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Henoch-Schönlein syndrome and selective IgA deficiency

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SUMMARY A 9 year old girl presented with clinical manifestations of Henoch-Schönlein syndrome and macroscopic haematuria. Laboratory investigations showed selective IgA deficiency and renal biopsy showed mesangial proliferative glomerulonephritis with diffuse granular deposits of C3 on immunofluorescence. IgA deposits were absent.

It is well documented that patients with IgA deficiency have an increased incidence of immune mediated diseases.¹ As far as we know, however, an association between selective IgA deficiency and the clinical picture of Henoch-Schönlein syndrome has not been previously reported. This is understandable since the syndrome is believed to be caused by deposition of IgA-containing immune complexes.² We describe an unusual case of a girl with selective IgA deficiency who presented with clinical features closely resembling Henoch-Schönlein syndrome which we believe represented an unusual variant of acute post-streptococcal glomerulonephritis.

Case report

In April 1983 a 9 year old girl presented with a mildly sore throat and low grade fever of three days' duration. One week later she had a transient erythematous rash on her face, buttocks, and legs and polyarthritis affecting the ankles, knees, and wrists; the joints were swollen, hot, and red. Over the next few days she developed diffuse colicky abdominal pain, a petechial rash on the legs, and macrohaematuria and was admitted to hospital. She was not feverish on admission and her blood pressure was 115/70 mm Hg. Family and personal

history were unremarkable; in particular there was no history of recurrent respiratory or other infections. Physical examination showed crops of non-pruritic rust coloured macules/papules and purpuric petechiae on the ankles and calves. There was diffuse abdominal tenderness. Joint examination was normal. Laboratory investigations were as follows: haemoglobin 11 g/dl, white cells $24.5 \times 10^9/l$ with 82% neutrophils, erythrocyte sedimentation rate 63 mm in the first hour, serum creatinine 70.7 $\mu\text{mol/l}$ (0.8 mg/100 ml), creatinine clearance 88 ml/minute/1.73 m², albumin 2.6 g/dl. Urine analysis showed 30 to 40 red cells per high power field and slight proteinuria (0.4 g/24 hours); the antistreptolysin 0 titre was positive at 1/1600; C3, C4, and CH50 values were normal. Serum IgG was 2297 mg/dl, IgM 237 mg/dl, while IgA was repeatedly undetectable in serum, saliva, and nasal secretions (serum IgA less than 5 mg/dl, secretory IgA less than 0.5 mg/dl). Determination of IgG subclasses by monoclonal antibodies (kindly provided by Dr Jefferies, Birmingham) failed to show any IgG subclass deficiency: cell mediated immunity, determined by E rosette formation and in vitro mitogen responsiveness, was normal. Rheumatoid factor, hepatitis B antigen, and circulating cryoglobulins were absent, while antinuclear antibodies and anti-double strand DNA antibodies were positive in low titres. Skin biopsy showed a leucocytoclastic vasculitis with vascular deposition of C3 and fibrinogen; IgA, IgG, and IgM were absent. Percutaneous renal biopsy showed segmental and focal proliferation of mesangial cells. On immunofluorescence, diffuse granular deposits of C3 and faint deposits of IgG with the same pattern were present, while IgA and IgM were absent.

The child was given no medication except a course

of penicillin. The clinical symptoms rapidly subsided, although microscopic haematuria lasted several months. Anti-double strand DNA antibodies became negative over the following weeks, while antinuclear antibodies have remained positive in low titres. After 15 months of follow up the clinical manifestations have not recurred; repeated tests have confirmed the absence of IgA in her serum.

Discussion

The clinical presentation in our patient was highly suggestive of Henoch-Schönlein syndrome. Complete IgA deficiency, however, and the lack of IgA in skin vessels and glomerular tufts make this diagnosis untenable. Other conditions in which glomerulonephritis and vasculitis may be associated such as hepatitis B, polyarteritis, essential mixed cryoglobulinaemia, and systemic lupus erythematosus were excluded by the clinical and laboratory findings—systemic lupus erythematosus in particular because of the clinical course, normal complement values, renal biopsy findings, and spontaneous resolution of anti-double strand DNA antibodies. Moreover it is well known that IgA deficient patients may have antinuclear antibodies and even anti-double strand DNA antibodies in serum.¹

In our patient the histological and immunohistological findings of the renal biopsy were similar to those observed in resolving acute post-infectious glomerulonephritis. These together with the preceding sore throat, the raised antistreptolysin O titre, and the clinical course strongly suggest that our patient had an unusual variant of acute post-streptococcal glomerulonephritis characterised by mild systemic vasculitis. Normal complement values, although atypical, are still compatible with the diagnosis since 15% of children with classic post-streptococcal glomerulonephritis have a normal C3 value.³ Indeed the association with extra-renal vasculitis has been reported in a few patients,⁴⁻⁵ and in two the clinical presentation mimicked many of the features of Henoch-Schönlein syndrome;⁵ severe renal involvement, a marker of the seriousness of the underlying immune complex disease was, however, always present. Our patient, on the contrary, presented with mild renal involvement. It was discovery of the IgA deficiency and circulating anti-double strand DNA antibodies that prompted more careful diagnostic tests without which a diagnosis of Henoch-Schönlein syndrome would probably have been made. In fact, it is not our usual policy to perform skin or kidney biopsy when clinical diagnosis seems obvious and renal involvement not severe.

It is possible that in our patient the absence of functioning mucosal immunity played a role in the vasculitis, which was not related to the severity of the immune complex disease. Henoch-Schönlein syndrome has been linked with a variety of infective agents and other factors (such as food allergy, drugs, and insect bites),² and in about a third of patients, as in our case, an appreciably raised antistreptolysin O titre has been observed² suggesting an aetiological role for streptococcus. The syndrome is considered to be secondary to vascular deposition of IgA-containing immune complexes. Our patient, however, had the clinical picture of Henoch-Schönlein syndrome despite selective IgA deficiency. This may suggest that in Henoch-Schönlein syndrome IgA deposition is an epiphenomenon rather than a cause. We do not believe, however, that our finding is sufficient to impugn the current theory that a clinical picture of Henoch-Schönlein syndrome is secondary to vascular deposition of IgA-containing immune complexes; it shows rather that the syndrome should be regarded as a true syndrome which can depend on different pathogenetic mechanisms. For example, one may ask how often Henoch-Schönlein syndrome occurring after a streptococcal infection is the expression of a pathogenesis unrelated to IgA deposition.

Meadow recently hypothesised that some children with Henoch-Schönlein syndrome who do not present with the characteristic rash may escape correct diagnosis, since when the skin is not affected this diagnosis is rarely suspected.² On the other hand, our patient suggests that some children presenting with the typical clinical picture of the syndrome may have a vasculitis unrelated to IgA deposition in the vessels.

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