The Bench to Bedside Transition – Exceptional Case

Sudden death due to subarachnoid haemorrhage in an infant with autosomal dominant polycystic kidney disease

Kah Mean Thong1,2 and Albert C.M. Ong1,2

1Kidney Genetics Group, Academic Nephrology Unit, University of Sheffield Medical School, Sheffield, UK and 2Sheffield Kidney Institute, Sheffield Teaching Hospitals Foundation Trust, Sheffield, UK

Correspondence and offprint requests to: Albert C.M. Ong; E-mail: a.ong@sheffield.ac.uk

ABSTRACT

Intracranial aneurysm rupture is the most serious and potentially lethal extra-renal manifestation of autosomal dominant polycystic kidney disease (ADPKD). Almost all cases of ruptured intracranial aneurysm occur in adult patients with a median age of rupture of 40 years. We report the occurrence of sudden death in a newborn infant born to a mother with typical ADPKD in the first week of life. Post-mortem examination revealed the cause of death to be subarachnoid haemorrhage with focal glomerular and tubular cysts detected in the kidney. This is the earliest reported case of intracranial aneurysm rupture in ADPKD and should raise awareness of this rare but lethal complication in younger patients.

Keywords: autosomal dominant polycystic kidney disease, intracranial aneurysm rupture, subarachnoid haemorrhage

INTRODUCTION

Autosomal dominant polycystic kidney disease (ADPKD) is the most commonly inherited renal disease, occurring in 1:400 to 1:1000 live births. It is a multi-systemic disease with cystic and non-cystic manifestations. The most serious and potentially lethal extra-renal manifestation of ADPKD is intracranial aneurysm rupture. Almost all cases of ruptured intracranial aneurysm have been reported in adult patients. However, there have been three previous reports in young children [1–3]. In this paper, we describe a case of newborn infant with ADPKD who died of a ruptured intracranial aneurysm in the first week of life, the youngest case to be reported to date.

CASE REPORT

A 40-year-old mother with typical adult-onset ADPKD gave birth to a baby boy at 37-week gestation by an induced vaginal delivery due to hypertension. The pregnancy had been uneventful and she had only taken labetalol for hypertension during this period. The birth was not traumatic, and he was given intramuscular vitamin K at birth. There were no signs of fetal distress, and the baby had been feeding well (formula-fed) after birth. However 6 days later, he became acutely unwell, developed vomiting, lethargy, became comatose and died. Blood investigations were normal without thrombocytopenia or coagulopathy. Angiography was not performed prior to death, but a CT scan confirmed the presence of subarachnoid haemorrhage. At post-mortem, a massive subarachnoid haemorrhage running through the foramen magnum and spinal cord was revealed with compression of the left cerebellum and extension into the subdural space. There were no features to suggest an organizing haematoma, the ventricular system was not dilated and an intraventricular haemorrhage was not seen. The intracranial venous sinuses, falx and tentorium were normal. Although no discreet bleeding point or another aneurysm was identified, it was concluded that the bleed was most likely to have occurred from a ruptured intracranial aneurysm. There were no macroscopic changes visible in the kidneys or renal tract, but histological examination revealed cystic dilatation of Bowman’s capsule in several glomeruli (Figure 1). The family had been previously shown to have genetic linkage to PKD1. Her maternal great-grandmother had died at 58 years of age from a subarachnoid haemorrhage but no other relatives were known to be affected.
The cause of death in this infant was from a subarachnoid haemorrhage, most likely due to a ruptured intracranial aneurysm. However, at autopsy, no bleeding point was revealed and no other aneurysms detected. In ~15% of cases of subarachnoid haemorrhage (SAH), no intracranial aneurysm or arterial malformation can be identified on angiography [4]. Haemorrhagic disease of the newborn can present as subarachnoid haemorrhage [5]. This was unlikely since he was given vitamin K at birth and was formula-fed. There was also no evidence of a clotting disease as no generalized bruising or internal organ bleeding was detected. His mother was not on other medication such as anticonvulsants, anticoagulants or antiplatelet drugs that could increase the risk of bleeding. Although uncomplicated vaginal delivery can be associated with asymptomatic intracranial bleeding in 26% of births, this is usually limited to subdural haematoma (and occasional SAH), which resolve spontaneously in the first 5 weeks of life [6].

Intracranial aneurysm rupture is a rare but devastating extra-renal manifestation of ADPKD, which may be fatal. Aneurysms have been reported in patients with both PKD1 and PKD2 mutations [7], and reflect a primary vascular defect due to abnormal polycystin expression in disease [8, 9]. This also explains the increased incidence of other vascular abnormalities in some ADPKD adult patients such as aneurysms in other arterial beds, intracranial arterial dolichoectasia, arteriovenous malformations and spontaneous artery dissection.

Patients with ADPKD are at four to seven times increased risk of developing intracranial aneurysms compared with the general population [10]. From the literature, the prevalence is higher in those with a positive family history of aneurysms or SAH (22%) than in those without a family history (8–10%) [10, 11]. Despite the increased prevalence, aneurysms in ADPKD patients do not appear to have an increased incidence of rupture compared with other causes [12].

Aneurysm rupture accounts for 4–7% of deaths in the ADPKD population with a mean age of death of 37 years [13]. The most important factors determining the risk of rupture of an asymptomatic aneurysm are its size and position and a history of previous subarachnoid haemorrhage [14]. In one survey, the risk of rupture was 0.05% per year for aneurysms <10 mm and 1% per year for those >10 mm. Posterior circulation aneurysms are more likely to rupture than those found in other locations. For
those with a history of SAH, the risk is much higher and does not appear to be dependent on aneurysm size [15].

In ADPKD, intracranial aneurysm (ICA) rupture may occur independently of impaired renal function or the presence of hypertension. In one retrospective study cohort, 10% of patients were aged 20 years or less [16]. In the 12 months prior to rupture, blood pressure was normal in 29% of patients with half having normal renal function. Familial clustering of aneurysm rupture in ADPKD is well recognized [17]. Ring et al. have proposed that the individual risk of aneurysm rupture can be estimated based on family history using a Bayesian random effects model [18]. Current guidelines recommend that patients with a previous history of rupture should undergo lifelong surveillance. For asymptomatic patients, only those with a strong family history of rupture (one or more first degree relatives) should be considered for screening [19]. In addition, some authors advocate screening prior to major elective surgery (including renal transplantation) and before undertaking high-risk occupations [20].

To our knowledge, only three cases of children with ADPKD and aneurysm rupture have been reported in the literature (Table 1). The youngest affected child was 3 years old and suffered two intracranial bleeds at the ages of 3 and 5 years [2]. He was diagnosed with PKD in the neonatal period with associated hypertension and impaired renal function. There was a positive family history of ADPKD (father) with similar very-early-onset disease in his brother who was born prematurely at 28 weeks and died shortly after birth. However, unusually for ADPKD, the child was described to have abnormal facies and was found to have a complex arteriovenous malformation. Two other children have been reported: a girl with a typical ruptured aneurysm at the age of 4 years [1] and the other, a boy who suffered a SAH at the age of 6 years [3]. Of interest, a male infant with very-early-onset PKD who died of unexpected causes at 13 weeks of age was found to have an unruptured 1-mm basilar artery aneurysm at post-mortem examination [21].

Our patient is the youngest to have developed and died of this vascular complication to date. With this report, we hope to raise awareness that this complication can occur in infants with ADPKD. However, since this remains extremely rare, routine screening of children or infants with ADPKD would not be cost-effective or justified.

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**CONFLICT OF INTEREST**

The results presented in this paper have not been published previously in whole or part. The authors declared no competing interests.

**REFERENCES**


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