Successful outcome using rituximab as the only immunomodulation in Henoch-Schönlein purpura: case report

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Abstract

In the current report, we describe a patient with moderate nephritis and severe skin Henoch Schönlein purpura (HSP) who has been treated with rituximab. Complete and sustained skin and renal remission resulted from the treatment. Thus, further studies are required to confirm the efficacy of rituximab as first-line treatment in HSP, and it might be an interesting new therapeutic option.

Keywords: Henoch Schönlein purpura; nephritis; rituximab; skin

Background

Henoch-Schönlein purpura nephritis is a rare kidney disease leading to end-stage renal disease in up to 30% of adult patients during long-term follow-up [1]. Management of Henoch Schönlein Purpura (HSP) remains controversial. In children, various treatment regimens have been proposed in cases of severe digestive involvement or nephritis, including corticosteroids, azathioprine, cyclophosphamide, cyclosporine and mycophenolate mofetil [2,3]. Results have been conflicting. A recent meta-analysis concluded that data for any intervention used to improve kidney outcomes are very sparse except for short-term prednisone and that there was no evidence of benefit of prednisone in preventing serious long-term kidney disease in HSP [4]. However, we recently suggested, in a prospective randomized trial, that the addition of cyclophosphamide provides no additional benefit for adults with severe HSP compared to steroids alone [5]. No other randomized study has been undertaken to evaluate the efficacy of any treatment modality. In fact, our knowledge of treatment of HSPN is quite limited. The efficacy of rituximab (RTX) in standard treatment-refractory chronic Henoch-Schönlein purpura has been recently reported in three children [6].

Case report

In November 2008, a 22-year-old man was admitted to our hospital to investigate purpuric lesions of the legs that appeared 1 week before.

He had no relevant medical history. He had no fever or abdominal pain. He complained of arthralgia of the knees and ankles with no clinical evidence of arthritis. Blood pressure was 130/75 mmHg. Laboratory tests showed haematuria (15 mm³), proteinuria (0.25 g/day) and a normal renal function (creatinine 87 μmol/L). Serum albumin was 43.2 g/dL and CRP 53 mg/L. Serologic tests for hepatitis B virus, hepatitis C virus, HIV were negative. Anti neutrophil cytoplasmic antibodies and antinuclear antibodies were negative. Skin examination showed a palpable purpura with
small necrotic and bullous lesions limited to the legs. Skin biopsy revealed a small-vessel neutrophilic vasculitis with IgA deposition, consistent with HSP. He was discharged with a symptomatic local treatment and 5 mg of ramipril. Four months later, he described four others episodes of rash. Skin examination showed some ulcerations on the legs, the largest of them measuring 7 cm associated with smaller necrotic and bullous lesions (Figure 1A). The palpable purpura extended to the arms and abdomen. Blood pressure was still normal. Laboratory tests showed persistent haematuria and increased proteinuria (1.1 g/day), serum creatinine was 95 μmol/L, albumin 44.9 g/L and CRP 51 mg/L. A renal biopsy was performed and revealed focal proliferative glomerulonephritis with a segmental crescent formation in 15% of the glomeruli (Figure 2A). The remaining glomeruli were either normal or exhibited minimal mesangial prominence. There was no interstitial fibrosis or infiltrates and no tubular necrosis. Blood vessels were normal. Immunofluorescence study showed mainly mesangial deposits of IgA and fibrin (Figure 2B).

The patient received, as a single therapy, only two doses of 1000 mg of RTX at 2-week intervals. Three months later, the patient noticed no new rash and the skin only showed scars (Figure 1B). He had no more haematuria or proteinuria and serum creatinine was 70 μmol/L, albumin 41.7 g/L and CRP 9 mg/L. Peripheral B lymphocyte levels were normal before RTX infusion (290 cells/μL); 4 weeks later they had decreased to 0 cells/μL and remained below the normal limit for 6 months (68 cells/μL).

He went back to work after 6 months of incapacity. Twenty-two months after treatment, he still showed complete and sustained renal and skin remission: blood pressure was 128/72 mmHg, serum creatinine was 75 μmol/L and there was no proteinuria or haematuria.

Discussion

To our knowledge, this is the first case report describing successful treatment of adult HSP with the B-cell-depleting antibody RTX as unique therapy. In the previous case reporting success of RTX, therapy with RTX had been initiated after the failure of steroids ± cyclophosphamide or azathioprine; all three children were being treated for
severe gastrointestinal involvement, one for nephritis and two for central nervous system vasculitis [6].

HSP is an immunoglobulin-A vasculitis that affects the small vessels. It is a multiorgan system disease that may include cutaneous purpura, arthralgia, acute enteritis and nephritis [7]. Most of the clinical trials to define the best treatment of HSP are conducted in severe forms of the disease, including digestive and renal involvement and the results are still conflicting [4]. Although retrospective studies suggest beneficial effects of some therapies, prospective randomized clinical trials proving treatment efficacy are scarce and inconclusive. As on the one hand, spontaneous complete recovery has been described even in the case of severe initial presentation and/or extended histological lesions and late evolution to chronic kidney disease has been reported with less severe initial symptoms on the other hand, the interpretation of treatment effect is difficult [8]. Concerning skin lesions, it is well documented that steroids are not effective or their effect only transient. Nevertheless, skin lesions can be very crippling and can alter significantly the patient's life quality.

IgA plays a central role in the pathogenesis of HSP. Levels of galactose-deficient polymeric IgA1 are commonly elevated in the serum of the patients, resulting from an increase in their production and a defect in their clearance. The pathogenesis of the nephropathy involves the deposition of this aberrant glycosylated IgA1 and/or of IgA1 immune complexes in the glomerular mesangium [9]. No study has been designed up to now to show drug efficacy on the production of IgA1 or GalNac-IgA1.

Our hypothesis that B-cell depletion with rituximab may reduce circulating IgA could be a promising new therapeutic approach in this disease. Although its biological functions have not been clearly defined, and its incapacity to deplete differentiated immunoglobulin-secreting plasma cells, an increasing number of clinical trials have reported the benefits of RTX in other forms of vasculitis and autoimmune disease [10] and recently in three children with standard treatment-refractory chronic HSP [6].

Our patient, who never received any previous immunosuppressive treatment or steroids, had responded dramatically to two pulses of RTX given as a single agent, without any clinical sign of nephritis 22 months later. No complications have been observed.

This case report suggests that the inhibition of IgA production might be a good approach to treat HSP and offers hope that RTX might also be efficacious in the treatment of severe renal forms of HSP and points out the need to conduct some further studies to evaluate its benefit.

Conflict of interest statement. None declared.

References


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