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A 72-Year-Old Kidney Transplant Recipient With Visual Changes

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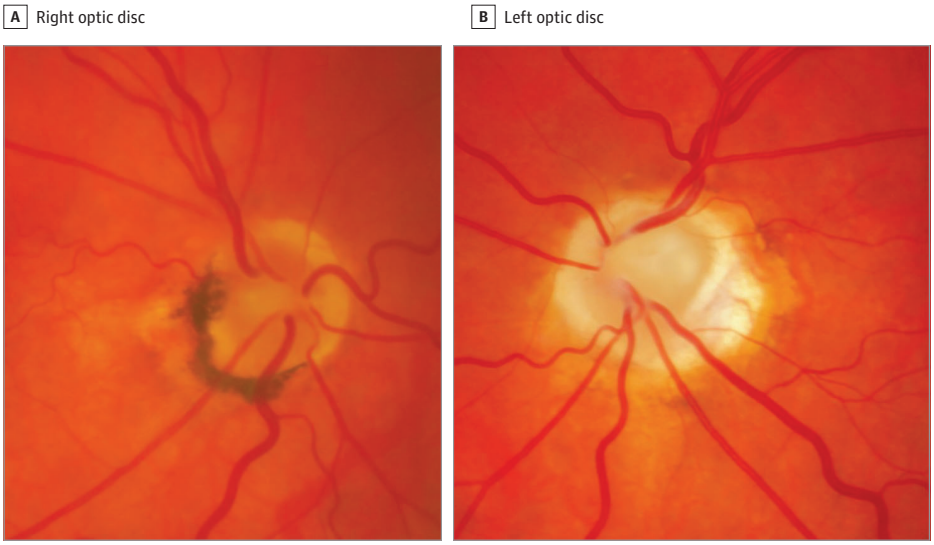

Figure. The right optic disc is dysplastic, with a subtle appearance of the peripheral location of blood vessels emanating from the central disc. There is a central excavation of the left optic disc, with peripherally located blood vessels and the absence of central vessels.

A 72-year-old woman was referred for an eye examination because of visual changes in the left eye. Her medical history was notable for end-stage kidney disease requiring a kidney transplant at age 50 years and a second transplant at age 65 years. She had received her medical care at outside facilities, the records of which were not available. She could not recall being given any precise diagnosis but reported having proteinuria since age 7 years. Her other medical conditions included hyperlipidemia, arterial hypertension, and pulmonary *Mycobacterium avium* complex infection. She was taking tacrolimus, amlodipine, atorvastatin, ethambutol, rifampin, and clarithromycin. Her family history was unremarkable. She had 2 healthy adult children.

One year after the first kidney transplant, she noted an inferior visual field defect in the left eye and was diagnosed with nonarteritic anterior ischemic optic neuropathy. Several years later, she underwent uncomplicated bilateral cataract procedures.

Visual acuity with distance correction was 20/25 OD and 20/30 OS. Color vision was 14/14 plates for each eye. There was a left relative afferent pupillary defect. Confrontation visual field was full for the right eye and demonstrated an inferior defect for the left eye. External and slitlamp examinations were notable only for bilateral pseudophakia. Both optic discs were anomalous in appearance, with central excavation in the left eye greater than the right eye (**Figure**). The remainder of the posterior pole examination, including the retinal vessels, appeared normal in both eyes.

WHAT WOULD YOU DO NEXT?

A. Cranial magnetic resonance imaging

B. Genetic testing

C. Vasculitis serological evaluation

D. Positron emission tomography

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Diagnosis

Papillorenal syndrome due to a *PAX2* gene variant

What to Do Next

B. Genetic testing

Discussion

The appearance of the patient's optic discs (particularly of the left eye) is consistent with a vacant optic disc associated with the autosomal dominant papillorenal syndrome (PAPRS; OMIM 120330). Sequence analysis identified a heterogeneous pathological variant (c.335G>A) in the *PAX2* gene, confirming the clinical diagnosis (choice B). Cranial magnetic resonance imaging is not indicated, as this is not a morning glory disc anomaly (MGDA) that can be associated with a basal encephalocele or moyamoya disease (choice A). There are no historical or examination findings to suggest an underlying vasculitic condition; therefore, serological testing is not indicated (choice C). A vacant optic disc is not associated with an underlying malig-

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nancy, and for that reason, positron emission tomography is not needed (choice D).

PAPRS—also known as *renal-coloboma syndrome*, *coloboma-ureteral-renal syndrome*, *optic nerve coloboma with renal disease*, *coloboma of the optic nerve with renal disease*, and *optic coloboma-vesicoureteral reflux-renal anomalies*—was first reported by Reiger[1] in 1977, with a more extensive clinical description by Weaver et al[2] in 1998. In 1995, Sanyanusin and colleagues[3] discovered a variant of the *PAX2* gene as the cause of PAPRS. Because of the phenotypic heterogeneity of PAPRS, experts have suggested it be termed *PAX2-related disorders*.[4] However, not all patients with PAPRS have a known *PAX2* variant.[5]

Clinically, the syndrome is characterized by kidney and eye (one or both) abnormalities. Approximately 70% of patients will have optic disc abnormalities and approximately 10% will have retinal findings.[4] A forme fruste of the disease may present with only 1 of these conditions. Kidney dysfunction resulting in end-stage kidney disease can occur at any age and can be manifested by a variety of pathology, including kidney hypoplasia or dysplasia, multicystic dysplastic kidney, oligomeganephronia, vesicoureteral reflux, focal segmental glomerulosclerosis, and uric acid nephrolithiasis.[4] Systemic manifestations include hearing loss, growth retardation, microcephaly, developmental delay, gout, joint laxity, and soft skin.[4]

The hallmark eye finding is an anomalous optic disc, which was initially termed a *coloboma*, but *vacant optic disc* is a more appropriate term, given the clinical features and proposed embryogenesis.[6] In some cases, retinal coloboma, scleral staphyloma, optic nerve cyst, foveal hypoplasia, macular changes, and microphthalmia have been reported in conjunction with PAPRS.[7]

Excavated or cavitary optic disc anomalies comprise a group of congenital, morphologically distinct conditions, which include vacant optic disc, MGDA, optic disc coloboma, megallopapilla, optic disc pit, and peripapillary staphyloma. However, some have considered these anomalies to be along a spectrum because certain optic discs do not conform to any one particular entity.[8]

Located on chromosome 10, the *PAX2* gene is within the *PAX* family of genes that includes 8 other members. The *PAX2* gene encodes a transcriptional factor that is important in the development of the eye, kidneys, and central nervous system.[9] Parsa and colleagues[5] have hypothesized that the vacant optic disc arises from deficiency in vascular development during embryogenesis, resulting in the absence of central retinal vessels within the excavated optic disc, with the peripheral vasculature representing cilioretinal vessels. In comparison, an optic disc coloboma demonstrates an absence of tissue in the inferonasal quadrant of the disc and the central retinal vessels emerge superotemporally from the unaffected portion of the disc. Recognizing a vacant optic disc and differentiating it from MGDA and optic disc coloboma is essential, as it can lead to early recognition and treatment of unrecognized kidney disease.[10]

Patient Outcome

The patient was evaluated by a geneticist to discuss the implications of the *PAX2* gene variant and was explained the 50% risk of transmitting the genetic variant to her children.

ARTICLE INFORMATION

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