The Role of Streptococcal Infection in Henoch–Schönlein Purpura

Henoch–Schönlein purpura (HSP) is the most common vasculitis of childhood characterized by purpuric rash, articular, gastrointestinal and renal involvements. In contrast to its well-defined clinical manifestations and prognosis, the etiology of the disease remains obscure.[1–3] Epidemiological studies report that the disease may follow an upper respiratory tract infection.[1,4–7] This coexistence cannot be proved by controlled studies and a specific infectious agent is rarely identified.[1,4–7]

Streptococci are the most common bacterial agents causing upper respiratory infections in childhood.[8] Few studies have examined the role of streptococcal infections in the pathogenesis of HSP.[5–7] The aim of this study was to investigate the possible role of streptococcal infections in the etiopathogenesis of HSP using different types of anti-streptococcal antibodies [anti-streptococcal DNase B (ADNB) and anti-streptococcal hyaluronidase (AHD)] in addition to throat culture and antistreptolysin O (ASO) titers.

The study was conducted in a prospective manner. All children studied were clustered into three main groups, as seen in Table 1. A diseased control group was made up of 10 acute rheumatic fever (ARF) and acute post-streptococcic glomerulonephritis (APSGN) patients whose disease had a well-defined relationship with streptococcal infections. All studied patients were in the acute phase of their disease. In all patients and control subjects throat cultures and serum samples for ASO, ADNB, and AHD detection were obtained.

ASO, ADNB, and AHD levels were determined using Turbiquant ASL, ADNB and AHD reagents with ELISA and turbimetric methods in Pediatric Biochemistry Laboratory.

TABLE 1
Demographic characteristics of the study groups

Study group	*n*	Female/male ratio	Mean age at investigation (years)
Henoch–Schönlein purpura group	35	12/23	6.77 ± 2.25 (range 3–11.5)
Healthy controls	20	10/10	7.87 ± 2.1 (range 3.5 – 11)
Diseased controls	10	4/6	10.53 ± 3 (range 5.5 – 15)
Total	57	22/33	

All anti-streptococcal antibodies levels of all subjects are shown in Table 2.

All anti-streptococcal antibody titers in the HSP group were found to be higher than in the healthy control group. The differences between ASO and AHD levels were also statistically significant ($p < 0.001$ and $p = 0.012$, respectively).

Throat cultures in five of 35 (14.2 per cent) patients with HSP were positive for group A streptococcus, while in the healthy controls only one (5 per cent) culture positivity was detected. The difference between the two groups was not statistically significant ($p = 0.27$, Fischer's χ^2).

When patients with HSP were compared with the patients who had ARF and APSGN; all anti-streptococcal antibody levels of the HSP group were lower than the diseased control group. Only the

TABLE 2
The results of the anti-streptococcal antibody levels and throat cultures in all study groups

Group	ASO (Ul/ml)	ADNB (Ul/ml)	AHD (Ul/ml)	Throat culture Positive/negative (%)
Henoch–Schönlein purpura group	415 (47–1650)	75 (45–1650)	150 (40–1650)	5/35 (14.2%)
Healthy controls	107 (47–983)	150 (50–300)	50 (50–400)	1/20 (5%)
Diseased controls	669.5 (354–1480)	225 (150–400)	400 (150–600)	1/10 (10%)

Values are median (range).

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difference between the ASO levels was statistically significant ($p = 0.028$).

In the diseased control group only one patient (10 per cent) had throat culture positivity for group A streptococci. There was no significant difference between the two groups according to throat culture positivity ($p = 0.54$).

In patients with HSP, levels of ASO and AHD were statistically higher than those of the healthy control subjects. Although ADNB levels were also higher than those of the controls, this was not statistically significant. This result may be due to the lower anti-streptococcal response in HSP. There was no statistically significant difference between the HSP group and the healthy control subjects with regard to the positivity rate of throat cultures for group A streptococci. This observation agrees with the report by Al-Sheyyab, *et al*.[6] who also observed similar throat culture positivity rates between HSP and the control group. This observation led to the hypothesis that HSP could result from an immunological insult by the organism rather than the direct effect of the organism during acute infection.

In conclusion, the higher levels of streptococcal markers in HSP patients than in healthy subjects led to the hypothesis that streptococcal infections could have a role in the etiology of the disease. Since patients who had ARF and APSGN (although the sample size was low) were found to have higher levels of streptococcal markers than those of HSP patients, we concluded that for pathogenesis of HSP, a relatively small amount of streptococcal insult could be sufficient. Our results also demonstrated that environmental and host factors, or other infectious agents, could play a role in the pathogenesis in addition to streptococcal infections.

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Minimal Electron Microscopic Changes of the Jejunal Mucosa Following Cows' Milk Provocation

Histological changes of the jejunal mucosa following cows' milk provocation, is accepted as the objective criteria for the diagnosis of cows' milk allergy (CMA).[1] In our previous studies we noted that a subset of infants following challenge, clinically tolerated cows' milk protein (CMP) and had normal histological appearance of the jejunal mucosa, but had depressed mucosal oligosaccharidases and impaired xylose absorption.[2]

We proposed that these infants probably had subcellular changes in the mucosa that were not detected histologically. We are not aware of any studies on the subcellular changes of the enterocytes in small bowel mucosa of infants with normal histology following CMP challenge. Here we report EM findings in three infants who had normal histology following cows' milk provocation.

We studied three infants aged 19–23 weeks admitted with persistent diarrhoea of 9–12 days duration. All three infants were bottle-fed from birth. Prior to referral to our center the infants had been placed unsuccessfully on low lactose and soy-based formula.

At the onset of illness they had vomiting but no fever. They passed six to seven watery stools per day. The stools had mucus but no blood. They had mild abdominal distension and marked perianal excoriation. The stools tested positive for reducing sugars in all three infants and positive for *Salmonella* organisms in one.

After rehydration with rice-starch oral rehydration solution, they were regraded to their respective pre-illness cows' milk formula. All three infants failed to tolerate successively the CMP formula, low-lactose CMP formula, and soy-based formula. However, they tolerated and thrived well on a protein-hydrolysed hypoallergenic formula (Pregestimil, Mead-Johnson). They were clinically presumed to have CMA and were maintained on

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