupy the anterior chamber, presenting as a black pseudohypopyon, as occurred later in our patient.[8] This case had an atypical clinical picture at initial evaluation, as a peripheral, single, diffuse, friable-looking pigmented patch covering the retina. A differential diagnosis of such presentation is an extensively necrotic primary ciliary body melanoma. Differentiation between primary and metastatic intraocular melanoma is not possible by cytopathologic examination of melanoma cells, if obtained by fine needle biopsy.[1–3] However, the presence of associated bowel, visceral, and brain melanoma metastases, in addition to the histopathologic finding of retinal infiltration with melanoma cells without uveal involvement, highly suggested the diagnosis of metastatic melanoma to the retina. Interestingly, there was no definite history of a cutaneous melanoma in this patient. Nevertheless, the forearm pigmented skin lesion, which spontaneously regressed after pregnancy 20 years earlier, is presumably the origin of her metastatic disease. Time between diagnosis of a primary skin melanoma and ocular metastases has been reported to be within 5 years in almost 75% of cases.[1] In a few cases, however, the time interval approached 20 years.[1,5,6] Spontaneous regression has been reported to occur in less than 1% of cutaneous melanoma cases.[9] The underlying mechanism of such regression is not fully understood and has been attributed to various immunologic, endocrine, and metabolic causes. Nevertheless, spontaneous regression of cutaneous melanoma during pregnancy has been previously reported.[9,10]

This atypical presentation of metastatic melanoma to the retina is to be distinguished from a primary intraocular melanoma. Metastatic melanoma to the retina can be secondary to a spontaneously regressed cutaneous melanoma, and may herald the presence of other occult non-ocular melanoma metastases.

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