The Bench-to-Bedside Transition

Bilateral cysts in the choroid plexus in a patient with autosomal dominant polycystic kidney disease

Niek F. Casteleijn¹, Edwin M. Spithoven¹, Maarten B. Rookmaaker², Mervyn D.I. Vergouwen³ and Ron T. Gansevoort¹

¹Department of Nephrology, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands,
²Department of Nephrology and Hypertension, University Medical Center Utrecht, University of Utrecht, Utrecht, the Netherlands
and ³Department of Neurology, University Medical Center Utrecht, University of Utrecht, Utrecht, the Netherlands

Correspondence and offprint requests to: Ron T. Gansevoort; E-mail: r.t.gansevoort@umcg.nl

ABSTRACT

Autosomal dominant polycystic kidney disease (ADPKD) is a genetic systemic disorder, which is associated with cyst formation in several organs, renal function decline and a higher prevalence of intracranial aneurysms. We report a 52-year-old, otherwise healthy, man with ADPKD who had asymptomatic, bilateral, multiple cysts in the choroid plexus, which is an extremely rare abnormality. Recent evidence suggests that the polycystin proteins, which are dysfunctional in ADPKD, are found in ciliated choroid plexus cells that are involved with regulation of cerebrospinal fluid homeostasis. We hypothesize therefore that choroid plexus cysts may be part of the ADPKD phenotype, which has not been described before.

Keywords: autosomal dominant polycystic kidney disease, brain cysts, choroid plexus, PKD1, PKD2

INTRODUCTION

Autosomal dominant polycystic kidney disease (ADPKD) is an inherited systemic disease with a predominant feature of cyst formation in both kidneys, leading to renal function decline, haematuria and pain. The prevalence of ADPKD is estimated to be 1 in 1000 people. Two different genes, located at chromosomes 4 (PKD2) [1] and 16 (PKD1) [2], have been linked to ADPKD that account for 78 and 13% of the cases, respectively [3]. The remaining 9% of ADPKD patients have the typical phenotype, but lack a yet known mutation in the PKD1 or PKD2 gene. These two genes code for the proteins polycystin-1 and polycystin-2, respectively, which, when malfunctioning, lead to ciliary dysfunction and subsequent aberrant growth and organization of ciliated renal tubular cells. ADPKD is therefore part of the spectrum of the so-called ciliopathies.

In affected patients cyst formation can also be found in other organs, such as the liver, spleen and pancreas [4]. In addition, the association of ADPKD and intracranial aneurysms is well known [5]. It is generally advised to screen ADPKD patients who have an affected family member with a haemorrhagic cerebral vascular incident before the age of 65 years. When a patient is screened for cerebral intracranial aneurysm by magnetic resonance (MR) imaging [6], other brain abnormalities can be found by coincidence. An association with arachnoid and pineal cysts has been described in ADPKD patients [7], but the presence of cysts in the choroid plexus is rare. To our knowledge, there have only been three reported cases with unilateral simple cysts [7].

Here, we report a case of a 52-year-old male ADPKD patient, in whom during screening for intracranial aneurysms multiple bilateral cysts of the choroid plexus were found.

CASE REPORT

A 52-year-old man with ADPKD was referred to our tertiary care hospital for participation in a randomized clinical trial to halt renal function decline. In 1992 the diagnosis of ADPKD was made by ultrasound in combination with a positive family history [8]. Recent genetic analysis showed a pathogenic truncating mutation in the PKD1 gene. He had no history of
macroscopic haematuria, kidney pain, urinary tract infections, cyst infections, cyst bleedings or neurological abnormalities. He inherited ADPKD from his maternal side. His mother died at the age of 71 from complications following ischaemic stroke. Medication comprised irbesartan 150 mg OD, atorvastatin 10 mg OD and alfacalcidol 0.25 mcg OD. Physical examination revealed a man weighing 98 kg and measuring 192 cm. Results from routine neurologic examination were normal. His estimated glomerular filtration rate was 30 mL/min*1.73 m². Urine analysis showed microscopic haematuria without proteinuria.

An MR imaging scan performed in the context of the clinical trial showed presence of multiple bilateral renal and hepatic cysts, leading to enlargement of kidneys and liver (Figure 1). Furthermore, multiple cysts were found in the spleen. Because of his positive family history for cerebral aneurysms, the patient was scheduled for MR angiography of the circle of Willis. This MR angiography showed no intracranial artery aneurysms. However, both ventricles were considerably enlarged (Figure 2). In evaluation of this finding, we considered xanthogranuloma, papilloma and cysts located in the choroid plexus. To differentiate between these causes, an MR imaging scan was performed. This scan showed multiple cystic lesions in both plexuses. The diagnosis of choroid plexus cysts was supported by the fluid-attenuated inversion recovery (FLAIR) images, which shows increased signal intensity of both choroid plexuses compared with cerebrospinal fluid (Figure 3). No mass lesions, enhancement of the choroid plexuses or flow voids reflecting tumour vascularity were found, excluding the diagnoses xanthogranuloma and papilloma.

A possible hereditary component was investigated. Unfortunately, the computed tomography images from his mother, which were made after her cerebral vascular accident 20 years ago, were not available anymore. His son, who was also diagnosed with ADPKD, refused screening for cerebral aneurysms and choroid plexus cysts.

**DISCUSSION**

The association between cysts of the plexus choroid and ADPKD is rare and has been reported in only one manuscript [7]. Schievink et al. investigated the prevalence of intracranial abnormalities in ADPKD patients. Three patients had unilateral simple cysts of the plexus choroid. In our case there were...
multiple cysts of the plexus choroid bilaterally that almost totally filled the ventricles, which makes it an exceptional finding.

Choroid plexus cysts are found incidentally on imaging studies with a prevalence of 0.1–1% in the general population [9, 10]. These cysts are usually benign and do not cause complaints. Such asymptomatic cysts are in general <1 cm in diameter [9], and do not need follow-up. Spontaneous regression has been reported [7]. Larger cysts may cause cerebral spinal fluid flow obstruction leading to ventricular dilation, and can be complicated by intracystic bleeding, which both can lead to complaints such as headache, nausea and visual disturbances [11]. In these cases, cyst elimination by neurosurgical procedures or removal of the obstruction may be necessary. Multiple, bilateral, large choroid plexus cysts, as in our case, are extremely rare and the exact prevalence is unknown.

A possible association of multiple choroid plexus cysts and chromosomal abnormalities has been postulated. Especially fetuses with trisomy 18 and patients with Klinefelter syndrome have a high prevalence of these brain abnormalities [10, 12, 13]. Our patient did not have a phenotype that is compatible with these conditions. Furthermore, multiple choroid plexus cysts can be found in fetuses with the Meckel–Gruber syndrome, a hereditary condition caused by mutations in the MKSI gene that lead to cilia dysfunction [14]. Interestingly, this rare autosomal recessive disease, which is lethal at young age, belongs to the same spectrum of ciliopathies as ADPKD. A possible association between ADPKD and choroid plexus abnormalities is furthermore supported by recent observations in a mouse model that indicate that polycystin-1, the product of the PKD1 gene that is dysfunctional in the majority of ADPKD patients, is localized not only in kidney tissue, but also in ciliated choroid plexus cells [15]. These ciliated cells are supposed to be important for the rate of secretion, movement and reabsorption of cerebrospinal fluid [15]. It may well be, therefore, that mutations in the genes coding for polycystins, especially polycystin-1, can lead to cyst formation in the choroid plexus. Given these recent observations we hypothesize that the association that we found in our case between ADPKD and multiple, bilateral choroid plexus cysts is not coincidental, but that these choroid plexus cysts may be part of the ADPKD phenotype, especially in ADPKD patients with a PKD1 mutation.

In conclusion, by screening for intracranial aneurysms in patients with ADPKD, cerebral cysts can be found, such as arachnoidal and pineal cysts. We observed in an otherwise healthy patient, with ADPKD due to a PKD1 mutation, multiple bilateral choroid plexus cysts, which are an extremely rare abnormality in the general population. Recent evidence suggests that the polycystin-1, that is dysfunctional in ADPKD patients with a PKD1 mutation, is present in ciliated choroid plexus cells that are involved with regulation of cerebrospinal fluid homeostasis. We hypothesize therefore that choroid plexus cysts may be part of the ADPKD phenotype, which has not been described before.

CONFLICT OF INTEREST STATEMENT

On behalf of all authors, the corresponding author states that there is no conflict of interest.

REFERENCES


Received for publication: 11.4.2014; Accepted in revised form: 3.7.2014