Histopathologic, Immunohistochemical, Ultrastructural, and Cytogenetic Analysis of Oncocytic Uveal Melanoma

The histological findings of malignant melanoma may be highly variable, and the tumor can mimic many other neoplasms. Oncocytic change is defined histologically by abundant, eosinophilic, finely granular cytoplasm due to densely packed mitochondria. Oncocytic change has rarely been described in dermal nevi, meningial melanocytoma, cutaneous melanoma, or metastatic melanoma. To our knowledge, we give the first description of exclusively oncocytic uveal melanoma.

Report of a Case. A 73-year-old man visited the outpatient department of ophthalmology with signs of a para-central scotoma, decreased vision, and metamorphopsia in his left eye for 1 month. Best-corrected visual acuity was 40/40 OD and 20/40 OS. On dilated funduscopic and ultrasonographic examination of the left eye, a mushroom-shaped hypopigmented subretinal mass was seen superior and temporal to the fovea with a thickness of 7.1 mm, a diameter of 11.4 mm, and medium to low internal reflectivity (Figure, A). No atypical cutaneous pigmented lesions were observed. Systemic radiologic evaluation revealed no metastatic lesions. The patient opted for enucleation. After a follow-up of 24 months, there were no signs of metastases.

Sections of the eye confirmed a mushroom-shaped tumor (Figure, B) exclusively composed of a trabecular arrangement of epithelioid cells with abundant, finely granular, eosinophilic cytoplasm (Figure, C). Mitotic figures were present at 2 per 10 high-power fields. Intracytoplasmic brown pigment stained positive with Masson-Fontana stain. The cytoplasm stained positive with periodic acid–Schiff stain with resistance to diastase treatment. Vascular mimicy with a closed loop pattern was present. The tumor did not show extrascleral extension. Tumor cells stained positive for Melan-A, HMB-45 (Figure, D), and tyrosinase, confirming melanocytic lineage. They stained negative for keratin A1/A3, CD56, chromogranin, and synaptophysin, excluding epithelial (neuroendocrine) metastasis.

Ultrastructural studies on formalin-fixed, paraffin-embedded tumor tissue that was deparaffinized, postfix-
ated with osmium tetroxide, and re-embedded in Epon (Hexion Specialty Chemicals, Inc, Danbury, Connecticut) showed cytoplasm densely packed with mitochondria and sparse melanosomes (eFigure, http://www.archophthalmol.com). No epithelial features were observed.

Fluorescence in situ hybridization experiments on tumor tissue indicated 2 copies of chromosomes 1, 3, 6, and 8. Multiplex ligation-dependent probe amplification testing with the Salsa P027 uveal melanoma kit (MRCP-Holland, Amsterdam, the Netherlands) confirmed this normal disomic state for a total of 31 different regions tested on multiple chromosomes. Single-nucleotide polymorphism array analysis revealed no copy number alterations or regions of heterozygosity on any of the chromosomes. These investigations have been carried out according to the tenets of the Declaration of Helsinki.

Comment. The many histologic faces of melanoma include primary and metastatic carcinoma, neuroendocrine tumors, sarcoma, leukemia, and germ cell tumors. Intraocular oncocytoma has been considered in the differential diagnosis of mesectodermal leiomyoma of the ciliary body. A granular cell tumor of the iris and ciliary body has been described. The diagnosis of choroidal melanoma and exclusion of other cancers was based on the tumor’s characteristic mushroom shape, positive immunohistochemical staining for HMB-45, Melan-A, and tyrosinase, and a 2-year follow-up without evidence of another primary cancer.

The prognostic significance of oncocytic change in uveal melanoma is not clear. Our case displayed unfavorable histological prognostic parameters in tumor size, epithelioid cell type, and vascular pattern. This was not corroborated with cytonuclear negative parameters as no cytogenetic aberrations were present. Earlier, it was reported that cytogenetic aberrations were detected in 80% (59 of 74 cases) of a series of uveal melanoma. In cutaneous melanoma, no prognostic significance could be determined. Oncocytic change is generally proposed to be a reactive degenerative adaptation; however, the fact that no cytogenetic changes were observed in this tumor poses the possibility of a distinct tumor variant as opposed to a degenerative change.

In conclusion, to our knowledge we give the first description of an oncocytic uveal melanoma that is not to be mistaken histologically for other tumors, including metastatic carcinoma.

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Solitary Epithelioid Histiocytoma (Reticulohistiocytoma) of the Eyelid

Solitary epithelioid histiocytoma of the dermis (and rarely of the mucosae but not the visera) was previously designated as a reticulohistiocytoma. There are reports of 2 solitary corneoscleral lesions and 1 small recurrent lesion in an eyelid. Among the rarest of histiocytic disorders, it typically affects the truncal region of young men (uncommonly the face and digits) and is unassociated with any systemic disease. Among 12 of 44 noneyelid lesions of solitary epithelioid histiocytoma with follow-ups, none recurred despite incomplete excision. Multicentric reticulohistiocytoma, on the other hand, has a predilection for the face and digits of middle-aged women and displays an associated disabling multifocal arthropathy and internal carcinoma in approximately 27% of patients. It has been described in all 4 eyelids. Current opinion holds that both unicentric and multicentric epithelioid histiocytomas are nonneoplastic, arising from the macrophagic rather than the dendritic histiocytic compartment.

Report of a Case. A healthy 39-year-old woman was referred for evaluation of a 3-month-old lesion on her left lower eyelid. The patient had no other skin lesions. The examination of the eyelids revealed a smooth, 10-mm-elevated, flesh-colored, firm lesion (Figure, A) in the lateral one-third of the eyelid. Most of the eyelashes were missing. Visual acuity was 20/20 OU. There was no head and neck lymphadenopathy. Computed tomographic results of the neck, chest, and abdomen/pelvis were