Poststreptococcal nephritis—a rare disease?

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Meadow, S. R. (1975). *Archives of Disease in Childhood*, 50, 379. **Post-streptococcal nephritis—a rare disease?** Forty-three children presenting with acute nephritis were studied for evidence of preceeding streptococcal infection. They were compared with a group of control children of similar age. Two-thirds of those with nephritis gave a history of a preceeding respiratory infection (compared with one-third of the controls). A significant rise of antistreptolysin O titre occurred in only 16 children with nephritis and within this minority several did not show a fall of serum C3 level. It is probable that only one-third of the children with acute nephritis had poststreptococcal glomerulonephritis. Poststreptococcal glomerulonephritis is no longer the main cause of childhood acute nephritis in the Leeds area. There may be many different aetiological factors and this diversity calls for more rigorous investigations and a more guarded prognosis.

Poststreptococcal glomerulonephritis is generally stated to be the most common cause of acute nephritis in childhood, but in recent years fewer children have been seen with acute nephritis, and in those who have presented a streptococcal aetiology has often been uncertain. Therefore, a prospective study was begun of all children presenting at hospitals in the Leeds area with acute nephritis, with particular reference to streptococcal aetiology.

Streptococcal aetiology can be inferred from a combination of the following features: history of preceeding sore throat (classically 1–2 weeks before onset of nephritis); isolation of a β -haemolytic streptococcus from pharyngeal swab; sequential rise of antistreptolysin O (ASO) titre, and depression of the C3 complement level. Of these features, the last is probably the most pathognomic of acute streptococcal glomerulonephritis (Lange, Wasserman, and Slobody, 1960; West, Northway and Davis, 1964; Popovic-Rolovic 1973).

Patients studied

All the children developed acute nephritis during the 4-year period from April 1970–April 1974, and were seen at Leeds hospitals at that time. For inclusion in the study, they had to have sudden onset of haematuria plus at least two of the following features: hypertension (diastolic blood pressure > 80 mmHg); azotaemia (blood urea > 40 mg/100 ml); facial oedema; oliguria. Any child who had or who developed a

primary systemic condition such as systemic lupus erythematosus or Henoch-Schönlein syndrome was excluded. Children with evidence of pre-existing renal disease were also excluded.

The 43 children included 24 boys and 19 girls. Their ages ranged from 9 months to 14½ years. 28 children lived in the Greater Leeds area (population one million), but 15 lived in other areas of Yorkshire and were referred by regional paediatricians. The 28 local children are thought to represent all the children in the Leeds area presenting at hospital with acute nephritis during the 4-year period, and include cases of both mild and severe nephritis. The 15 referred children were mainly children with severe nephritis. The children with acute nephritis were compared with a similar number of control children. These were chosen on the basis of the next child of comparable age who presented at hospital requiring a venepuncture. Therefore, the controls are matched for season of the year and age only.

Methods

The parents were asked if their child had had a sore throat or respiratory illness in the preceeding month. All except 2 children had a throat swab taken within 3 days of presentation at hospital. The swabs were cultured on both blood agar and tellurite. In the first 2 years they were cultured also on heated blood agar ('chocolate'), and for the latter period on blood agar with added crystal violet, to promote streptococcal identification.

ASO titre was measured at least twice in all the patients except 5 who had a single measurement. The control group had a single estimation of ASO titre. The measurements were done by the standard method using Burroughs Wellcome solutions (Gooder and

Williams 1959). The third component of complement (C3) was measured as B₁C/B₁A globulin by a radial diffusion method (Mancini, Carbonara, and Heremans, 1965). All except 6 of the patients had two or more such estimations of which at least one was performed within 3 weeks of onset. 6 patients and most of the controls had a single C3 estimation only.

All the children were investigated at Leeds hospitals, but a minority of the results of the referred patients includes investigations performed at the first admitting hospital.

Results

ASO titre. ASO titre rose to above 1:200 in 16 out of 43 children with acute nephritis. It was found to be raised in 7 of the control children also (Fig. 1).

FIG. 1.—ASO titre in the two groups of children. Only the highest titre is recorded for those who had 2 or more estimations. Levels above the dotted line indicate previous streptococcal infection.

C3 complement. Serum C3 was significantly depressed (i.e. <80 mg/100 ml) in 10 of the children with acute nephritis and in one control (Fig. 2). In those children with acute nephritis and a lowered C3 concentration the complement concentration returned to normal within 10 weeks (Fig. 3). 9 of the 10 children with a depressed C3 concentration also had a significantly raised ASO titre.

Throat swab. β -Haemolytic streptococcus was isolated from 6 children with nephritis and from 2 controls.

Preceding infection. A history of a respiratory tract infection during the preceding month was given for 29 children with nephritis and for 14 of the controls. One child with nephritis had had impetigo 2 weeks earlier.

The results are summarized in the Table. The proportion of positive findings in the acute nephritis group was similar in the nonselected local children and in the selected referred children.

FIG. 2.—Serum C3 concentrations. The number of children with C3 concentrations in each 20 mg range is shown, and is the lowest recorded estimate for each child. The dotted line represents the lower limit of normal.

FIG. 3.—Serum C3 concentrations in the 10 children with initial low levels, during the first 9 weeks after onset of nephritis.

TABLE

Incidence of features suggesting streptococcal infection in children with acute nephritis compared with a similar number of control children

	Acute nephritis (43)	Controls (43)	P
Preceding respiratory illness	29	14	<0.01
β -haemolytic streptococcus	6	2	=0.02
ASO titre raised	16	7	<0.01
C3 depressed	10	1	<0.01

Discussion

Of 43 children with acute nephritis a streptococcal aetiology could not be shown in the majority. If low C3 complement concentration is taken as the

ultimate criterion, only 10 children satisfied that criterion. If raised ASO titre is taken as the most reliable indicator, then 16 children satisfy the criterion. Whatever combination of the criteria studied is taken, it seems unlikely that streptococcal infection was an aetiological factor in more than 16 of these children. Therefore it is important to allow for the limitations of each criterion.

ASO titre does not identify all previous streptococcal infections. It is alleged to miss 10–20% of such infections unless it is combined with a number of other serological tests such as anti-DNAseB and anti-DPNase (McCarty, 1954). The ASO titre itself may be lowered in an inconsistent and unpredictable way by penicillin therapy (Kilbourne and Loge, 1948; Weinstein and Tsao, 1946). Nearly half the children had had previous antibiotics and in some of them the ASO titre may have been misleadingly low. Despite these limitations, the ASO titre was the single most useful and reliable indication of preceeding streptococcal infection at the time of the study, though it may be replaced in future by the recently developed Streptozyme test (Silverman *et al.*, 1974). The low yield of streptococci from throat swabs is not surprising in view of the 2- to 3-week interval between respiratory illness and throat swab culture, and also the fact that many children had had antibiotic therapy. Serum C3 complement concentration is generally believed to be a reliable test, and to be depressed in the first 4 weeks of illness in over 90% of children with poststreptococcal glomerulonephritis (Cameron *et al.*, 1973). Yet only 10 children in this series had low C3 concentrations.

Allowing for the limitations of the methods, it seems that in these 43 children with acute nephritis, preceeding streptococcal infection could have occurred in a minimum of 10 (23%) and a maximum of 20 (45%). The cause of the acute nephritis in the remainder is uncertain. In 6 the illness followed an identifiable virus infection; in the rest some had a history of a preceeding respiratory infection and some did not. Though the children who were severely ill had detailed investigations, including renal biopsy, these results have not been included in this paper because they do not shed light on the cause of the nephritis. There is nothing specific about the appearance of poststreptococcal glomerulonephritis on routine light microscopy; the same sort of diffuse proliferative glomerulonephritis may be seen after a variety of different causes.

The survey included hospital cases only. The hospital services in the Leeds area are such that it is highly unlikely that a child with an acute illness

including haematuria would go to a hospital outside Leeds. However, the survey remains one limited to hospital patients rather than being a comprehensive community survey which might disclose more children with mild nephritis.

It might be suggested that during the period of the study there was endemic in the area a micro-organism which caused acute nephritis; however, no specific organism was identified. There is no reason to suspect that the aetiology of acute nephritis in the Leeds area is markedly different from other urban areas of Britain since discussion with colleagues suggests that in many other areas of Britain poststreptococcal nephritis has become rare (as has rheumatic fever). It is difficult to know whether this is due to lower prevalence of streptococcal infection in the community, decreased virulence of the organism, or decreased susceptibility in the host.

If poststreptococcal nephritis is no longer the main cause of acute nephritis in childhood, then we must alter our textbooks, as at present nearly all of them state dogmatically that acute nephritis is caused by a preceeding streptococcal infection. Secondly, and more importantly, we may need to be more rigorous in the investigation of children with acute nephritis and more guarded in our prognosis. Until careful long-term follow-up studies are available for children with 'modern' acute nephritis, it is probably unwise to assume that they will necessarily follow the same favourable course as 'old-fashioned' poststreptococcal nephritis.

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