Retinoma Underlying Retinoblastoma Revealed After Tumor Response to 1 Cycle of Chemotherapy

Retinoma is a benign, elevated, gray, translucent retinal mass with calcification and hyperpigmented retinal pigment epithelium. Histopathological features include abundant fleurettes and hyperpigmented retinal pigment epithelium. We report a case in which an underlying retinoma was revealed by collapse and massive vitreous dispersion of the overlying unilateral retinoblastoma after 1 cycle of chemotherapy. Pathological analysis of the enucleated eye confirmed retinoma.

Report of a Case. A 2-year-old boy had leukokoria in the left eye. The left eye contained group D retinoblastoma, an endophytic posterior pole tumor with inferior vitreous seeding (Figure 1A). The right eye appeared unaffected.

Because there was potential for useful vision, treatment with chemotherapy followed by laser therapy was initiated. Three weeks after 1 cycle of systemic carboplatin-etoposide–vincristine sulfate treatment with high-dose cyclosporine (Toronto Protocol), the main tumor showed marked reduction in size, revealing a translucent mass with moderate calcification overlying chorioretinal scarring (Figure 1B). However, the main active retinoblastoma had dispersed widely into the vitreous including anterior to the ora serrata inferiorly, so the eye was enucleated.

Pathological examination showed a solid posterior tumor tapering into the inner nuclear layer of the retina (Figure 2A). The residual retinal lesion had numerous fleurettes, consistent with retinoma (Figure 2B). Fleurette-rich regions were not reactive to Ki-67 and p53 antibodies, and mitotic figures were rare. At the edge of the gap in the tumor from which the necrotic vitreous seeds had emerged, small, round retinoblastoma cells with little cytoplasm and no fleurettes stained positive for Ki-67, indicating proliferation and p53. The vitreous contained necrotic cellular debris. The optic nerve, optic nerve head, subarachnoid space, and choroid were free of tumor.

We previously reported that molecular analysis of this retinoblastoma showed a homozygous splice mutation (IVS12 +1G>A); blood DNA had 2 normal RB1 alleles. Staining for pRb was negative, while the p73NTR tumor suppressor and senescence marker p16INK4a were highly expressed (case 5 in supplementary Table 2 from our previous article).

Comment. We concluded that the active retinoblastoma (Figure 1A) arose from retinoma (Figure 2B) originating in the inner nuclear layer of the retina (Figure 2A). Chemotherapy killed the dividing retinoblastoma cells, which collapsed into the vitreous. The nondividing translucent retinoma was unaffected by chemotherapy but became evident only after chemotherapy (Figure 1B). This retinoma shows all of the described features: clinical, histopathological, and molecular.

Clinically, retinoma is a translucent intraretinal mass with calcification and/or choroidal scarring that remains benign for the lifetime of the individual in 1.5% to 10% of predisposed persons. Several examples of clinically recognized retinoma that progressed to retinoblastoma have been documented. The transition from retinoma to retinoblastoma is usually so rapid that the benign lesions are rarely observed clinically, but we have previously shown that they are relatively common in eyes removed for retinoblastoma. Most eyes enucleated for retinoblastoma do not undergo therapy prior to removal, so the underlying retinoma is usually hidden by the proliferating tumor (Figure 1A).
Tso et al\textsuperscript{13} considered the fleurettes observed in pathological specimens with retinoblastoma to be radiation resistant rather than a sign of tumor regression. Later, Tso\textsuperscript{14} speculated that the proportions of fleurettes intermingled with Flexner-Wintersteiner and Homer Wright rosettes indicated to what degree the tumor was benign. We speculate that the intermingling of the fleurettes with rosettes results from retinoblastoma growing out of and invading the precursor retinoma. The idea that clinical retinomas represent spontaneous regression\textsuperscript{15-17} of retinoblastoma is not supported by pathological analysis given that they show no scarring or necrosis, whether treated or not.\textsuperscript{7}

Molecular analysis shows that retinomas and their adjacent retinoblastomas in enucleated eyes carry identical \textit{RB1} mutations, indicating a common origin followed by clonal progression from benign to malignant tumor.\textsuperscript{7} Genomic instability at low levels in retinoma may be the first consequence of loss of \textit{RB1}, which becomes more advanced in the adjacent retinoblastoma.\textsuperscript{7}

In our case, chemotherapy destroyed most of the malignant retinoblastoma, unveiling an underlying retinoma that was recognized clinically and confirmed by histopathological analysis and molecular studies. Although retinoma is frequently observed in eyes with retinoblastoma on pathological examination, it is rarely documented clinically because it is commonly overgrown by the malignant retinoblastoma, which obscures its detection.

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Progressive Eyelid and Facial Swelling Due to Follicular Lymphoma

Periocular swelling is a cardinal manifestation of Melkersson-Rosenthal syndrome and may occur in many other diseases, including severe acne, vasculitis, sarcoidosis, or impaired venous or lymphatic drainage complicating neoplasia or radiotherapy of the neck.

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