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Brief report

IgA nephropathy and idiopathic thrombocytopenic purpura with splenectomy: a case report

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Abstract. A 14-year-old boy who had had a splenectomy at the age of 2 years for idiopathic thrombocytopenic purpura, suffered from IgA nephropathy. Serum IgA and IgE levels were elevated and low levels of circulating immune complexes were detected. Splenectomy may play a role in the pathogenesis or susceptibility to IgA nephropathy by means of decreased clearance of circulating immune complexes or impaired immune regulation, such as increased IgA synthesis.

Key words: Splenectomy – IgA nephropathy – Immune complexes – Idiopathic thrombocytopenic purpura – Reticuloendothelial system

Introduction

Glomerular IgA deposition is well docomented in several systemic diseases. We report here a patient with IgA nephropathy (IgAN) who had undergone splenectomy 12 years earlier for idiopathic thrombocytopenic purpura (ITP).

Case report

A Japanese boy of 1 year 2 months was referred to our clinic for a tendency to bleed, and the diagnosis of ITP was made. Prednisolone therapy was initiated at a daily dosage of 2 mg/kg, with a partial response. However, splenectomy was performed at 2 years because of refractory ITP. After splenectomy the platelet number was maintained at more than 110,000/mm^3.

At 14 years, 12 years after the splenectomy, urinalysis as part of the school screening programme revealed that he had haematuria and mild proteinuria. Prior to this his annual urinalysis had shown no abnormalities. On admission, physical examination revealed systemic atopic dermatitis and a normal blood pressure. Laboratory investigation revealed: red blood cell count 417×10^4/mm^3, haemoglobin 11.3 g/dl, white blood cell count 10,200/mm^3 with an eosinophilia of 7%, platelets 175,000/mm^3, serum creatinine 1.3 mg/dl and urea nitrogen 23 mg/dl. Normal values were obtained for total protein, albumin electrolytes, transaminases and alkaline phosphatase. The anti-streptolysin O titre and platelet-associated IgG were within the normal ranges. Urinalysis revealed mild proteinuria and a urinary sediment with many erythrocytes, some leucocytes and red cell casts. Urinary excretion of protein was 0.4 g/24 h.

Renal biopsy findings

Light microscopy revealed diffuse mesangial hypercellularity, focal segmental mesangial sclerosis and adhesion of glomerular tufts to Bowman's capsule; Fibrocellular crescent formation was observed in 6 of 38 glomeruli. Immunoflourescence studies revealed diffuse mesangial depositis of IgA and C3 associated with mild deposition of IgM.

Electron microscopy showed small electron-dense deposits in the mesangial region; the glomerular basement membrane was almost intact. The diagnosis of IgAN was made.

Immunological studies

The serum IgG level was 1,580 mg/dl (normal range 770–1,550 mg/dl), IgA 447 mg/dl (normal 76–376 mg/dl), IgM 39 mg/dl (normal 47–217 mg/dl) and IgE 536 IU/ml (normal $<$103 IU/ml). Complement components (C1q, C4, C3 and C5) were within the normal range. Cryoglobulins were not detected. Analysis of peripheral mononuclear cell subpopulations by fluorescence-activated cell sorter showed: mature T cells (CD3) 42.4%, helper T cells (CD4) 29.2% (normal range 40%±8%), suppressor T cells (CD8) 14.4% (normal 27%±6%), pan B cells (CD20) 19.9% (normal 14%±5%), monocytes/granulocytes (OKM1) 31.4% and HLA-DR (OKla1) 3.8%. An anti-C3d enzyme immunoassay, using mouse anti-human C3d monoclonal antibody to react with the C3d component of immune complexes [1] detected low levels of circulating immune complexes (CIC). Precipitates of the serum (obtained with 4% polyethylene glycol) contained 455 mg/dl IgG, 32 mg/dl IgA and 39 mg/dl IgM as measured by single radial immunodiffusion.

Discussion

Glomerular IgA deposits are well documented in several systemic diseases, such as anaphylactoid purpura and liver

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cirrhosis. However, to our knowledge there is no report of IgAN with ITP, with or without splenectomy.

About half of the patients with IgAN have an elevated serum IgA level. Increased levels of monomeric IgA1 and IgA1-containing CIC have also been documented [2, 3]. The nephritogenic role of high levels of circulating polymeric IgA has been shown in the experimental model of "alcoholic" IgAN in the rat [4]. Hence, over-production of IgA could be an important factor in the pathogenesis of IgAN in the splenectomised patient. Drew et al. [5] showed that IgA synthesis was raised in peripheral blood mononuclear cells from splenectomised patients. Decreased numbers of suppressor T cells or increased numbers of primed B cells resulting from splenectomy [5], both of which were observed in our patient, could affect the regulation of IgA production.

It has been suggested that IgA deposits in the mesangium could be derived from the circulation, probably in the form of IgA-containing immune complexes which are often detectable in the sera of IgAN patients [6]. Experimental studies show that, when the uptake of immune complexes by organs of the reticuloendothelial system (RES) is reduced, the amount deposited in the glomeruli is correspondingly increased [7]. Several studies, using aggregated IgA [8] or mixed aggregates of IgA and IgG [3] have shown the defective clearance capacity of IgAN patients. The spleen is also a major organ of the RES. In our patient small amounts of immune complexes composed of mixed immunoglobulins were detected. In human volunteers the site of clearance of aggregated human IgG was predominantly the liver, and to a lesser extent the spleen (a liver: spleen uptake ratio of 230: 100) [9]. However, although this suggests a lesser role for the spleen, the clearance defect of immune complexes resulting from splenectomy could not be negligible because of the high density of C3b and Fc receptors in the spleen [10]. Splenectomy may affect this clearance mechanism and may promote glomerular injury. Further investigations (such as the presence of cofactors for glomerular injury) to evaluate the long-term effect of splenctomy on nephritogenicity.

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Literature abstract

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Treatment of renal anemia by subcutaneous erythropoietin in children with preterminal chronic renal failure

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Eleven children aged 0.6–17 years with preterminal chronic renal failure and anemia (mean serum creatinine concentration 4.8 mg/dl; mean hemoglobin concentration 7.9 g/dl) were treated with s. c. injections of recombinant human erythropoietin (EPO, initial dose 150 U/kg/week) over a mean period of 13 months. When a target hemoglobin concentration of 11.5–13.5 g/dl was reached, the dose was adapted. Iron deficiency was corrected. Hemoglobin concentration increased by >2 g/dl in all patients within 14–119 (mean 45) days. The last maintenance dose ranged between 75 and 300 (mean 133) U/kg/week. No major adverse effects were observed, except for hypertension which occurred in about half of the patients and necessitated interruption of EPO in one child with advanced renal failure. Additional antihypertensive drugs were given to five patients. Body height increased in two patients by 0.6 and 1.3 SDS/year, respectively. In six patients with a mean observation period of 14 months before and 16 months after the start of EPO, the mean slope of the reciprocal serum creatinine concentration curve improved slightly ($p = 0.05$). The proposed schedule appears to be safe for the treatment of renal anemia in most pre-dialysis patients. Frequent monitoring of hemoglobin, blood pressure, serum creatinine and ferritin is required.