Renal papillary necrosis in infancy

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Husband, P., and Howlett, K. A. (1973). *Archives of Disease in Childhood*, 48, 116. **Renal papillary necrosis in infancy.** Two infants developed renal papillary necrosis after acute illnesses associated with dehydration. After a short oliguric phase there was a longer phase characterized by impaired urinary concentration, hyponatraemia, metabolic acidosis, and a raised blood urea. Intravenous urograms showed contrast collecting in the papillae, with subsequent sinus formation extending into the medulla. In one case impaired urinary concentration was still present 21 months after the initial illness.

Renal papillary necrosis was originally described by Friedreich (1877) in a man aged 70 years. Since then the majority of further cases reported have also been in adults. It has been thought to be uncommon and usually to have a fatal outcome in infancy and childhood (Davies, Kennedy, and Roberts, 1969). In the newborn infant renal papillary necrosis has occurred with asphyxia (Bernstein and Meyer, 1961; Mauer and Nogrady, 1969), hyperbilirubinaemia (Watanabe and Sakaguchi, 1969), and haemorrhagic shock (Marks, 1960). In older children it has followed severe and prolonged hypotension with dehydration (Davies *et al.*, 1969) or sepsis (Stirling, 1958; Swartz and Hoogstraten, 1959). Chrispin *et al.* (1970) described the radiological appearances of papillary necrosis in 3 infants who survived. This report describes the clinical features and radiological appearances of two further cases in infancy.

Case histories

Case 1. This 9-week-old male infant was the fourth child of healthy parents born after a normal pregnancy and delivery at 42 weeks' gestation, birthweight 3.4 kg. He was admitted to hospital at the age of 6 weeks, severely ill and dehydrated after 3 days of vomiting, and 24 hours of loose stools. On that admission serum sodium was 158 mEq/l., potassium 5.7 mEq/l., chloride 124 mEq/l., bicarbonate 11 mEq/l., and blood urea 138 mg/100 ml. He made a rapid recovery with intravenous fluids and 4 days later serum electrolytes were normal and blood urea was 32 mg/100 ml. He was discharged home weighing 4.8 kg. He was re-

admitted to hospital 9 days later after he had been found in his cot, grey, with respiratory distress and a high temperature. 3 days before he had diarrhoea and vomiting for 24 hours but subsequently tolerated feeds of full cream Cow and Gate milk, 180 ml 5 times a day. He was again extremely ill: temperature 40.3 °C, pale, cyanosed with a rapid respiratory rate, but not dehydrated. He weighed 4.7 kg. Serum sodium was 164 mEq/l., potassium 6 mEq/l., bicarbonate 10 mEq/l., and blood urea 118 mg/100 ml. Bacteriological evidence of infection was not found. With intravenous fluids his blood urea fell to 39 mg/100 ml and electrolytes became normal over the next 48 hours by which time he started to take feeds by mouth.

His condition deteriorated 4 days after admission, and he was grossly dehydrated, with 280 g loss of weight since the previous day, though there had been no diarrhoea or vomiting. He again needed intravenous fluids and for the next 2 weeks had a persistent electrolyte disturbance with a raised blood urea, hyponatraemia, and metabolic acidosis, in spite of additional sodium supplements of 30 to 40 mEq/day (Fig. 1). At no time was there any evidence of a urinary tract infection. An intravenous urogram (IVU) (Fig. 2) 13 days after admission showed no abnormality on the preliminary film. The length of the right kidney was 78 mm, the left 75 mm. The pelvicalyceal systems were incompletely shown but contrast was seen extending from the calyces into the papillae in places.

When his electrolytes were normal, 19 days after admission he became pyrexial with a tense anterior fontanelle, and he was found to have pneumococcal meningitis which was successfully treated with penicillin. The meningitis was complicated by a right subdural effusion and left-sided fits; the subdural effusion was treated with repeated aspirations.

A further IVU 17 months after the original illness showed no abnormality on the preliminary film. The right kidney measured 78 mm, the left 77 mm.

Received 26 June 1972.

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FIG. 1.—Case 1. Serum sodium, bicarbonate, blood urea, and weight.

Most of the calyces showed better cupping, presumably because of a reduction in papillary swelling. Contrast-filled cavities were seen in almost all papillae.

He was readmitted at the age of 21 months for reassessment. He had thrived well and his intellectual development was normal though motor development was delayed probably due to understimulation at home. The blood pressure was normal. Renal function was normal except for impaired urinary concentration. After 14 hours of fluid deprivation, he only achieved a urine osmolality of 566 mOsm/kg and 528 mOsm/kg on two separate occasions.

FIG. 2.—Case 1. IVU during the acute illness. Contrast is seen extending from the calyces into the papillae in places.

FIG. 3.—Case 1. IVU 17 months after the illness. Contrast-filled cavities are now seen in almost all the papillae.

Case 2. A 3-month-old male infant was admitted to hospital after he had been found in his cot, limp, white, sweating profusely, and with marked respiratory distress. For the preceding 10 days he had had a slight cough not severe enough to interfere with feeding. He had been born after a normal pregnancy and delivery, birthweight 3.7 kg, and had been well until this illness.

On admission he was a pale, ill-looking infant with a rectal temperature of 40.5 °C. His respiratory rate was 70 per minute with scattered coarse crepitations in the chest. Chest x-ray was normal. WBC 23,000/mm³ with 76% neutrophils. A heavy growth of *Haemophilus influenzae* was cultured from a throat swab.

He was treated with oral ampicillin and his temperature became normal in 36 hours. There was some clinical improvement but he continued to feed poorly and had some small vomits. 8 days after admission, his condition suddenly deteriorated; he was lethargic and moderately dehydrated with sunken eyes and anterior fontanelle, and he had lost 280 g in weight since the previous day. For 3 days before this there had been a decrease in the number of wet nappies. Serum sodium was 123 mEq/l., potassium 7.2 mEq/l., chloride 90 mEq/l., bicarbonate 14.5 mEq/l., and blood urea 128 mg/100 ml. He was treated with intravenous fluids and kanamycin and penicillin. He improved over the next few days but for 4 days he was hyponatraemic and acidotic in spite of added supplements of sodium 45 mEq per day to his feeds. Blood urea fell to 42 mg/100 ml 3 days after this sudden deterioration (Fig. 4).

An IVU 17 days after admission (Fig. 5) showed no abnormality on the preliminary film. The length of the right kidney was 64 mm; the left 72 mm. Both kidneys excreted the contrast and were of normal size and shape and in normal position. All the calyces were blurred. There was a pronounced increase in the

FIG. 4.—Case 2. Serum sodium, bicarbonate, blood urea, and weight.

density of the papillae as compared with the rest of the kidney. The contrast in some places extended into the medulla.

He subsequently made satisfactory progress. A further IVU was performed 9 months after the illness (Fig. 6). Both kidneys excreted the contrast. The right kidney measured 72 mm, the left 76 mm. Some of the calyces were now more sharply cupped than previously but contrast collected in virtually all the papillae. Irregular cavitation of the papilla was seen in the left upper calyx. Sinus formation was shown in the left middle and lower calyces. One year after the illness he was thriving normally and was free of symptoms.

FIG. 5.—Case 2. IVU during the acute illness. Dense opacification of papillae is shown.

FIG. 6.—Case 2. IVU 9 months after the illness. Contrast collects in virtually all the papillae with irregular cavitation and sinus formation.

Discussion

Renal papillary necrosis is less common in children than in adults and has a different aetiology (Davies *et al.*, 1969). In adults it usually occurs with the repeated ingestion of analgesics, diabetes mellitus, and prolonged urinary tract obstruction. In children most cases occur under the age of 1 year and most commonly in association with episodes of asphyxia, dehydration, and septicaemia (Davies *et al.*, 1969). A fairly characteristic clinical picture emerges from a consideration of our cases and others where clinical details are recorded (Stirling, 1958; Chrispin *et al.*, 1970). The patients are usually under the age of 6 months and have an acute illness associated with shock and dehydration, most commonly due to diarrhoea and vomiting. They either make a poor recovery from this illness or relapse after a few days treatment.

The diagnosis of acute renal failure is easily missed when the clinical picture is overshadowed by the primary disease and if accurate measurements of urinary output are not available (Kerr, 1968). This author also comments on the short oliguric phase in acute tubular necrosis in infancy; in our second case oliguria was present for only 3 days. After the oliguric phase, there is a more prolonged phase characterized by failure to conserve water, hyponatraemia, metabolic acidosis, and a raised blood urea. A worsening clinical state with dehydration occurs in the absence of any further diarrhoea or vomiting and, because of the hyponatraemia, this can be mistaken for acute adrenal hypofunction. This phase lasted for 8 and 4 days in our two cases, and two of the cases described

by Chrispin *et al.* (1970) were hyponatraemic for 4 and 7 days. Two of the cases reported by Stirling (1958) remained persistently hyponatraemic till death. Hyponatraemia in this condition probably usually occurs from the excessive administration of water during acute renal failure. Weight gain during the period of hyponatraemia in our two cases suggests that this had happened. It may also result from acute tubular damage or dilution due to excessive production of water. In Case 1 a defect in urinary concentrating ability could still be shown 21 months after the initial illness.

The common factor in most of the reported cases has been an episode of severe vascular collapse causing renal ischaemia (Davies *et al.*, 1969). The selective ischaemia of the papillae is due to the arrangement of the arterial blood supply to the medulla. The papillae are supplied by the arteriolae rectae spuriae which are a continuation of the efferent glomerular arterioles in the juxta-medullary zone; they enter the papillae and run towards the apex. With severe hypotension, if there is little or no constriction of the interlobar arteries, the blood flow in the medulla will be less than in the cortex as the capillary resistance of the medulla is higher than that of the cortex (Thurau, 1964). The margin and tips of the papillae, however, are fed by spiral branches direct from the interlobar arteries (Baker, 1959) and are therefore less vulnerable to ischaemic change than the centre of the papillae. Salm and Voyce (1970) have implicated the liberation of prostaglandins by ischaemia in the production of renal papillary necrosis.

If infants with renal papillary necrosis recover, the presence of extensive renal damage may not be appreciated unless excretion urography is performed (Chrispin *et al.*, 1970). The characteristic radiological finding in the acute stage of renal papillary necrosis is prolonged and heavy opacification of the renal parenchyma with a pronounced increase in the density of the papillae. Renal papillary necrosis has been produced experimentally in rats with ethyleneimine (Risdon, Berry, and Chrispin, 1970; Sherwood, Swales, and Tange, 1971). Intravenous urograms showed dense medullary opacification in the early stages of the lesion. This selective opacification of the renal papillae does not occur when there is acute tubular necrosis alone. With renal cortical necrosis there is failure to visualize the kidneys on IVU and subsequently a distinct pattern of calcification of the renal cortex is seen (Leonidas, Berdon, and Gribetz, 1971). After clinical recovery the papillae may show a central cavity filled with contrast medium

producing the 'egg in a cup' appearance. If there has been more complete destruction of the pyramids, then irregular, broad, expanded, or clubbed calyces may be seen. Shrinkage of the kidney may occur rapidly. These radiological features of renal papillary necrosis depend on separation of papillae; if the necrotic papillae do not separate there may only be a reduction in the size of both kidneys or the papillae (Fairley and Kincaid-Smith, 1968).

The extent of the lesions will influence survival after renal papillary necrosis. In 3 of the 18 cases recorded by Davies *et al.* (1969) the changes were unilateral and it was noted that the site and size of the area of infarction varied. In those with prolonged survival, apart from an occasional congested vessel, the appearance of the surviving parts of the medulla was normal. Swartz and Hoogstraten (1959) found that, even in patients dying with extensive lesions, there might be marked healing characterized by re-epithelialization of the remaining basilar portion of the papillae. The ultimate prognosis for children who survive the acute episode is uncertain. In two of the cases described by Chrispin *et al.* (1970) IVUs 4 months after the initial illness did not show normal renal growth. A repeat IVU after 9 months in Case 2 of the present study showed normal renal growth. In Case 1 there was no increase in the length of the kidneys 17 months after the acute illness. This might be due to generalized renal enlargement at the first examination as the kidneys may be swollen during the acute episode (Chrispin *et al.*, 1970). In Case 1 there is persistent impairment of urinary concentration. This is an easily performed and useful test of tubular function in this condition. The concentrating ability of the kidney is dependent upon the countercurrent mechanism which in turn depends on the active reabsorption of sodium from the distal tubule which is a medullary function.

The long-term radiological appearances of the kidneys in these infants are not known. It is conceivable, however, that they will need to be distinguished from those of atrophic pyelonephritis (Hodson, 1971). The possibility of severe neonatal or childhood illness with subsequent renal papillary necrosis should be borne in mind in older patients with inexplicable calyceal deformity or renal atrophy, particularly if there is no reflux or evidence of previous obstruction.

We wish to thank Drs. Herbert Barrie and Hugh Jolly for permission to report these cases admitted under their care. We are grateful to Drs. P. E. Gower and H. M. Saxton for their help in the preparation of this paper.

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