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BRIEF REPORT

# Bilateral progressive cystic nephroma in a 9-month-old male infant requiring renal replacement therapy

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**Abstract** We report the case of a 3-year-old boy who presented at 9 months of age with abdominal distension and was found to have a triad of bilateral cystic nephroma, pleuropulmonary blastoma (PPB) and juvenile intestinal polyps. There have been three previous reported cases of patients with the same associated diagnoses. Our patient is the first reported patient with PPB who received renal replacement therapy and progressed to successful renal transplantation. The potential increased risk of progression of malignancy of PPB (type 1) with immunosuppression following transplantation remains unknown.

**Keywords** Bilateral cystic nephroma · Juvenile intestinal polyp · Lung cysts · Pleuropulmonary blastoma · Renal cysts · Renal transplant

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## Introduction

Cystic nephroma (CN) is a rare (possibly congenital) cystic kidney tumour of uncertain aetiology [1]. It was first described in 1892 by Edmunds who called the lesion cystadenoma of the kidney. CN frequently presents in early infancy and childhood [2], and the most common presenting symptoms are painless abdominal mass, abdominal or flank pain and haematuria [1, 3].Pleuropulmonary blastoma (PPB) is a rare mesenchymal tumour involving the lungs and pleura which primarily affects children under 5 years of age [4]. It is often associated with synchronous tumours in the lungs or other organs, notably kidneys (CN) and small bowel (juvenile polyps) [5–7]. The association of CN and PPB has been reported [5], but the triad of PPB, CN and small bowel juvenile polyps is a unique subset that has been previously reported in only two cases [5].

## Case report

A 9-month-old Caucasian boy presented with a history of vomiting, fever, poor appetite and a left-sided abdominal mass. The antenatal history and ultrasound scans were unremarkable. He was born by normal vaginal delivery with a birth weight of 3.8 kg (75th centile). His parents

have no medical problems. He has four older brothers, all of whom are healthy. At presentation he weighed 8.6 kg (25th centile), was clinically (5%) dehydrated and had pallor, mild respiratory distress, tachycardia, a blood pressure of 95/55 mmHg and a left upper quadrant mass. The remainder of the physical examination was unremarkable. Initial investigations revealed profound anaemia (haemoglobin of 5 gm/dl). The results from renal and liver function tests were normal except for a low serum albumin level of 27 gm/l. Urinary catecholamines and lactate dehydrogenase levels were normal. Echocardiography, magnetic resonance imaging of the head and ophthalmic reviews revealed no abnormalities. An abdominal ultrasound scan showed bilateral multilocular cystic kidneys with multiple anechoic spaces traversed by thin septations (Fig. 1), and a computerized tomography (CT) scan of the chest performed showed bilateral multiple lung parenchymal cysts of different sizes (Fig. 2). An enhancing solid mass within the second part of duodenum (intra luminal polyp) was demonstrated by an oral contrast meal. The patient underwent a laparotomy, with an open biopsy of the left renal mass (multiple cysts, acute and chronic inflammatory changes). The duodenal polyp was excised through a duodenostomy (hamartomatous polyp). No malignant or dysplastic cells were seen in either the renal or duodenal biopsies. Histological examination of the diagnostic open lung biopsy confirmed Type 1 PPB. Over the following 2 months the left renal mass increased rapidly in size. This resulted in marked respiratory distress and failure to tolerate nasogastric tube feeding. A dimercaptosuccinic acid scan (DMSA) showed less than 10% function in the left kidney, leading to a left nephrectomy. The histological results were consistent with a diagnosis of cystic nephroma with severe xanthogranulomatous inflammation; there was no evidence of tuberous sclerosis (TS), malignancy or dysplasia. There was marked improvement in respiratory symptoms following the removal of the left kidney; however, the patient developed narrowing at the second part of the duodenum following removal of the polyps. A feeding jejunostomy was performed to aid nutrition. Over the next few months, there was rapid increase in the size of the right kidney. A right nephrectomy was performed at age 18 months because of deteriorating renal function, recurrent urinary tract infections, increasing respiratory distress and symptoms of gastric outlet obstruction. Haemodialysis was established via a tunnelled right internal jugular central venous line.

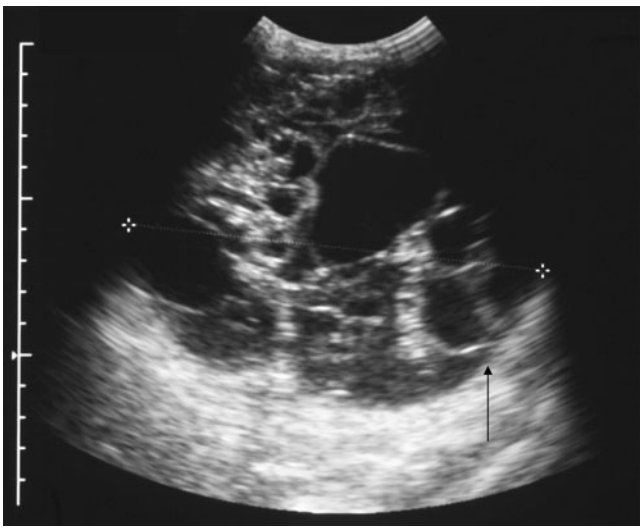

**Fig. 1** A sagittal ultrasound image of the left kidney shows a renal mass with multiple anechoic areas and posterior acoustic enhancement. The "beak sign" (*arrow*) suggests the renal origin of the mass

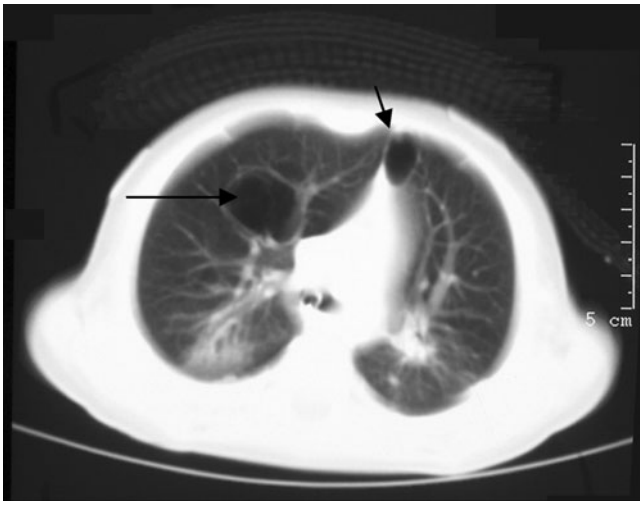


**Fig. 2** Computerized tomography chest scan shows multiple lung parenchymal cysts (*arrows*) of various sizes bilaterally

After extensive consultation among nephrologists, the transplant surgeon and anaesthetists, it was decided to offer him renal transplantation. Two major concerns remained: (1) low weight (11.8 kg) at the time of transplant (10.8 kg at the time of listing); (2) risk of malignant progression of PPB following transplantation and consequent immunosuppression. The risk of malignant progression of PPB was not quantifiable as no previous precedence for transplantation existed for this condition. The patient received a deceased donor renal transplant at 3 years of age. The HLA mismatch was 000. Implantation was extraperitoneal to the inferior vena cava and aorta. The cold ischemic time was 11 h and 35 min, while the warm ischemic time was 42 min. Six months post-transplant this child has good graft function (creatinine 52 μmol/l) and is receiving standard immunosuppression treatment consisting of tacrolimus, azathioprine and steroids. We plan to carry out continued surveillance of his lung cysts in view of the potential risk of malignant progression with immunosuppression.

## Discussion

Cystic nephroma is a rare benign cystic kidney tumour of uncertain aetiology and is a distinct entity from developmental cystic kidney diseases [1–3]. Paediatric CN is most frequent in young boys under the age of 4 years and girls older than 4 years [3, 8]. It usually affects one kidney; bilateral CN (BCN) is extremely rare and has been reported in only a few cases in both children and adults [9]. To the best of our knowledge, only two separate cases have been reported in children with BCN [10, 11]. A report from the PPB Registry identified only one out of 15 cases to be bilateral [6]. Diagnostic criteria for CN were initially proposed by Powell et al. [12] and subsequently modified by Joshi and Beckwith [13]. These criteria include multilocular, non-communicating cysts with normal residual renal tissue between the cysts. The locules are lined with epithelium with incompletely developed nephrons in the interlocular septae, and they have no communication with the renal collecting system or the renal pelvis [13]. There are two theories on the origin of CN. A developmental origin explains CN as a form of renal dysplasia related to polycystic kidney disease or a result of maldevelopment of the ureteric bud [14]. The second theory of neoplastic origin explains CN as a beginning of a continuous spectrum of cystic renal tumours which also includes cystic partially differentiated nephroblastoma through to cystic variants of Wilms tumour at the malignant end [14].

Pleuropulmonary blastoma was first described in 1988 [4, 15]. It is an intrathoracic malignant neoplasm that typically occurs in children less than 5 years of age. These tumours arise from the lungs and/or the pleura and develop from blastemal elements [4, 15, 16]. Histologically PPB exhibits a primitive, variably mixed blastematous and sarcomatous appearance [17]. There is a wide spectrum of PPB, varying from cystic Type I PPB (an early malignancy with scattered malignant cells in the walls and septa of multilocular pulmonary cysts) through to cystic/solid Type II PPB (an aggressive sarcoma) and solid Type III PPB (an even more aggressive sarcoma). In general, PPB is understood to progress during approximately the first 4 years of life from Type I to Type II to Type III. The standard of care for Type I PPB is to consider it an early malignancy, to resect the pulmonary cysts and to consider adjuvant chemotherapy [18]. However, not all Type I PPB cases progress to advanced disease. It has been reported recently that some Type I PPBs "regress" and lose their potential to progress [7, 19]. Given the diagnostic dilemma posed by PPB and its association with other tumours, we recommend consulting with the PPB Registry in suspected cases. A review of the International Pleuropulmonary Blastoma Registry (IPPBR) (www.ppbregistry.org) revealed that CN or related tumours were found in 9.2% of 152 registry-reviewed PPB cases [5]. The Registry identified 18 patients with PPB associated with 20 renal tumours (15 CN), either in the same patient or in a family member. Eleven children had both PPB and renal tumours (7 CN). The frequent association of PPB with other neoplasms in the same patient or in close family members suggests an oncogenetic factor.

A recent report has mapped the PPB locus to chromosome 14q based on a family-based linkage study on four families with inherited predisposition to PPB. Of the 72 genes within the 7-Mb region of interest, *DICER1* was an attractive candidate because of its role in lung development [20]. Although approximately 75% of PPB cases appear to be sporadic, the remaining 25% appear to result from a genetic predisposition to dysplasia or neoplasia in the patient and/or family, suggesting that screening other family members of affected children should be considered [6, 21]. PPB and CN can occur in one patient or in kindreds [5, 17, 21]. Personal communication with Dr. J.R. Priest (IPPBR, Minnesota) resulted in the identification of two other cases of PPB, bilateral and progressive cystic renal disease and intussusceptions because of small bowel polyps. One of the patients died of progressive lung and renal cysts [22], and the other patient received VAC (vincristine, adriamycin and cyclophsphamide) chemotherapy. This second patient also underwent a unilateral nephrectomy and partial nephrectomy on the contralateral side. To the best of our knowledge, she currently has stable renal function and has not required renal replacement therapy. Given the bilateral nature of some of the cases, we would recommend nephron-sparing surgery, where possible, to preserve native renal function. Our patient is unique in several ways. He exhibited the rare triad of PPB, CN and juvenile intestinal polyps. This is the only reported case with this association in which the patient received renal replacement therapy and then has gone on to be successfully transplanted. There is no precedent for transplantation in patients with this condition and the potential for malignant progression of PPB following long-term immunosuppression remains. A close surveillance of such patients (not just the lungs) is recommended because of elevated risk of other tumours, such as gonadal tumours, medulloblastoma, leukaemia, lymphoma, thyroid follicular and papillary carcinoma, as reported by Priest et al. [7].

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