Progression of a posterior communicating artery infundibulum into an aneurysm in a patient with Alagille syndrome

Case report

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The authors present a case in which a posterior communicating artery (PCoA) infundibulum progressed into an aneurysm in a patient with Alagille syndrome (arteriohepatic dysplasia). The 3-mm PCoA infundibulum had been noted on angiography studies obtained 5 years earlier, prior to clip occlusion of a basilar tip aneurysm. Recently, the patient presented to the emergency department with the sudden onset of headache and decreased mental status. A computerized tomography scan of the head with three-dimensional angiography revealed no gross subarachnoid hemorrhage, but did demonstrate a 5-mm PCoA aneurysm. Lumbar puncture demonstrated xanthochromia and a large quantity of red blood cells. The patient underwent open surgery for aneurysm clip occlusion and obtained a good recovery. This case illustrates the small but growing number of examples of infundibulum progression. It also indicates the need for a close follow up in patients with congenital abnormalities that may pose an increased risk for what has traditionally been considered a benign lesion.

KEY WORDS • infundibulum • Alagille syndrome • intracranial aneurysm • aortic coarctation • ruptured aneurysm

Case Report

History. This 23-year-old man presented in June 2003 to our emergency department with the sudden onset of headache and decreased mental status. The patient was known to suffer from Alagille syndrome, also known as arteriohepatic dysplasia. In 1998 he underwent an emergency left frontotemporal craniotomy for a ruptured basilar tip aneurysm and made an excellent recovery. At that time, it was noted on preoperative angiography as well as intraoperatively that the patient had a 3-mm infundibulum of the left PCoA (Fig. 1). In 1999 the patient underwent a thoracic aorta bypass graft with renal revascularization for an aortic coarctation. Subsequently, he underwent follow-up magnetic resonance angiography, which revealed occlusion of the basilar tip aneurysm; however, the left PCoA infundibulum was not adequately visible.

Examination. The results of a neurological examination revealed mild lethargy, nuchal rigidity, and photophobia. Other aspects of the examination were normal. A laboratory investigation revealed elevated levels for prothrombin (16.1 seconds) and partial thromboplastin (40.6 seconds) and elevated levels of alkaline phosphatase (314 U/L), alanine aminotransferase (113 U/L), aspartate aminotransferase (105 U/L), total bilirubin (8.6 mg/dL), and creatinine (1.2 mg/dL); the level of albumin (2.7 g/dL) was low.

An unenhanced CT scan of the head did not reveal any gross evidence of SAH. A lumbar puncture, however, yielded more than 25,000 red blood cells in all tubes plus the findings of xanthochromia. Gram stains and cultures of cerebrospinal fluid were nondiagnostic. A three-dimensional CT angiogram demonstrated a 5-mm PCoA aneurysm at the site of the previously noted infundibulum (Fig. 2A). This was confirmed on conventional angiography (Fig. 2B). A decision was made to delay surgery to optimize the patient’s medical condition.

Operation. The patient underwent a left pterional craniotomy for clip occlusion. The PCoA aneurysm was noted to have a wide neck and an approximately 5-mm dome, which adhered to the tentorium. Interestingly, the aneurysm displayed no overt evidence of previous rupture on inspection. A bayoneted clip was used to occlude the aneurysm completely. A Doppler probe confirmed good proximal and distal blood flow.

Postoperative Course. The patient experienced a cerebral spinal fluid leak that required washout and reclosure, but otherwise had a good postoperative recovery. At the 3-month follow-up examination, he exhibited no new neurological symptoms.

Discussion

We present the case of a young man with Alagille syndrome and a history of aortic coarctation and aneurysm rupture in whom a PCoA aneurysm developed at the site of a
Infundibulum and Alagille syndrome

previously documented infundibulum. Based on our review of previous case summaries by Marshmann, et al.,10 and an additional report by Martins and colleagues,11 this represents the 13th known case presented in the literature. The developments in the present case emphasize the need to follow up patients with risk factors for aneurysm formation and rupture who have infundibula.

Alagille syndrome,13 also known as arteriohepatic dysplasia or syndromic paucity of the interlobular bile ducts, is an autosomal-dominant inherited disease with variable expression, which occurs in approximately one person per 100,000 live births.16 The syndrome is defined as a paucity of intrahepatic bile ducts and is associated with characteristic facies such as a broad forehead, hypertelorism, a pointed chin, or a straight nose with a bulbous tip. Various cardiovascular abnormalities are seen; the most common is peripheral pulmonic stenosis, but aortic, renovascular, hepatic, carotid, celiac, and subclavian arterial lesions have also been found.2 Other findings include chronic cholestasis, butterfly vertebrae, renal abnormalities, ophthalmological abnormalities, and growth retardation.3

Although the pathogenesis of Alagille syndrome has not been fully elucidated, it has been associated with defects in a single gene, Jagged1, which encodes a ligand to the Notch intercellular signaling pathway, which is important in cardiovascular development.7,8 Jagged–Notch signaling has a prevalent role in cardiovascular development.22 Zimrin, et al.,22 posit its involvement in the regulation of fibroblast growth factor–induced migration of endothelial cells necessary for angiogenesis. Loones, et al.,3 demonstrated that the Jagged1 gene is expressed in the developing heart and multiple vascular structures, including the descending aorta and the pulmonary vascular tree.

Interestingly, the intracranial hemorrhage rate in patients with Alagille syndrome is disproportionately high, and usually there is no obvious origin of the bleeding. Emerick, et al.,1 recently studied a series of 92 patients with Alagille syndrome. They reported an intracranial hemorrhage rate of 14% (13 patients) with three SAHs, all of which lacked established origins. In only six patients was trauma associated with the hemorrhage. There are only a few reported cases of cerebrovascular disease in patients with Alagille syndrome, including two reports of moyamoya disease, autopsy evidence of an intradural arteriovenous malformation, and a case of a cavernous carotid aneurysm.6,12,17,21

Additionally, mutations in the Notch receptor (a ligand of the Jagged receptor) have been associated with adult-onset cerebral autosomal-dominant arteriopathy with subcortical infarcts and leukoencephalopathy.7 Patients with this disorder have small, deep cerebral infarcts with nonatherosclerotic, nonamyloid angiopathy involving the media of small cerebral arteries; this implicates the Jagged–Notch signaling pathway in pathological cerebrovascular conditions.

Aortic coarctation, first described by Eppinger4 in 1871, is an established risk factor for cerebral aneurysm formation. It is found in patients with unruptured intracranial aneurysms at a rate of 0.19 to 1.9% and in those with ruptured aneurysms at a possibly higher rate of 4.8%.5,14,18,20 To date, only four cases of aortic coarctation have been reported in association with Alagille syndrome.1,15,19

Conclusions

This case highlights the need to follow up in patients with infundibula who have risk factors for aneurysm formation and rupture. Our report adds to the growing body of literature indicating that infundibula may not represent benign intracranial variants.

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References


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