Infantile Polycystic Disease of the Kidneys

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SUMMARY

Infantile polycystic disease is not a single entity, but rather a spectrum of disease with variable presentations. This is illustrated by 7 cases reported in this article seen over an 8-year period at the Transvaal Memorial Hospital for Children. Associated congenital hepatic fibrosis was confirmed in 5 of the patients. Six of the children have survived for periods of 16 months to 14 years.

The inheritance of this disease as an autosomal recessive characteristic differentiates this from adult polycystic disease which is of autosomal dominant inheritance. The typical appearances on excretory urography are described. Adequate treatment of the associated problems (in particular the hypertension) is discussed. It would appear that these children are not condemned to die in infancy, as has been supposed, but may live to adult life.


Early diagnosis is of importance for the assessment and treatment of children suffering from infantile polycystic disease (IPCD). The prognosis and the life expectancy for these children have been materially altered in the last decade.

With the progress of renal transplantation, a better understanding of immunology, and the adequate control of hypertension, these children are now offered greater hope for the future.

The objective of this article is to stress the major clinical features, evaluate the use of early excretory urography, assess any congenital hepatic fibrosis (CHF), which might be present, discuss the treatment of the associated hypertension, and consider the prognosis for these children.

We wish to review 7 cases of infantile polycystic disease who presented at this hospital in the past 8 years.

CASE HISTORIES

Patient 1

A male infant, aged 4 days, presented with bilateral abdominal masses which were enlarged kidneys. There was no hepatomegaly. Hypertension was a feature and soon the child developed severe congestive cardiac failure.

Initial serum creatinine was 1.6 mg/100 ml and blood urea was 43 mg/100 ml. Excretory urography performed on the 8th day of life demonstrated the typical appearance of infantile polycystic disease. The ECG was within normal limits.

The child remained poorly during the first 13 months of life, but by 6 months of age he had almost doubled his birth-weight. The major problem was to control the hypertension which was initially managed with a combination of alpha-methyl dopa 125 mg q.i.d. and chlorothiazide 50 mg b.d. With an increase in his protein load the blood rose to 59 mg/100 ml. When he was followed up at a renal clinic his hypertension increased and could not be controlled, despite the addition of guanethidine 25 mg daily. By 6 months of age he had also developed a gallop rhythm and was in overt cardiac failure. He was digitalized. The problem of the hypertension persisted and the drugs were changed to hydralazine and propranolol which eventually controlled his blood pressure. He was weaned off digoxin with no ill effects. Now at the age of 3 years, his hypertension is well controlled and he is thriv­ing reasonably well. His kidneys are still easily palpable and he has a large liver (8 cm below the xiphisternum).

Patient 2

This girl presented first at 13 months with pneumonia and enlarged kidneys. The birth-weight was 2.7 kg. She was the result of a normal pregnancy and forceps delivery. She was the only patient whose blood pressure was normal initially.

At 2 years and 4 months of age she became hypertensive. This state persisted until she was treated with hydralazine (20 mg t.d.s.) and propranolol (20 mg t.d.s.) plus chlorothiazide, and potassium replacement, which controlled her hypertension. Her liver was enlarged. The blood urea was 58 mg/100 ml and serum creatinine 0.9 mg/100 ml.

At 3 years and 1 month she remains normotensive. Her liver is enlarged 5 cm below the xiphisternum, but she is thriving.

Patient 3

An infant girl first presented at 6 weeks of age, with vomiting. She was operated on for a hypertrophic pyloric stenosis. After the operation it was noted that the infant did not feed well and bilateral abdominal masses were palpable. Bilateral polycystic kidneys were demonstrated by excretory urography. At 5 months of age she became significantly hypertensive and this state was eventually controlled with guanethidine 20 mg daily, hydralazine 30 mg t.d.s. and potassium replacement, which controlled her hypertension.

Her liver was enlarged. The blood urea was 58 mg/100 ml and serum creatinine 0.9 mg/100 ml.

At 3 years and 1 month she remains normotensive. Her liver is enlarged 5 cm below the xiphisternum, but she is thriving.

Patient 4

This patient's birth-weight was 3.6 kg. He was born at term and the delivery was normal. He was first seen at 6 months of age. He had been vomiting intermittently since birth, and had had recurrent attacks of upper respiratory tract infection. He was slightly hypertensive. The blood urea was 82 mg/100 ml. He had enlarged kidneys. Excretory urography demonstrated typical infantile polycystic disease. His main problem has been repeated urinary tract infection. His hypertension has been well controlled. The lower urinary tract has been investigated and there are no discovered causes for his recurrent urinary tract infection, a problem seldom seen in uncomplicated infantile polycystic disease. His renal function has deteriorated as a result of the repeated urinary infections.
**Patient 5**

This patient’s birth-weight was 2.5 kg. The pregnancy and delivery were normal. This child was first admitted with acute gastro-enteritis and dehydration, at the age of 10 months when enlarged kidneys were palpated. She was hypertensive. Her liver was easily palpable. She is now 20 months and is thriving. Her hypertension is controlled by propranolol 20 mg t.d.s. A diuretic given earlier was withdrawn because of her tendency to become salt-depleted.

**Patient 6**

This patient had a normal birth. She was first seen at the age of 2 years, for continuous crying. A liver biopsy performed at another hospital, disclosed tissue hamartoma. Shortly thereafter, she was admitted to the Transvaal Memorial Hospital for Children for investigation of bilateral abdominal masses. She had mild hepatomegaly and a 2-finger breadth firm, non-tender spleen. She was mildly hypertensive (blood pressure 130/90 mmHg) and an intravenous pyelogram demonstrated ‘horseshoe’ kidneys affected by infantile polycystic disease. When last seen she was 14 years of age, normotensive, and well.

**Patient 7**

This patient, a male, was admitted at 1 month of age, with pneumonia. On examination bilateral abdominal masses were palpable and there was hepatomegaly. A retrograde pyelogram demonstrated infantile polycystic disease. At the age of 4 months this child died from an infection and at autopsy the previous findings were confirmed.

**PATHOLOGY**

What is infantile polycystic disease and how is it related to (a) adult polycystic disease, and (b) congenital hepatic fibrosis. The clinicopathological classification presents a problem to pathologist and clinician, and no satisfactory solution has been found.

Kissane and Smith described a heterogeneous group of patients who present usually in early childhood: these represent Osathanondh and Potter’s type 1 and type 2 polycystic disease.

Macroscopically, the kidneys are uniformly enlarged and spongy in texture. Microscopically, there are multiple cystic lesions, arising from saccular or cylindrical dilatations of the enlarged collecting tubules throughout the cortex. The pelvis and ureters appear normal.

Histology of liver tissue shows the features of congenital hepatic fibrosis, i.e. microbiliary dilatation surrounded by cellular mesenchymal fibrous tissues. The liver lobule retains its architecture.

In the cases reported here autopsy material was received from case 7 in whom polycystic kidneys were found. Both kidneys had numerous cysts, the largest measuring 1 cm in diameter (Fig. 1). These were observed throughout the cortex and medulla, and some contained purulent material. Histology of this material showed irregularly dilated cortical tubules. The adjacent glomeruli and tubules were surrounded by fibrous tissue.

Microscopy of the liver tissues showed proliferation and microcystic dilatation of the bile ducts in the portal triads, with perportal fibrosis (Figs 2 and 3).
In 5 further cases, liver biopsies showed the characteristic appearance of congenital hepatic fibrosis. In 1 patient the liver biopsy was normal.

It should be noted that whereas microscopy is essential for the diagnosis of congenital hepatic fibrosis, needle biopsy may not help in some cases because of the tough consistency of the liver. An open wedge resection is indicated in such cases.6

Animal experimentation has shown that toxins may induce polycystic disease in the foetus.4

GENETICS

Infantile polycystic disease is stated to be inherited as an autosomal recessive characteristic. In the 7 patients reviewed here there was no history of consanguinity and most of the parents were in the younger age group. All the parents were examined, all had intravenous pyelograms and no abnormality was discovered except a double collecting system in one parent.

CLINICAL PRESENTATION

We have studied 7 cases of infantile polycystic disease. This hospital is a referral hospital and all cases had survived the initial 3 days of life. All cases were products of normal pregnancies and deliveries. In no case was labour obstructed by the large abdominal masses. There were no other congenital abnormalities apart from the renal and hepatic abnormalities.

The ages of presentation and the presenting signs and symptoms are shown in Table I. It can be seen that bilateral abdominal masses and hepatomegaly were present in all cases of infantile polycystic disease. Respiratory distress in the neonatal period should alert the paediatrician to the possibility of underlying renal pathology.6 Only 2 children remained uraemic although 6 cases showed elevated serum urea levels.

In 4 cases the hypertension was early and severe and control was difficult. The children tended to develop cardiac failure, and digitization was necessary, although they were later weaned off it after the hypertension had been brought under control. Urinary tract infection is uncommon and was seen in only 2 cases. Patients 1 to 5 had thorough liver function investigations. These were completely normal. Calcium, phosphate, and blood gases were usually normal. Australia antigen was absent and alpha-antitrypsin was normal in all.

RADIOLOGICAL ASSESSMENT

The excretory urogram is typical early in the course of the disease, but with survival of the child the urogram later appears to resemble that seen in adult polycystic disease.

Excretory urography there is a marked delay of excretion of contrast medium by the kidneys. There is a prolonged nephrogram with alternating streaks of radio-
density and radiolucency radiating from medulla to cortex (Fig. 4). The pelvis and ureters are not adequately demonstrated, due to the poor excretion of contrast medium. It is necessary to obtain delayed X-ray films over 24 - 36 hours in order to show the kidneys. Tomography is recommended (Fig. 5).

Retrograde pyelography will confirm the diagnosis (Fig. 6). This shows typically blunted calyces, distorted infundibula and there may be distortion of the calyceal pattern by larger cysts. (Fig. 7).

Although there are microscopic changes present in the liver, scanning with $^{99m}$Tc showed no intrinsic abnormality, but demonstrated the central position of the liver resulting from the medial displacement by the abdominal masses.

**TREATMENT**

Treatment of the respiratory distress and cardiac failure is routine. Combination of hydralazine and propranolol, orally, with or without a diuretic, has been used with good effect for the control of hypertension. Hydralazine 3 - 15 mg/kg/day, propranolol 3 - 12 mg/kg/day and spironolactone 3.75 mg/kg/day, were all given in 3 divided doses. Spironolactone should be given with care if renal function deteriorates. Hyperkalaemia may result.

There have been no significant side-effects with the above 3 drugs, even with hydralazine at the highest dosage of 15 mg/kg/day (twice the maximal recommended oral
dosage, but less than a total daily dose of 200 mg). Loggie found no children with hydralazine-induced lupus syndrome with a long-term dose of not more than 200 mg/day. We had a poor response, generally, to large doses of alphamethyldopa and guanethidine. In these children, alphamethyldopa, even in the massive dosage of 200 mg/kg/day in 4 divided doses, did not control the hypertension, but made them irritable and drowsy. Guanethidine was effective at dosages of 1-2.5 mg/kg/daily, but with side-effects of diarrhoea and postural hypotension being troublesome. Chlorothiazide was administered in the usual dosage of 10-40 mg/kg/day as a daily or twice-daily dose. If the latter was used, potassium replacement was usually necessary. Sodium depletion can be caused so that diuretics should be administered with care. One patient had the diuretic changed from chlorothiazide to spironolactone because of hyperuricaemia. In our cases there has been evidence of some improvement of renal function with age.

It should also be noted that there is no significant increase in kidney size, as there may be in the adult type.

Good liver function has been present in all these patients, but the possibility of portal hypertension developing later must be borne in mind. Although urinary tract infection is uncommon, it is difficult to control when it does occur.

**DISCUSSION**

In this series of 7 cases, 5 are thriving and leading normal lives with their hypertension well controlled. One child is uraemic although his hypertension is well controlled. Only 1 patient has died.

Osathanondh and Potter attributed all cystic conditions to polycystic disease. One form of polycystic disease is characterized by dilated collecting tubules, and another by abnormal nephrons. Some are discovered only in adult life. The authors quote Bunting's comments on polycystic disease, in which he states: 'The attempts to explain the pathogenesis of the congenital cystic kidney have been so numerous and so varied that one is inclined to question whether pathologists have been dealing throughout with a single pathological process'.

Blyth and Ockenden, and Lumdin and Olow suggest that there may be several forms of infantile polycystic disease. In their few groups they indicate that each has a characteristic age distribution with decreased cystic involvement of the kidney and increased hepatic fibrosis with advancing age. In the cases presented here, all are compatible with the groups appearing in the perinatal (1 case), neonatal (2 cases), and infantile (4 cases) periods. There were no children presenting with the adult type of polycystic disease.

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**REFERENCES**