INCREASED SERUM IgD CONCENTRATIONS IN CHILDREN WITH HENOCH–SCHÖNLEIN PURPURA

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SUMMARY

Serum IgD concentrations were measured in 39 children with Henoch–Schönlein purpura (HSP) and 40 control children by means of radial immunodiffusion. Serum IgG, IgA and IgM concentrations in the HSP patients were measured by nephelometry. The geometric mean IgD concentration in children with HSP (16.7 μg/ml) was significantly higher than in control children (9.1 μg/ml; P = 0.03). Serial testing in 10 HSP patients revealed no significant change in IgD concentrations over periods ranging from 1 to 12 months. There was no relationship between IgD and IgA concentrations in the HSP patients. Nineteen of the 39 HSP patients (49%) had nephritis. The mean IgD concentration in patients with nephritis (10.7 μg/ml; P = 0.03). Serial testing in 10 HSP patients revealed no significant change in IgD concentrations over periods ranging from 1 to 12 months compared to control values, but was significantly lower than the mean IgD level in the remaining 20 patients who did not have nephritis (25.4 μg/ml; P = 0.02). These results indicate that serum IgD levels are increased in children with HSP who did not have nephritis. IgD concentrations in patients with nephritis were similar to levels in control children.

KEY WORDS: IgD, Henoch–Schönlein purpura, Nephritis.

HENOCH–SCHÖNLEIN purpura (HSP) is a systemic vasculitis that primarily affects children. The dominant clinical manifestations include cutaneous purpura, arthritis, abdominal pain and nephritis. The aetiology is unknown, but it is clear that IgA plays an important role in the immunopathogenesis of HSP. HSP is associated with increased serum IgA concentrations, IgA-containing immune complexes, IgA rheumatoid factor, and IgA deposition in vessel walls and renal mesangium [1]. Although there are two subclasses of IgA, it is noteworthy that HSP is associated with abnormalities involving only IgA1, but not IgA2 [2, 3]. Despite extensive literature with respect to IgA, there is very little information concerning IgD concentrations in HSP. Interest in IgD derives from the fact that IgA1 and IgD are the only immunoglobulin isotypes that contain O-linked oligosaccharides in the hinge region [4, 5]. Moreover, recent studies demonstrated alterations in the O-linked oligosaccharides of IgA1 in patients with HSP [6]. The present study was performed to determine serum IgD concentrations in children with acute HSP.

PATIENTS AND METHODS

Study subjects

The patients were 39 children (19 boys and 20 girls) with acute HSP, ranging in age from 2 to 12 yr (mean ± 1 s.d. of 6.3 ± 2.6 yr). The diagnosis of HSP required the presence of typical cutaneous purpura plus one or more major manifestations. Thirty-five patients had arthritis, 32 had abdominal pain, 13 had gastrointestinal bleeding and 19 had nephritis. Nephritis was defined as the presence of gross or microscopic haematuria (>5 red blood cells per high-power microscopic field), with or without proteinuria (protein concentration > 30 mg/dl). Controls were 40 healthy children ranging in age from 2 to 15 yr (mean ± 1 s.d. of 7.8 ± 4.2 yr). Sera were stored at −20 °C until tested.

Immunoglobulin concentrations

Serum IgD concentrations were measured by radial immunodiffusion (The Binding Site Inc., San Diego, CA, USA). Serum IgG, IgA and IgM concentrations in the HSP patients were measured by nephelometry. Values beyond 2 s.d. from the mean for age were considered abnormal.

Statistical analyses

Because of a non-Gaussian distribution of serum IgD concentrations, the results were log transformed and statistical analyses were performed on the logs of the data. Student’s t-test was used to compare the geometric mean IgD levels between groups. The relationship between IgD concentrations and the age of patients and controls was measured by the Spearman rank correlation.

RESULTS

The geometric mean IgD concentration in children with HSP (16.7 μg/ml) was significantly higher than that in control children (9.1 μg/ml; P = 0.03). There was no significant correlation between IgD levels and the age of HSP patients or controls. Serum samples from 10 HSP patients were available for serial testing. IgD concentrations did not change significantly over periods ranging from 1 to 12 months compared to values obtained during the acute phase of the illness, despite resolution of symptoms in 8/10 patients (Fig. 1).

Serum IgG and IgM concentrations were normal in...
Increased serum IgA concentrations have been reported in ~50% of children with acute HSP [7]. In the present study, 24 of 39 patients (62%) had serum IgA levels >2 s.d. above the mean for age. There was no relationship between IgD and IgA concentrations in patients with HSP.

Nephritis occurs in 20–50% of children with HSP, and it is virtually the only manifestation of the syndrome that is prone to result in chronic problems [1]. Thus, the long-term prognosis of HSP is intimately linked to the presence or absence of nephritis. Unfortunately, there are presently no markers that predict which patients with HSP are at risk of developing nephritis. In the present study, 19 patients (49%) had nephritis. Interestingly, HSP patients with nephritis had significantly lower IgD levels than patients without nephritis. In fact, IgD concentrations in patients with nephritis were not significantly different from IgD levels in control children. It is possible that urinary losses of IgD could account for the lower levels in the patients with nephritis, but this is unlikely since there was no significant difference in IgD concentrations in the 10 patients with proteinuria (12.3 μg/ml) compared to the nine patients with haematuria alone (8.9 μg/ml). Urinary immunoglobulin concentrations were not measured, however. The reasons for the lower IgD levels in HSP patients with nephritis will require further study.

IgD was discovered in 1965 [10], but the role of IgD in the defence against infection or the regulation of the immune response remains unclear. Moreover, the factors influencing the rate of production and catabolism remain largely unexplored. Increased serum IgD levels have been reported in a number of conditions, including atopic diseases, AIDS, malignancy and chronic infections [9, 11, 12]. Marked elevations of serum IgD concentrations are characteristic of the hyperimmunoglobulin D syndrome. Interestingly, the vast majority of patients with hyperimmunoglobulin D syndrome also have increased serum IgA levels [13]. The dominant features of this rare syndrome include periodic fever, abdominal pain, arthralgia, lymphadenopathy and skin rash [13]. Vasculitis is common [14], and typical HSP has been reported in two children with hyperimmunoglobulin D syndrome [15]. The IgD concentrations in the present study involving children with HSP were far below those reported in patients with hyperimmunoglobulin D syndrome [14].

The present report indicates that HSP should be included in the list of conditions associated with elevated IgD levels. IgD levels should be examined in other

**TABLE I**

<table>
<thead>
<tr>
<th>IgD concentration (μg/ml)</th>
<th>Controls (N = 40)</th>
<th>HSP patients (N = 39)</th>
<th>With increased serum IgA (N = 24)</th>
<th>With normal serum IgA (N = 15)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>9.1 (6.1–13.6)</td>
<td>16.7 (11.5–24.3)†</td>
<td>17.0 (10.5–27.4)</td>
<td>16.2 (8.2–31.9)</td>
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<tr>
<td></td>
<td></td>
<td>10.7 (5.6–20.6)‡</td>
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<td>25.4 (17.9–35.9)</td>
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*Values are expressed as geometric means with 95% confidence intervals in parentheses.
†P = 0.03 compared to controls.
‡P = 0.02 compared to HSP without nephritis.

33 (85%) and 34 (87%) patients, respectively. By contrast, serum IgA concentrations were increased in 24 of 39 (62%) HSP patients. There was no relationship between IgA and IgD levels; the geometric mean concentration of IgD was 16.9 μg/ml in the 24 patients with increased serum IgA levels, and 16.2 μg/ml in the 15 patients with normal IgA levels (Table I).

Nineteen of the 39 HSP patients (49%) had nephritis. Fifteen of the 19 patients with nephritis had microscopic haematuria and four had gross haematuria. Ten of the 19 patients with nephritis had proteinuria. The geometric mean concentration of IgD in patients with nephritis (10.7 μg/ml) was significantly lower than the mean IgD level in the remaining 20 HSP patients who did not have nephritis (25.4 μg/ml; P = 0.02).

**DISCUSSION**

Overwhelming evidence indicates that IgA, particularly IgA1, plays a critical role in the immunopathogenesis of HSP [1–3]. Nevertheless, the factors accounting for increased serum IgA concentrations and tissue deposition of IgA in HSP remain unknown. Recent studies have demonstrated alterations in the O-linked oligosaccharides of IgA1 in patients with HSP [6]. IgA1 and IgD are the only immunoglobulin isotypes that contain O-linked oligosaccharides in the hinge region [4, 5]. To date, however, there has been very little information concerning IgD in HSP.

In the present study, serum IgD concentrations were increased in children with acute HSP compared to control children. Many previous studies have examined serum immunoglobulin levels in patients with HSP, but very few have provided information concerning IgD. In two previous studies, IgD concentrations were reported to be normal in children with HSP [7, 8]; however, neither study measured IgD in control children. In agreement with other reports, there was no correlation between IgD levels and age of the children in the present study [9]. IgD concentrations did not change significantly over time, despite resolution of symptoms.
vasculitis syndromes associated with nephritis in order to confirm the present observation that IgD levels were lower in HSP patients with nephritis compared to those with no renal involvement.

REFERENCES