Screening for intracranial aneurysms in patients with isolated polycystic liver disease

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Object. Isolated polycystic liver disease, that is, polycystic liver disease without kidney cysts, is an entity distinct from polycystic kidney disease. It is not known whether patients with isolated polycystic liver disease are at an increased risk for developing intracranial aneurysms, similar to patients with polycystic kidney disease. The authors screened individuals for intracranial aneurysms in a family in which isolated polycystic liver disease occurred to study the relationship between these two disorders.

Methods. Six siblings requested screening for intracranial aneurysms. Their father had died of a middle cerebral artery aneurysm. Isolated polycystic liver disease was found at autopsy. Their paternal aunt had died of a basilar artery aneurysm, but no autopsy had been performed in that case. Screening with magnetic resonance (MR) angiography and subsequent conventional angiography showed a 5-mm posterior communicating artery aneurysm in one sibling in whom abdominal ultrasound examination yielded normal findings and a posterior communicating artery infundibulum in another sibling in whom an ultrasound examination detected isolated polycystic liver disease. Screening did not detect aneurysms or polycystic liver disease in the other siblings. Thus, of the two patients with isolated polycystic liver disease in this family, one had a ruptured aneurysm and the other had an infundibulum.

Conclusions. Findings in this family suggest an association between isolated polycystic liver disease and intracranial aneurysms. However, because of the delay in onset of the appearance of liver cysts in individuals who carry the disease gene, abdominal ultrasonography is not a useful method to exclude those family members at risk for aneurysm development.

Key Words • cerebral aneurysm • polycystic liver disease • screening • subarachnoid hemorrhage
59 years of age following surgery for the attempted repair of a middle cerebral artery aneurysm. At postmortem examination, numerous cysts were noted in the liver but not in the kidneys. The siblings’ paternal aunt (II-3) had died at 57 years of age following the rupture of a basilar artery aneurysm. This individual was not known to have liver or kidney disease, and an autopsy was not performed at that time. There was no history of aneurysms or subarachnoid hemorrhage in the maternal side of the family.

All six siblings underwent MR angiography. An area suspected of being an aneurysm was found in three individuals (III-3, III-4, and III-5). Subsequent catheter angiography displayed normal findings in one sibling (III-5), an infundibulum of the posterior communicating artery in another (III-3), and a 5-mm posterior communicating artery aneurysm in the third (III-4). This last individual underwent uneventful clipping of her aneurysm. The individual with an infundibulum was advised to undergo repeated MR angiography in 1 year, and the remaining siblings were advised to undergo repeated MR angiography in 5 years.

Abdominal ultrasonography was performed in five siblings (III-2 through III-6). One (III-3) was found to have polycystic liver disease with a total of eight cysts, ranging in size from 0.5 to 4 cm; this sibling also had a posterior communicating artery infundibulum. Another sibling (III-5) had a single 1.5-cm liver cyst, which was an indeterminate finding; angiography was normal in this patient. Normal ultrasound results were found in the remaining three individuals, including the patient with an intracranial aneurysm; none had any cysts in the kidney or other organs.

**Discussion**

Polycystic liver disease generally is defined as the presence of more than three cysts in the liver parenchyma.\(^{11}\) Renal cysts are found in 20 to 60% of patients with polycystic liver disease and in the remainder of patients the polycystic liver disease is considered to be an isolated disorder.\(^{1,2,4,6,11}\) Isolated polycystic liver disease may occur sporadically or as a familial form with autosomal dominant transmission. In contrast to ADPKD, isolated polycystic liver disease often remains asymptomatic throughout the patient’s life.\(^{1,4,6,11}\)

It is unclear whether intracranial aneurysms are associated with isolated polycystic liver disease. In the autopsy series reported by Karhunen and Tenhu,\(^{4}\) intracranial aneurysms were found in six of 12 cases of ADPKD with or without polycystic liver disease but in none of 10 cases of isolated polycystic liver disease. Pirson and colleagues\(^{6}\) screened two siblings with isolated polycystic liver disease for intracranial aneurysms by using MR angiography and found no aneurysms. However, Torres and colleagues (Torres VE, personal communication, 1998) detected intracranial aneurysms in two of 30 patients with isolated polycystic liver disease who were screened with MR angiography. Of the two patients with isolated polycystic liver disease in the family reported here, one had a ruptured intracranial aneurysm and the other had an infundibulum, possibly a precursor to aneurysm development. However, in another family member who was 49 years old and in whom an intracranial aneurysm was detected by screening, there was no evidence of polycystic liver disease on ultrasonography. Clearly, in this family abdominal ultrasonography was not a useful method to exclude those family members at risk for intracranial aneurysm development. Perhaps, the association of intracranial aneurysms and isolated polycystic liver disease in this family was coincidental. On the other hand, the progression of polycystic liver disease in this family may be very protracted and middle-aged persons may not yet have developed liver cysts, even though they carry the disease gene.
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and have developed intracranial aneurysms. The frequency of liver cysts in patients with ADPKD has been shown to increase with age from approximately 20% in the third to 75% in the seventh decade of life.\textsuperscript{2,11} On average, liver cysts appear 20 years later than renal cysts in ADPKD.\textsuperscript{2} In some families whose members have ADPKD, even kidney cysts are not detectable with ultrasonography until late in life. For example, Parfrey and colleagues\textsuperscript{5} reported that in ADPKD linked to \textit{PKD2} only approximately 20% of patients carrying the disease gene have detectable kidney cysts at age 30 years. There are only a few families in which isolated polycystic liver disease has been described and the natural history of the disease is poorly understood. For example, the growth rate of the liver cysts is not known, although they have been shown to become more numerous and larger with age. The identification of the autosomal dominant polycystic liver disease gene will provide significant advances in our understanding of the disease and, perhaps, will allow the development of a simple test to select those family members at risk for aneurysm development.

In families with intracranial aneurysms, abdominal ultrasonography is routinely performed to rule out polycystic kidney disease. We suggest that during this ultrasound examination, attention should also be directed to the liver to search for liver cysts.

References


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