the IS/OS line at an earlier stage by the pathological changes in a typical case of AZOOR. We should note that care should be taken in evaluation of the COST line because its visibility is dependent on the intensity and direction of the laser light that reaches the photoreceptor layer. However, in patients with AZOOR, the COST line and the foveal bulge observed by OCT could help as indicators of early cone photoreceptor dysfunction in cases with minimal ophthalmoscopic and angiographic abnormalities.

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**Adult Ovarian Retinoblastoma Genomic Profile Distinct From Prior Childhood Eye Tumor**

We report the first case of a woman, previously cured of childhood intraocular retinoblastoma, who developed tumor in the ovary with histological and genomic characteristics suggesting an independent retinoblastoma, not a metastasis.
Report of a Case. Bilateral Retinoblastoma. In a 10-month-old girl with esotropia for 6 months, the right eye was classified as group IVb (Reese-Ellsworth classification)/group D (International Intraocular Retinoblastoma Classification) and the left eye was classified as group Vb/group D. There was no extraocular disease on computed tomography or bone marrow and cerebrospinal fluid examinations. She was cured by irradiation of the right eye and enucleation of the left eye. There was no tumor extension into the choroid or optic nerve.

Ovarian Tumor. At age 19 years, she had constipation and abdominal distention, with a large abdominal mass on computed tomography (Figure 1A and B). After an open biopsy, she underwent laparotomy for resection of a left ovarian tumor and fallopian tube, mesentery, and lymph nodes, which were involved by tumor, and drainage of 5 L of ascites containing no tumor cells. She was cured by irradiation of the right eye and enucleation of the left eye. There was no tumor extension into the choroid or optic nerve.

Molecular Analyses. The patient was heterozygous in blood and homozygous in the eye and ovarian tumors for a C to G point mutation causing an immediate nonsense codon in exon 23 of the \( RB1 \) gene (TAC→TAG, Tyr790X).

The DNA from the ovarian and eye tumors was tested by quantitative multiplex polymerase chain reaction for copy number changes in the \( KIF14, \ DEK, \ E2F3, \) and \( MYCN \) oncogenes and the \( CDH11 \) tumor suppressor gene, which constitute post-\( RB1 \) mutations in retinoblastoma.
tumorigenesis.\textsuperscript{2,3} ACVRL1 and RLBP1 were used as 2-copy controls (Figure 2), normal blood was used as a negative control, and a retinoblastoma with known KIF14, DEK, E2F3, and MYCN gains and CDH11 loss was used as a positive control. Distinct profiles were observed: the eye tumor showed gain of KIF14 (mean copy number, 2.77) and MYCN (mean copy number, 4.80) with single-copy CDH11 (mean copy number, 1.04), whereas the ovarian tumor showed no KIF14 gain, amplification of MYCN (mean copy number, 19.50), and 2-copy CDH11 (mean copy number, 2.21) (Figure 2). DEK and E2F3 were not gained in either tumor.

Comment. We consider 2 possible explanations for our observation of retinoblastoma manifesting in the ovary: late metastasis or independent malignant transformation. Late metastasis is unlikely 18 years after cured retinoblastoma. Metastasis usually occurs in the first few years after diagnosis. Ovaries are extremely rare sites, reported in only 1 other case after 2 years.\textsuperscript{4} Malignant transformation of retinal cells within an ovarian teratoma 15 years after cured retinoblastoma has been reported, but without the molecular characterization we show.\textsuperscript{5}

Our patient had no teratoma. She developed an ovarian tumor with histological (Figure 1) and molecular (Figure 2) features of retinoblastoma. Ovarian markers were observed only in uninvolved ovarian tissue, while the proliferative tumor stained for retinoblastoma markers and displayed Homer Wright and Flexner-Wintersteiner rosettes, pathognomonic for retinoblastoma. The eye and ovarian tumors both shared the same first (M1) and second (M2) RB1 mutations, likely from loss of the normal RB1 allele and reduplication of the mutated allele (loss of heterozygosity), which is observed in 52% of retinoblastoma cases.\textsuperscript{6}

The different pattern of post-RB1 mutational events in the ovarian tumor suggests a separate clonal origin from the eye tumor. Common for retinoblastoma, the eye tumor displayed gains of KIF14 and MYCN with loss of 1 copy of CDH11.\textsuperscript{5} The ovarian tumor showed only MYCN

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure2}
\caption{Molecular analysis with quantitative multiplex polymerase chain reaction to determine copy numbers of MYCN, KIF14, DEK, E2F3, and CDH11 in eye and ovarian tumors. The copy number for each gene is assessed by comparing with the internal 2-copy control ACVRL1 (blue asterisk), RLBP1 (the other 2-copy internal control not shown), normal blood (normal 2-copy negative control), and a well-characterized retinoblastoma control with known gains and loss (not shown). Lines indicate equivalent positions on each plot of normal blood and eye and ovarian tumors; arrows, gains and amplification. The copy number gains are shown in red, amplification in red and bold; and copy number loss in italics. Two separate quantitative multiplex polymerase chain reaction peaks were observed for CDH11 in the patient’s ovarian tumor and peripheral blood (not shown), representing 1 normal allele and 1 variant allele, an infrequent polymorphism from a 2–base pair insertion in intron 1. The single peak in the eye tumor represents the polymorphic variant.}
\end{figure}
amplification with a normal CDH11 copy number (Figure 2). MYCN amplification may account for the aggressiveness of the ovarian tumor, as it does for highly fatal neuroblastomas.

The evidence indicates that the ovarian tumor was an independent retinoblastoma rather than a metastasis. While our analysis did not attempt to reveal the cell of origin that underwent malignant transformation, marker analysis revealed that it was not of ovarian origin. Instead, we speculate that it may have been a retinal cell displaced into the ovary by an unknown mechanism. Alternatively, a primitive pluripotent cell persisting in the ovary may have acquired the second RB1 and subsequent other mutations allowing the malignant transformation.

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Acute Exudative Polymorphous Paraneoplastic Vitelliform Maculopathy in a Patient With Carcinoma, Not Melanoma

Paraneoplastic retinopathy occurs when autoantibodies against cancer cross-react with normal retinal antigens and lead to retinal degeneration and subsequent vision loss. Two main categories of paraneoplastic retinopathies have been described, including cancer-associated retinopathy and melanoma-associated retinopathy. Cancer-associated retinopathy is found most often in patients with small cell lung carcinoma and affects both rod and cone function, while melanoma-associated retinopathy occurs with metastatic cutaneous or uveal melanoma and affects primarily rod function. Autoantibodies against recoverin and bipolar cells are typically found in cancer-associated retinopathy and melanoma-associated retinopathy, respectively, although other retinal antigens have also been described. Herein, we illustrate a case of a more recently recognized paraneoplastic retinopathy, termed acute exudative polymorphous paraneoplastic vitelliform maculopathy (AEPPVM).

Report of a Case. A 69-year-old woman noted gradually progressive blurred vision in both eyes over 2 years. Three months previously, she experienced subjective loss of peripheral vision bilaterally. Other symptoms included mild decreased night vision and photopsia. Stage I breast cancer was diagnosed 5 years prior and treated with excisional biopsy and radiotherapy. She had a second cancer, stage IV lung cancer with liver metastasis, that was diagnosed 2 years prior and was treated with chemotherapy.

On examination, best-corrected visual acuity was 20/80 OD and 20/70 OS. The anterior segment, optic disc, and retinal vessels were unremarkable bilaterally. Fundus examination revealed multiple small, round, amelanotic (vitelliform) lesions approximately 500 µm in diameter in the postequatorial region bilaterally that superficially appeared like choroidal metastasis or retinal pigment epithelial detachments (Figure 1). There was no vitritis. Ultrasonography showed multifocal regions of chorioretinal thickening. Optical coherence tomography revealed multiple areas of localized subretinal fluid with debris overlying flat retinal pigment epithelium (Figure 2). Autofluorescence disclosed hyperautofluorescence corresponding to the serous retinal detachments (Figure 1), whereas fluorescein angi-