whether the damage to the liver cell and renal tubule is caused by lactose or by another unknown substance. Lactose is not normally found in the blood and its presence may have toxic effects similar to fructose-1-phosphate in fructose intolerance, and galactose-1-phosphate in galactosaemia. Russo et al.7 and Hirashima et al.8 noted cataracts in children with lactosuria and in some of their relatives.

References

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Typhoid glomerulonephritis

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SUMMARY 15 patients with typhoid glomerulonephritis were studied and compared with a group of children with poststreptococcal nephritis. Useful criteria distinguishing the two diseases are given. The diseases may present in a similar manner and therefore it is important to remember typhoid as a cause of glomerulonephritis in endemic areas or in patients travelling from endemic areas.

Although both typhoid fever and poststreptococcal glomerulonephritis (PSGN) are common among the underprivileged in South Africa, rarely does the former present as nephritis.1 The clinical findings of acute PSGN have been well described but those of typhoid nephritis have not. Failure to distinguish one from the other affects management and may determine the outcome. We therefore report 15 cases of typhoid glomerulonephritis comparing them with a matched group of children with PSGN, and put forward criteria helpful in distinguishing the two diseases.

Patients and methods

A study of 15 patients with typhoid glomerulonephritis admitted to King Edward VIII Hospital, Durban, and observed by one or both of us between 1973 and 1978 was carried out. 15 patients matched for race, age, and sex, and admitted to the same hospital in 1978 with PSGN were randomly selected as the comparison group. The age range of patients was 2-13 years. 10 were girls.

A diagnosis of glomerulonephritis was made on the clinical criteria of periorbital and peripheral oedema, oliguria with evidence of hypertension in nearly all cases, together with haematuria, casts, albumin <2 g/l, and leucocyturia in some patients. An antistreptolysin O titre (ASOT) of >200 U/l was used to confirm the diagnosis of poststreptococcal disease. (93% of children with PSGN at this hospital had a positive response to ASOT).2

A diagnosis of typhoid was made as follows: Salmonella typhi was cultured from blood in 5 patients, in blood and stools in 2, in blood and urine in 2, in urine alone in one patient, and in stool alone in one patient. The Widal test was positive (S. typhi O titre >320) in 9 patients. Six of these 9 patients had negative blood cultures. However, in the presence of pyrexia >39°C, abdominal findings of pain, tenderness and guarding, with constipation or diarrhoea, and an initial leucocytosis (absolute neutrophil count
<2000 in 4 patients with an initial Widal test >320), we felt that a diagnosis of typhoid was extremely likely.

**Results**

**Typhoid glomerulonephritis.** In this group 8 patients presented with a history of oedema of longer than one month’s duration, 2 had had oedema for 2 weeks, and 3 patients had had oedema for a week or less. The oedema was of moderate severity affecting mainly periorbital areas and feet, with oedema of hands and sacral areas in some cases. All of these children had urinary proteins <2 g/l on Labstix testing. 12 children had serum albumin <3.5 g/l. Many of our children are malnourished, so suboptimal protein intake could be the reason for these low values. The remaining 2 patients did not present with oedema. They each had a history of general malaise, weakness, headache, and abdominal pain for 2–3 months before admission. Both developed oedema of the eyelids and feet 10 days after admission, by which time a diagnosis of typhoid had been made. 12 patients had temperatures >37.5°C; 6 had splenomegaly; 12 presented with signs of volume overload associated with hypertension (this excludes the 2 patients who developed clinical nephritis 10 days after admission). One 4-year-old girl with BP 90/50 mmHg on admission developed hypertensive encephalopathy on day 10, with BP 150/120 mmHg. She was treated aggressively with antihypertensives and made a complete recovery, being discharged at 7 weeks.

All patients except one had a negative ASOT. The third component of serum complement (C3) was reduced in all but 2 patients in this group, the range of C3 being 0.18–1.12 g/l apart from one patient with C3 <0.01 g/l (mean: 0.56 g/l ± 0.38 SD) (normal 0.90–1.19).²

Two renal biopsies were performed; one because the aetiology of nephritis was obscure before the diagnosis of typhoid had been made; histology showed acute diffuse proliferative changes with weak deposits of Clq on the glomerular basement membrane and no deposits of IgG, IgM, IgA, IgE, fibrinogen, or C3 (serum C3 0.58 g/l). The second renal biopsy was performed after a 7-year-old boy developed acute renal failure requiring dialysis; histology showed focal interstitial nephritis with focal calcinosis in the tubules, fine granular deposits of IgG, C3, and Clq were present in the glomerular basement membrane (serum C3 0.26 g/l). The child recovered within 9 weeks and was discharged with normal renal function.

Three of these patients died. They were the 3 youngest of the group (2, 2, and 4 years). Two developed myocarditis after completion of a course of amoxycillin and died in intractable cardiac failure, one on day 27 after admission and the other on day 77. The third was apyrexial on admission with features of nephritis, hypertension, and volume overload. She responded initially by producing a diuresis but relapsed on day 7 becoming oliguric, oedematous, and drowsy. She died within 20 hours of these changes. Blood, urine, and stool cultures on days 1 and 7 were negative. Initial agglutination titres to *S. typhi* O were negative. A blood culture taken on day 8 showed *S. typhi*.

The remaining 12 patients each spent at least 4 weeks in hospital and all had recovered clinically by 12 weeks.

**Poststreptococcal glomerulonephritis.** All these children presented with a history of oedema of less than one week’s duration and had hypertension and evidence of volume overload on admission. No patient had a temperature greater than 37.5°C. Serum C3 was <0.01 g/l in all patients on admission. Statistics from this hospital show that 93% of patients admitted with PSGN have C3 <0.01 g/l. All these patients recovered within 2 weeks, with blood pressure, blood urea, and electrolytes again normal.

Three patients had microscopic haematuria on discharge, but no evidence of schistosomiasis.

**Discussion**

Typhoid fever with classical features presents no difficulty in recognition and, in fact, in endemic areas can be correctly diagnosed on admission in about two-thirds of cases.³ However, when it presents atypically in the guise of one of its rare complications, diagnosis becomes difficult and appropriate treatment is delayed.

There are various renal complications of typhoid. Cystitis, pyelonephritis, and pyelitis have been described. Dehydration if not managed correctly may lead to acute tubular necrosis. Henke and Lubarch⁴ described the pathological findings in the kidneys of typhoid patients at necropsy as a diffuse toxic damage affecting the tubules and loops of Henle, with localised small cell infiltration of the interstitium. The glomeruli were generally spared in these cases. Scragg et al.¹ described 2 patients with pyelonephritis complicating typhoid, both of whom had focal interstitial pyelonephritis at necropsy.

Huckstep⁴ and Rolleston and Ronaldson⁵ found that typhoid nephritis did not differ clinically from PSGN. However, in children presenting with glomerulonephritis the distinction between streptococal and *S. typhi* disease can be made on clinical
glomerulonephritis together with estimation of complement (Table 1). Patients with typhoid nephritis usually have had oedema for prolonged periods before admission, are likely to be pyrexial with splenomegaly, and nearly always have a lower serum level of the third component of complement. If the rank sum test is applied to the C3 values the figures are statistically significant (P < 0.01). Serum complement values (C3, C4, factor B, and total haemolytic complement) have been shown in our laboratory to be normal in typhoid fever uncomplicated by glomerulonephritis (Table 2). We have no satisfactory explanation for the prolonged history of oedema. The insidious onset of oedema together with these complement changes may suggest a less vigorous immunopathological process than occurs in PSGN. It is notable that 2 children were admitted with features of typhoid fever and only later developed nephritis, thus offering no problems in diagnosis. Typhoid glomerulonephritis although uncommon, is not rare, occurring in 4% of children with typhoid fever in our wards. 6 Gulati et al. 7 found a 2% incidence in adults, while Huckstep 4 reported it to be 1%. The overall mortality of typhoid fever in children seen during the last 16 years in our unit has been between 3 and 8%. 6 The mortality of typhoid complicated by glomerulonephritis was 20% in this study. However, 2 of the 3 deaths could not be directly attributed to glomerulonephritis. The mortality in mainly adult patients with typhoid glomerulonephritis varies between 23 and 30%. 4 8

Scragg et al. 1 were not convinced that typhoid caused nephritis and suggested a double pathology. There is little doubt that patients in this study (with the possible exception of the one typhoid child with a positive ASOT) had typhoid nephritis and that this disease was not due to streptococci. The suggestion that typhoid nephritis exists as an entity is supported by the data of Sitprija et al. 9 who performed renal biopsies on 3 adults with typhoid. They found evidence of possible immune complex glomerulitis in all 3 cases with Salmonella Vi antigen on the glomerular capillary wall.

We felt that routine renal biopsies were not justified in typhoid fever with nephritis. The histopathological changes noted in one child in whom we performed a biopsy were similar to the diffuse proliferative lesions noted by Sitprija et al. 9

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References


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Table 1 Features useful in distinguishing poststreptococcal from typhoid glomerulonephritis

<table>
<thead>
<tr>
<th>History of oedema</th>
<th>Poststreptococcal (n = 15)</th>
<th>Typhoid (n = 15)</th>
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<tr>
<td>&gt; one month</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>One week or less</td>
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<td>4</td>
</tr>
<tr>
<td>Pyrexia &gt; 37.5°C</td>
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<td>12</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>ASOT &gt; 200 U/l</td>
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<td>1</td>
</tr>
<tr>
<td>C3 (mean g/l)</td>
<td>&lt;0-01</td>
<td>0-56</td>
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</tbody>
</table>

(P < 0-01)

Table 2 Serum complement levels in typhoid glomerulonephritis compared with PSGN

<table>
<thead>
<tr>
<th>C3</th>
<th>C4</th>
<th>Factor B</th>
<th>Total haemolytic complement</th>
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<td>57-7</td>
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<td>24-5</td>
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<tr>
<td>Controls</td>
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