Preliminary Communications

Renal Tubular Necrosis and Papillary Necrosis after Gastroenteritis in Infants

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Summary: Three young infants who had severe gastroenteritis developed radiological and histological features of renal tubular necrosis. Characteristically the excretion urogram showed renal enlargement with prolonged and heavy opacification of the renal parenchyma and a pronounced increase in density of the pyramids. Subsequent radiological studies showed extensive papillary necrosis. Though these infants are now apparently fit, renal damage has occurred and this may eventually give rise to features indistinguishable from chronic pyelonephritis.

INTRODUCTION

In acute gastroenteritis the clinical features of renal failure may be masked by those due to diarrhoea and vomiting (Black, 1959). If the infant recovers the extent or indeed the presence of extensive renal damage may not be appreciated. Excretion urography has been used to show the extent and development of renal damage in the three cases presented in this report.

CASE 1

A male infant aged 4 months was admitted to hospital with pronounced dehydration due to severe diarrhoea and vomiting, but he continued to pass dilute urine containing a few epithelial cells only. Subsequently the urine contained a few white cells (0-100/cu. mm.) and the occasional red cell. No casts or proteinuria were present. For the first two days the serum sodium was high (160 mEq/l.); it then fell to below 120 mEq/l. for four days before returning to normal values. Initially the serum potassium was normal, but during recovery from gastroenteritis it rose to between 7 and 8 mEq/l., remaining at this level for one week. A raised 11-oxygenation index suggested associated adrenal damage. The blood urea was initially 320 mg./100 ml., but in the first week it fell to 75 mg./100 ml. and stayed at this level for the next three weeks. The kidneys were palpable and enlarged and the systolic blood pressure rose above 200 mm. Hg. Polyuria continued.

Three weeks after the start of the illness an excretion urogram was carried out. This entailed no preliminary dehydration and the injection of 15 ml. of Hypaque (sodium diatrizoate) 45% intravenously (Chrispin, 1968). All other radiological studies in this report were carried out in the same way. Prompt opacification of normal calices was seen, but increased density of the kidneys developed, reaching a peak one hour after injection. The renal pyramids were particularly heavily opacified (Figs. 1 and 2). A brisk diuresis occurred after the injection of contrast medium.

Six weeks after the onset of the illness the infant was submitted to open renal biopsy. The specimen contained some 103 glomeruli, all of which were of normal appearances for a 4-month-old infant. There were foci of tubular degeneration and regeneration (Fig. 3). The degenerate tubules were lined by atrophic epithelium and there was occasional nuclear pyknosis. Regenerating tubules were lined by a low cuboidal epithelium. In these areas the tubules were separated and there was focal lymphocytic and histiocytic interstitial infiltration and oedema. In many areas the tubules were normal, the damage appearing patchy. Blood vessels seemed to be normal. There was no histological evidence of any underlying renal disease. No papillary tissue was present in the biopsy specimen. The histological appearances were those of healing focal tubular necrosis with tubular epithelial regeneration.

During the subsequent four months the blood pressure gradually became normal, the ability to concentrate urine improved, and the infant thrived. A second urogram, however, then showed the kidneys to be smaller and there was extensive papillary necrosis (Fig 4).

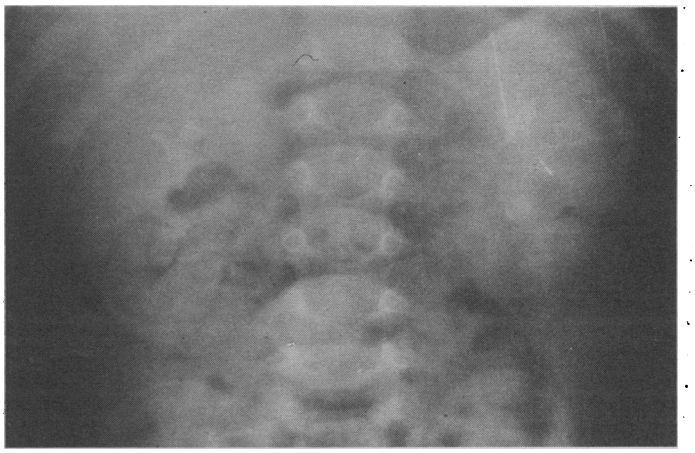

FIG. 1.—Case 1. Five minutes after injection of contrast medium the normal calices are seen to be well opacified, with a slight increase in density of kidney.

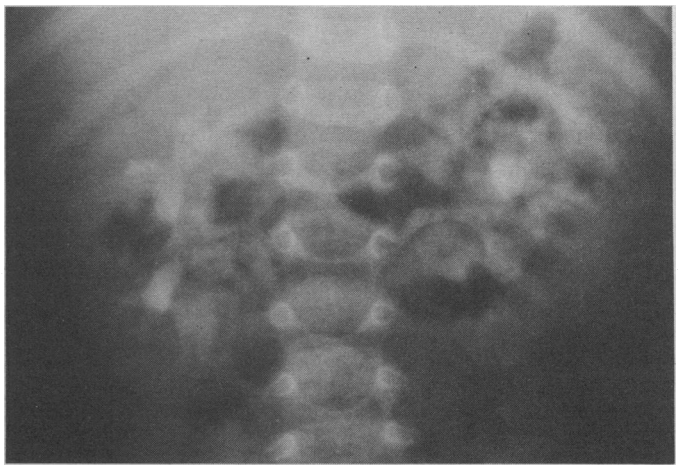

FIG. 2.— Case 1. Film at one hour showing pronounced increase in density of pyramids, with lesser increase in density of remainder of kidney. Continuing calix opacification. (At this study there was no measurable change in kidney size on the original radiographs.)

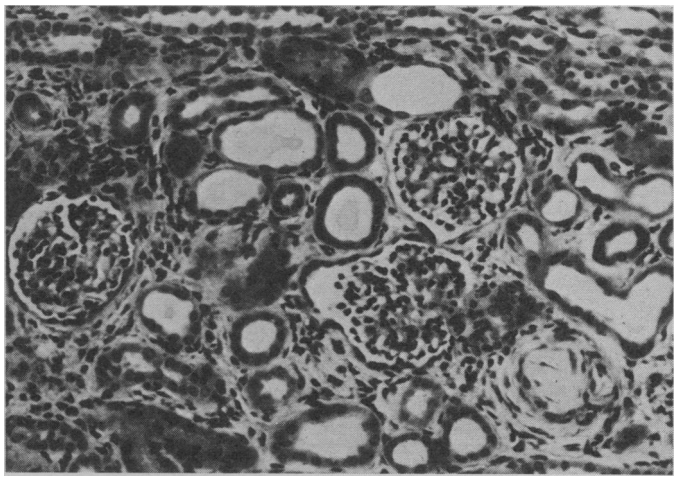

FIG. 3.—Case 1. Renal biopsy showing an area of cortex where there is tubular degeneration and interstitial oedema. At centre of the field two proximal convoluted tubules are lined by low regenerative cuboidal epithelium. These changes were of a focal nature.

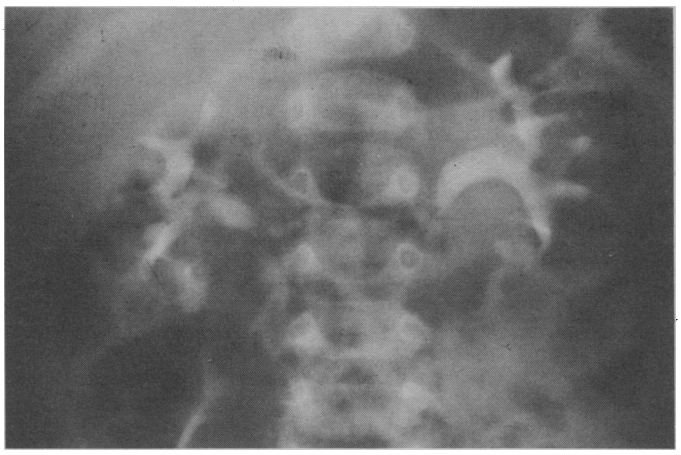

FIG. 4.—Case 1. Repeat study four months after acute illness. Papillary necrosis in upper pole of right kidney and middle segment of left kidney where partial separation of papillae has occurred. Caliectasis in other calices where separation of papillae is complete.

CASE 2

A female infant aged 3½ months was transferred from another hospital with a five-day history of gastroenteritis complicated by fits. The urine was dilute, containing an excess of sodium, and the serum sodium remained below 120 mEq/l. for one week before returning to normal levels. The urine contained a few white cells but no red cells, protein, or casts. The kidneys were palpable and enlarged. The blood pressure was normal. Initially the blood urea was 170 mg./100 ml., and it slowly fell to 70 mg./100 ml. during the first week.

Ten days after the start of the illness a urogram showed prompt opacification of normal calices. The density of the enlarged kidneys increased and reached a maximum four hours after the injection of contrast medium. The pyramids were slightly denser than the remainder of the kidney (Fig. 5). Contrast medium persisted in the kidney for four days. A second urogram has not yet been performed, but the infant was thriving.

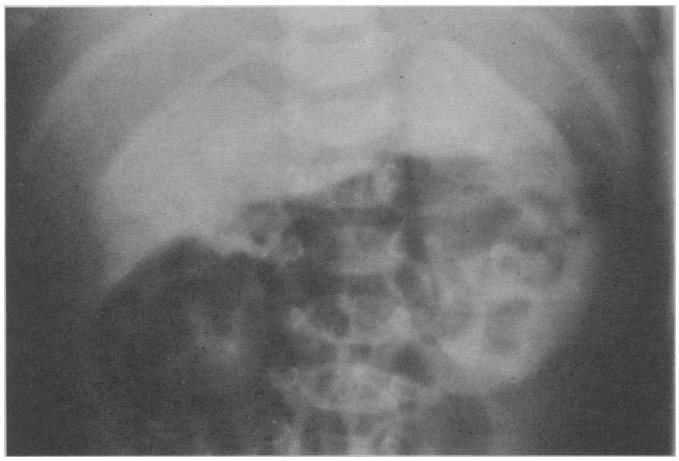

FIG. 5.—Case 2. Four hours after injection of contrast medium the kidneys are shown to be large, with increased density of the whole kidney and pronounced increase in density of the pyramids. The increased renal density has obscurbed the calices, but a considerable volume of contrast medium was entering the bladder, indicating continuing excretion of contrast medium.

CASE 3

This male infant aged 4 months was admitted to hospital after four days of vomiting and diarrhoea. Severe dehydration was present, the blood urea was 220 mg./100 ml., the serum sodium 160 mEq/l., and the urine output low. He made a good recovery with intravenous therapy. Initially, there was no urinary deposit or proteinuria. At the end of the second week, however, white cells were present (30-300/cu. mm.) and one cellular cast was seen. His ears were low-set and his kidneys were palpated easily.

At urography seven days after the start of the illness normal calices were promptly but faintly opacified. There was a slight to moderate increase in the density of the kidneys during the first 30 minutes. The pyramids were particularly dense. Pronounced diuresis ensued. Because of these findings a second urogram was performed four months later, when the infant was thriving. Extensive papillary necrosis was shown and the renal size had not increased (Fig. 6).

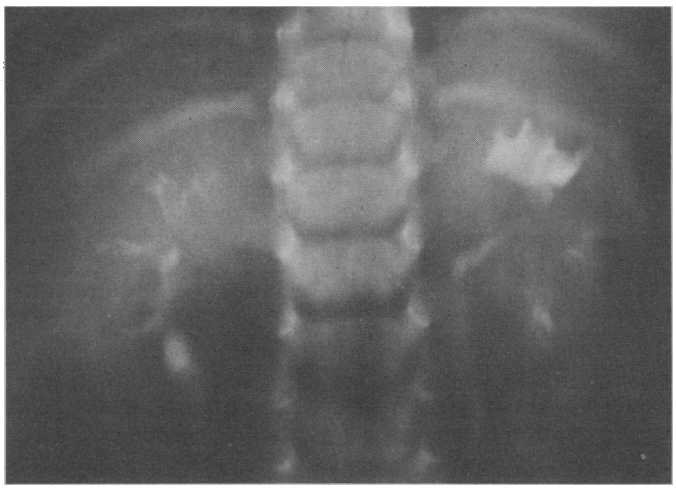

FIG. 6.—Case 3. Repeat study four months after acute illness. Tomogram 20 minutes after injection of contrast medium. Caliectasis in lower pole of right kidney. Normal calices in upper pole of left kidney. Elsewhere there is papillary necrosis with partially separated papillae outlined by contrast medium.

DISCUSSION

Kerr (1968) noted that the clinical presentation of acute tubular necrosis in infants differs in certain important respects from that observed in later life. In particular he pointed out that in infants the oliguric phase is short and lasts only three to five days. Gastroenteritis is well recognized among the common precipitating illnesses, and the dehydration and oliguria due to this may mask the oliguria of tubular necrosis.

Within four days of the onset of gastroenteritis two patients (Cases 1 and 2) had polyuria in the presence of dehydration. In Case 3 oliguria lasted 24 hours after admission, and following intravenous therapy his urine output was satisfactory. Numerous urine samples examined over many weeks contained no white or red cells, casts, or protein. On one occasion Case 1 had a urine count of 100 white cells/cu. mm., and Case 3 had one count of 300 white cells/cu. mm. All infants were treated with broad-spectrum antibiotics for their illness. One infant had hypokalaemia with hypertension, and in two infants sodium loss in the urine was excessive. None of these infants responded well to the initial treatment for gastroenteritis, which included intravenous therapy, but they had few features indicating serious renal damage. Without radiological study the extent of the renal lesion would have passed undetected.

At the first radiological study the calices were opacified promptly, though the density of contrast medium in them was reduced in one patient. The fact that contrast medium appeared in the calices and continued to be excreted from the kidneys must indicate that some nephrons were functioning in a generally normal way. This is entirely consistent with the patchy nature of the tubular damage noted in the biopsy specimen from Case 1. All these patients showed a considerable opacification of the kidney for a long period. They all showed heavier opacification in the pyramids than in the remainder of the kidney parenchyma. The abnormal persistence of contrast medium in the kidney may be accounted for by (*a*) obstruction of the lumen of the tubule and (*b*) leakage of contrast medium through the damaged tubular epithe-

lium into the interstitial tissues and then recirculation via the blood stream. The more pronounced opacification of the pyramids may be due to greater leakage of contrast medium in this region.

Chamberlain, Pringle, and Wrong (1966) observed a dense nephrogram in an adult with acute tubular necrosis. Subsequently Chamberlain and Sherwood (1967) showed uniform opacification of the kidneys in rats with tubular necrosis induced by ischaemia or mercuric chloride. We have found uniform opacification of the kidney in young patients with renal failure due to the haemolytic uraemic syndrome, and at necropsy their kidneys have not shown papillary necrosis. A dense uniformly opaque nephrogram has been observed at urography in normal patients who had oliguria and dehydration (Berdon, Schwartz, Becker, and Baker, 1969); this dense nephrogram was thought to be due to precipitation of Tamm-Horsfall protein by contrast medium in the tubules. Precipitation of Tamm-Horsfall protein, however, is unlikely to be a factor in the three cases we report, for none was oliguric or dehydrated at the start of the radiological studies.

Oliguria did not develop after injection of the contrast medium. Indeed, there was a brisk diuresis resulting in a 5% loss of weight in Case 1 and a 3% loss in Case 3, and this was accompanied by a transient rise in blood urea of about 20 mg./100 ml. Both weight and blood urea returned to the preceding levels within 36 hours. The injection of contrast medium did not have any other demonstrable untoward effects. There was no subsequent proteinuria or excretion of casts.

The clinical findings alone might suggest that a pre-existing urological lesion was present. There were, however, none of the features of obstructive uropathy, infantile polycystic disease, cystic change of Bowman's capsules, or renal dysplasia at radiology or at the one biopsy. The findings were not those of acute pyelonephritis in infancy (Reilly, 1967). Thus there was no evidence of any renal lesion being antecedent to the acute illness.

Radiological features similar to those described here were observed by Mauer and Nogrady (1969) in an infant with renal damage due to perinatal asphyxia. The underlying disorder may well be the same.

Clinical assessment alone in these infants did not indicate an underlying renal disorder of such magnitude and consequence. Tubular damage may be a relatively frequent complication of severe gastroenteritis or septicaemia in infancy or of asphyxia in the newborn. Such renal damage may, at the time, pass undetected. Of course, the remaining healthy renal tissue may grow and compensate for the damage, but a kidney so damaged may be subject to repeated infections or be the cause of hypertension in early adult life. Repeat radiological examination of two of the infants showed that the kidneys had not grown as might have been expected. It would not be surprising if the kidneys remained small with caliectasis and an irregular outline. The radiological features could then be indistinguishable from those of chronic pyelonephritis (Williams, 1958).

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Medical Memoranda

Post-vagotomy Diarrhoea?

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CASE REPORT

The patient, a surgeon aged 57, came under my care in March 1968 with severe pyloric obstruction, which had become extreme in a matter of weeks. Symptoms suggestive of a duodenal ulcer had been present for 35 years and a duodenal ulcer had been diagnosed radiologically in 1960.

Operation was carried out on 3 April 1968. The stomach was grossly enlarged. The duodenum was very scarred and narrowed and showed signs of active ulceration. In view of the enlargement of the stomach, the general state of the patient, and the oedema surrounding the duodenal ulcer, it was thought that the safest procedure would be to carry out a short-circuit operation. This was done, making a posterior, retrocolic gastroenterostomy with a short loop. Vagotomy was not carried out because of the gastric dilatation.

He made a good recovery and was discharged on 14 April. He felt well but was having a loose bowel action every morning.

On 11 June his diarrhoea became much worse and he had an attack during which he passed liquid stools at two-hourly intervals. This attack necessitated admission to hospital, where he was treated with Lomotil and mist. kaolin and morphine. There was a temporary improvement, but the condition relapsed and radiological investigations were carried out to make sure that all was well with the gastroenterostomy.

At this time his plight became known to various surgical friends and acquaintances—and some of these, without knowing the operative details, confidently diagnosed his case as an example of post-vagotomy diarrhoea.

He was readmitted under my care in June 1968, and I sought the aid of my medical colleague, Dr. G. Neale. A jejunal biopsy was carried out 1 ft. (30 cm.) distal to the stoma. Histology showed subtotal villous atrohpy. He was given a gluten-free diet and he made a rapid and uninterrupted recovery.

He wrote on 8 October 1969 that he was back to his preoperative weight of 10 st. 12 lb. (68·9 kg.). (It fell to 8 st. 7 lb. (54 kg.) when he developed pyloric obstruction.) He has occasional very slight indigestion "not enough to bother about." His bowels "open once daily—occasionally twice. The stool is bulky, a little pale, a bit fatty." He concluded by saying that his well-being and energy were normal and he was doing long and heavy lists.

COMMENT

There may be other patients in whom coeliac disease has been brought to light by a gastric operation, and this possibility should be considered before making the diagnosis of post-vagotomy diarrhoea.

The history of this patient has been described in order to draw attention to the fact that unsuspected coeliac disease may be unmasked by a gastric operation. This possibility should be more generally recognized.

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