Polycystic Kidney Disease Associated with Cervical Arteriovenous Shunt and Bilateral Jugular Vein Occlusion

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Abstract

A 59-year-old man with abnormal vascular features (intracranial aneurysm, a cervical arteriovenous shunt, bilateral internal jugular vein occlusions, and left transverse sinus hypoplasia), as well as left optic atrophy was suspected to have familial polycystic kidney disease. The possibility of autosomal dominant polycystic kidney disease complicated by Ehlers-Danlos syndrome type IV due to the coexistence of vasculopathy and polycystic kidneys was considered. However, the negative results of a skin fibroblast culture rendered the diagnosis of Ehlers-Danlos syndrome type IV unlikely. The cause of left optic atrophy in our patient remains unclear although it was suspected to be a secondary consequence of papilledema, which was caused by intracranial hypertension.

Key words: intracranial aneurysm, Ehlers-Danlos syndrome, transverse sinus hypoplasia, optic atrophy

Introduction

Autosomal dominant polycystic kidney disease (ADPKD) is a systemic disorder with potential vascular manifestations, in particular intracranial aneurysms (1). We present a probable case of ADPKD associated with diverse vascular features such as a basilar top aneurysm, an arteriovenous shunt between the right carotid artery and the right jugular vein, the occlusion of the bilateral jugular veins, and left transverse sinus hypoplasia. On the other hand, Ehlers-Danlos syndrome type IV (EDS-4) is a connective tissue disorder characterized by spontaneous rupture, dissection, or aneurysm formation of arteries, although the external signs of EDS-4 are frequently quite subtle (1). As a case study of a patient with EDS-4 accompanied by intracranial aneurysm and multiple renal cysts has been reported (2), we considered whether or not our patient also had ADPKD and/or EDS-4, and thus performed a dermal fibroblast culture. In addition, we considered the etiology of his optic atrophy in light of the conventional four-vessel arteriography results.

Case Report

A 59-year-old man was admitted to the hospital for further evaluation for severe left optic atrophy in August 1997. Nine months before admission, he first noticed a central scotoma. Seventeen months before admission, decreased left visual acuity had been noted at the time of his driver’s license renewal. Six months before admission, severe left optic atrophy was pointed out by an ophthalmologist. Multiple cysts in both kidneys were detected about 10 years prior to the 1997 hospital admission. The patient had been treated for hypertension for 15 years, and was an alcoholic (Japanese sake 360–720 ml a day) and a heavy smoker (one and a half packs of cigarettes a day) for 40 years. His family history revealed that his father died of liver cirrhosis, and his mother suffered from subarachnoid hemorrhage and hypertension. His brother and sister were also diagnosed as having renal cysts.

Physical examination on admission showed the following data: height, 168 cm; weight, 50 kg; temperature, 35.6°C; pulse rate, 66 beats/min; blood pressure, 154/90 mmHg. The patient was not anemic and not icteric. The liver edge was palpable two finger-breaths below the right costal margin; palpation of the spleen and both kidneys was negative. His consciousness was clear. Neurological examination revealed no abnormalities except for the central scotoma and severe optic atrophy in the left eye. Without his glasses, the patient’s left visual acuity was 0.01, and with his glasses, it was 0.1. Although the patient’s intraocular pressure was within normal limits, the medication prescribed by the ophthalmologist included timolol maleate, which is a type of eye drop for suspected glaucoma. The patient’s orally administered medication was mecobalamin (vitamin B12), 1,500 μg/day, and nifedipine (calcium channel blocker), 40 mg/day.
Laboratory tests revealed the following: serum creatinine, 1.4 mg/dl; glomerular filtration rate, 34 ml/min; uric acid, 9.3 mg/dl; vitamin B₁₂, 3.3 μg/dl (normal; 2.0–7.2); vitamin B₁₂, 1,020 pg/ml (normal; 249–938); folic acid, 6.5 ng/ml (normal; 2.4–9.8); protein S, 7.3 μg/ml (normal; 6.7–14.8). The prothrombin time was 10.6 seconds, with a control of 10.4 seconds; the activated partial thromboplastin time, 29.3 seconds, with the control of 30.3 seconds. Fibrinogen was 313 mg/dl. The results of complete blood cell count, erythrocyte sedimentation rate, urinalysis, and tests for thrombin-antithrombin complex and protein C antigen were all normal.

Computed tomography (CT) of the abdomen demonstrated multiple cysts in the liver and bilateral kidneys (Fig. 1). No cysts in the spleen or pancreas were found. Magnetic resonance images (MRI) of the brain revealed a pineal cyst with partial enhancement at the periphery and old cerebral infarctions at the pons and left thalamus; the MRI findings were hyperintense on T₂-weighted images and hypointense on T₁-weighted images without gadolinium-DTPA enhancement. There was no abnormal lesion adjacent to the left optic nerve. The angiogram of the right vertebral artery revealed a saccular aneurysm at the basilar top, 4.6 mm×5.0 mm×4.8 mm in size. In addition, conventional four-vessel arteriography demonstrated an arteriovenous shunt between the right carotid artery and the right jugular vein (Fig. 2), a complete occlusion of both internal jugular veins, and left transverse sinus hypoplasia together with several collateral circulations. The abdominal magnetic resonance angiogram did not disclose any abnormalities, including aneurysm formation of the major arteries. A previous report discussing a patient with EDS-4 who had both renal cysts and an intracranial aneurysm indicated the usefulness of performing fibroblast culture and skin biopsy upon receiving the patient’s consent. Here, the abdominal skin biopsy revealed hyperelastosis of the dermis, which suggested the possibility of a variant of EDS. The dermal fibroblast culture revealed no significant results. The patient declined endovascular coiling treatment for the intracranial aneurysm, which was recommended by the neurosurgeons. We could not obtain the patient’s approval for a genetic analysis, nor could we obtain another family members’ consent to examination of the cerebral artery. The patient was discharged from the hospital in September 1997.

**Discussion**

The patient described here was suspected to have ADPKD based on a positive family history and multiple cysts in the pineal gland, the liver, and both kidneys. Intracranial aneurysm is the hallmark of vascular complications and is detected in approximately one-fourth of patients with ADPKD at postmortem examination (1). Persistent fetal carotid-basilar anastomoses such as persistent hypoglossal artery, and persistent primitive trigeminal artery are relatively frequent findings in patients with ADPKD (1, 3, 4). Other cerebrovascular abnormalities reported thus far have included moyamoya disease, intracranial arteriovenous malformations, intracranial vascular ectasia, and extracranial carotid artery aneurysms (1). According to the literature, neither cervical arteriovenous shunts, nor jugular vein occlusions appear to be vascular complications of ADPKD.

In 85–95% of the cases of ADPKD, the disease is caused by heterogeneous mutations in the PKD1 gene, which encodes polycystin 1, an 11-pass membrane protein. Recently, Kim et al reported that polycystin 1 was required for the structural integrity of blood vessels, and that the vascular abnormality in ADPKD is caused in part by the nature of the PKD1 mutation by using mice homozygous for a targeted mutation in the mouse homologue of PKD1 (5). On the other hand, Imahori et al reported that a 42-year-old
woman with EDS-4 had adult polycystic disease of the kidneys and liver, as well as an intracranial aneurysm (2). Therefore, we also suspected the possibilities of ADPKD and/or EDS-4 in the present patient. Although the complications of a cervical arteriovenous shunt and jugular vein occlusion have not been reported in patients with EDS-4, other vascular manifestations, including cervical arteriovenous fistula, carotid-cavernous sinus fistulas, and cervical artery dissections as well as varicose veins have been reported (2, 6, 7).

To confirm the diagnosis of ADPKD and/or EDS-4 in the present case, we performed a dermal fibroblast culture and an abdominal skin biopsy. Fibroblasts from affected patients with EDS-4 secrete reduced amounts of type III procollagen (8). As collagen studies of cultured skin fibroblasts produced normal results (data not shown), we considered the diagnosis of EDS-4 unlikely. The biopsy specimen did show hyperelastosis of the dermis; as there are nine major types and several subtypes of EDS (1), it is possible that this finding was consistent with a diagnosis of another type of EDS. However, it should be noted that the coexistence of vascular anomalies and polycystic kidneys in types of EDS other than EDS-4 has not been reported.

Regarding optic atrophy, bilateral cases have been found to be 2.5 times as common as unilateral cases among 484 patients (9). Optic neuritis and pseudotumor cerebri were the main cause of unilateral secondary optic atrophy in males; head injury and periocular trauma were the main cause of primary optic atrophy. As there is no relevant past history, the cause of optic atrophy in our patient remains unclear. However, we considered that optic atrophy might have occurred secondarily due to the cascade of events following bilateral internal jugular vein occlusion and left transverse sinus hypoplasia, namely, left-side dominant intracranial hypertension might have been caused by an impairment of cerebral venous drainage according to the angiogram findings, and the MRI features. Another possibility is that optic atrophy was an incidental complication due to optic neuritis or retrobulbar optic neuritis.

Aneurysmal rupture in patients with ADPKD occurs at an earlier age than it does in patients with intracranial aneurysms in the general population; however the mortality rate is similar (10). As our patient presented with various types of vascular involvement, it might be of clinical value for family members of such patients to undergo examination of the cerebral artery.

References