CASE REPORT

IgA vasculitis (formerly Henoch-Schönlein purpura) in an adult with systemic lupus erythematosus

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Accepted 28 August 2015

SUMMARY

We report a case of a 65-year-old man with systemic lupus erythematosus (SLE) and antiphospholipid syndrome, presenting palpable purpuric lesions, necrotic blisters and swelling ankles, after a previous tracheobronchitis episode. Laboratory data were remarkable for mild proteinuria and imaging studies were normal. A skin biopsy showed IgA deposits on superficial dermal capillaries and IgA vasculitis (IgAV) (former Henoch-Schönlein purpura) was assumed. The patient was treated with colchicine, deflazacort and azathioprine, but as a regression in the purpuric lesions was noted, a decline in renal function was detected. A kidney biopsy revealed mesangial proliferation with IgA deposition and IgAV nephritis was considered. Immunosuppressive treatment was adjusted, with progressive normalisation of renal function and disappearance of proteinuria over a monthly follow-up; after 6 months, total remission was achieved. To the best of our knowledge, this is the first reported case of IgAV in an adult patient with SLE.

BACKGROUND

We focus on a disease usually affecting children and often inadvertently forgotten as a potential damaging disorder in adults. To the best of our knowledge, this is the first reported case of IgA vasculitis (formerly Henoch-Schönlein purpura, HSP) in an adult patient with systemic lupus erythematosus (SLE).

CASE PRESENTATION

A 65-year-old man with SLE and antiphospholipid syndrome (APS) presented to the emergency department, with a 2-week history of purpura and swelling of the ankles associated with fatigue and abdominal pain, worsened after meals. He described a previous event of tracheobronchitis, 1 week before the onset of purpura, treated with amoxicillin/clavulanic acid and clarithromycin, after which he experienced watery diarrhoea. By this time, the purpuric lesions worsened, with the appearance of necrotic blisters and haematochezia but no other bleeding, and the patient was admitted to the hospital. There was no fever, weight loss, anorexia or sweating, or any other acute systemic symptoms.

SLE had been diagnosed 2 years prior to admission, on the basis of photosensitivity, discoid lupus developing in the previous 6 years, non-erosive arthritis of the left knee, antinuclear antibodies (ANAs) (titre of 1/640, homogeneous immunofluorescent pattern) and double-stranded DNA.

Systemic Lupus International Collaborating Clinics (SLICC) damage index performed 1.¹ APS diagnosis was based on a deep vein thrombosis that occurred 8 years before, and persistently positive anticardiolipin antibodies and lupus anticoagulant. The patient also had osteoporosis, vitiligo and essential hypertension, controlled with medication. He was a smoker, with tobacco use estimated at 60 pack-years. Medication consisted of deflazacort 6 mg/day, bromazepam, losartan and alendronate. The patient had stopped hydroxychloroquine some months prior due to gastrointestinal intolerance. Follow-up was irregular owing to the patient's absenteeism on regular consultation.

On clinical examination, we found a haemodynamically stable patient, with painful palpable purpura affecting mainly the limbs, including hands and plants, but sparing the trunk. The rash was confluent in the ankles, where it formed blisters with some necrotic areas (figures 1–3), turning the feet swollen and tender from oedema. Vitiligo lesions on upper limbs were also found (figure 4), as well as arthritis on the second and third proximal interphalangeal joints.

Laboratory data revealed normal red and white cell count (WCC), and normal platelet count, with normal differential cell count; the blood smear was normal. Blood clot factors and coagulation studies were normal. Erythrocyte sedimentation rate was 12 mm/h and C reactive protein was 3.8 g/dL (N<1.0). Serum electrolytes, renal and hepatic function tests were normal. The protein electrophoresis was normal. Analysis of urinary sediment revealed haematuria and leucocyturia; 24 h proteinuria was 525 mg. There was no evidence of HIV, or hepatitis B or C infection. The immunological profile showed the presence of ANA 1/640 with a homogenous immunofluorescent pattern,

Figure 1 Left palm with palpable purpura lesions.

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To cite: Bernardino V, Mendes-Bastos P, Rodrigues A, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2015-210121

Figure 2 Right ankle with confluent purpuric lesions forming erythematous plaques with burst blisters and necrotic areas.

anti-dsDNA of 191.3 U/mL ($N < 100$), antinucleosome antibody of 130.98 U/mL ($N < 20$), circulating immunocomplexes of 24.13 RU/mL ($N < 2.0$) and Lupus anticoagulant, but negative anticardiolipin and anti- β_2 glycoprotein antibodies; anti-ribonucleoprotein (anti-RNP) anti-Sjögren's-syndrome-related antigen A (anti-SSA) and anti-Sjögren's-syndrome-related antigen B (anti-SSB) antibodies were negative. Fractions C1q, C3 and C4 of complement levels were normal but a low level of immunoglobulin (Ig) M was found (21.9 mg/dL, N : 34–210), with normal IgA (400 mg/dL, N : 88–410) and IgG (1390 mg/dL, N : 690–1400).

Abdominal ultrasound revealed fatty liver and renal ultrasound was normal; thoracic CT revealed central lobular emphysema on the apex. A skin biopsy revealed leucocytoclastic vasculitis. Immunohistochemistry staining revealed linear deposits of IgG and C3 along the dermoepidermal transition (typical finding in patients with SLE), as well as IgA deposits on

Figure 3 Right ankle with posterior necrotic lesions.

Figure 4 Right elbow with purpuric lesions and vitiligo patches.

superficial dermal capillaries.² IgA vasculitis was then assumed, without lupus flare or increased SLE activity.

The patient was treated with colchicine 1 mg twice daily for a week, and deflazacort 30 mg and azathioprine 100 mg daily, in order to treat the IgA vasculitis (IgAV). Within a few days, a regression in purpuric lesions was noted and no further haematochezia occurred; after 9 days, the patient was discharged. A week later, he was reevaluated on follow-up consultation and further improvement was noted, although his ankle blisters persisted for some weeks. Long-term smoking cessation was reached.

However, during the first 4 months of monthly follow-up, an increasing decline in renal function was detected, with serum creatinine reaching up to 1.5 mg/dL and urea 53 mg/dL. Proteinuria in 24 h increased to 1260 mg/24 h and the patient was readmitted for kidney biopsy. Histology revealed a tubular atrophied area in the subcortical fibrotic region and an interstitial mononuclear infiltrate with fibrotic thickening of the intima arterial layer (figure 5). There was mesangial proliferation with IgA deposition (figure 6). No suggestive lesions of lupus or APS-related nephritis were found. IgAV nephritis (IgAVN) was considered and azathioprine was increased to 150 mg/day (< 3 mg/kg), maintaining deflazacort at 30 mg/day. The antihypertensive therapy was changed, replacing losartan with ramipril. There was progressive normalisation of renal function and disappearance of proteinuria over monthly follow-up, and after 6 months, total remission was achieved. The medication was

Figure 5 Kidney biopsy, periodic acid-Schiff staining, on optic microscopy, with mesangial proliferation (courtesy Dr Fernanda Carvalho).

Figure 6 Kidney biopsy, immunofluorescent staining on optic microscopy, revealing glomerular deposits of IgA (courtesy Dr Fernanda Carvalho).

slowly adjusted for corticoid reduction and azathioprine dose optimisation.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis included lupus vasculitis, thrombocytopaenic purpura, malignancy and IgAV.

A complete blood count with normal peripheral smear, coagulation studies, biochemistry and liver function test eliminated platelet disorders and coagulopathies. Given the patient's previous history of SLE, lupus vasculitis was also considered. Normal erythrocyte sedimentation rate and complement levels revealed low SLE activity. Skin and kidney biopsy rendered SLE vasculitis unlikely. Normal WCC, protein electrophoresis and thoracic CT scan made malignancy improbable.

DISCUSSION

IgAV, recently renamed after Chapel Hill Consensus in 2012, is a systemic vasculitis involving small vessels, and can affect different organs, including the kidneys.³ SLE is an autoimmune systemic disorder affecting multiple organs, including the skin and kidneys. To the best of our knowledge, there is only one paediatric case reported, with ours being the first reported case of HSP in an adult patient with SLE.⁴

IgAV is a leucocytoclastic vasculitis involving small vessels, mediated by immune complexes containing polymeric IgA1 that deposit in small vessel walls and in turn activate the alternate complement pathway, leading to neutrophil accumulation.⁵ This inflammation and vasculitis affects mainly dermal, gastrointestinal and glomerular capillaries.⁶ Its pathogenesis is unclear, being associated with infections, drug therapy and tumours.⁷ IgAV is more frequent in children, with an incidence of approximately 10 cases/100 000 children per year; in adults, data on this disease are confined to small series, but vary from 3.4 to 14.3 cases per million.^{8,9} Clinical presentation of IgAV is usually more severe in older adults; it is characterised by the tetrad of non-thrombocytopaenic palpable purpura, arthritis/arthralgias, gastrointestinal and renal involvement, and, seldom, that of other systems. Cutaneous manifestations include symmetrical erythematous, and urticarial and macular rash, evolving to non-blanching purpura with petechiae and ecchymoses; rarely, haemorrhagic bullae, ulcerations and dermal scarring may be seen.⁵ Gastrointestinal involvement includes abdominal pain, nausea, vomiting, haematemesis, melena and haematochezia, and is due to vasculitis on splanchnic circulation.¹⁰ Joint involvement is

frequent, presenting as non-migratory, non-destructive, symmetrical polyarthralgias, affecting mostly the knees and ankles. IgAVN in adults is frequent, affecting from 45% to 85% of patients.¹¹ The risk of progression to renal insufficiency ranges from 5% to 30%.^{5,12} Initial signs of IgAVN are haematuria and proteinuria in 50% of patients, acute nephritic syndrome in 8%, nephrotic syndrome in 13% and both in 29%.¹³ Haematuria and proteinuria may follow relapses of purpura or may recur long after the extrarenal manifestations have resolved, with variable intensity.⁶ Histologically, IgAVN is described in light microscopy as a disease with glomerular mesangial proliferation, crescent formation and leucocyte margination, associated with deposition of IgA1 and C3.¹⁴ Although IgAVN and IgA nephropathy (IgAN) have long been considered to be related diseases, recent data have established the differences between these two disorders, as IgAVN is often a one-hit disease, whereas IgAN is a chronic progressive glomerular disease.^{14–16}

The diagnosis of IgAV is based on clinical manifestations. However, if the presentation is atypical, tissue biopsy may help, as positive immunostaining for IgA in renal biopsy gives more support to clinical diagnosis. IgAV is self-limiting in nature in up to 89% of adults, and symptomatic treatment is sufficient for most. Acetaminophen and non-steroidal anti-inflammatory drugs can be used for symptoms such as rash or arthritis.¹⁷ Oral steroids (prednisone or methylprednisolone) are recommended in patients with severe rash, oedema, severe colicky abdominal pain, or renal, scrotal or testicular involvement.⁵ Steroids decrease gastrointestinal symptoms and may prevent major complications such as gastrointestinal bleeding or intussusceptions.¹⁸ However, corticosteroids given at onset do not prevent nephritis.¹⁹ In fact, very limited evidence is available regarding the value of steroids, cyclophosphamide or other immunosuppressive agents for persistent IgAVN.¹⁶ In a few studies, high-dose intravenous pulse steroids, ranging from 500 mg to 1 g, revealed complete remission of nephritis.²⁰ Floege and Feehally,¹⁶ adapting KDIGO guidelines, further suggest a 6-month course of corticosteroid therapy to be given if proteinuria >1 g/day persists despite renin-angiotensin system blockade and blood pressure control. A randomised controlled trial in adults at significant risk of progression to end-stage renal disease (ESRD) proved no additional benefit when cyclophosphamide was added to steroids.²¹ Other immunosuppressive drugs, such as azathioprine, cyclosporine A and mycophenolate mofetil, have been recommended in combination with high-dose intravenous pulse steroids in ESRD, and haemorrhagic involvement of the lungs and brain; plasmapheresis or high-dose intravenous immunoglobulin therapy have also been recommended for the same purpose, but all of these are grade D recommendations based on meta-analytic studies.²²

As for the prognosis of IgAV, renal involvement is the most important factor in determining morbidity and mortality.²³ Some predictors of a poor renal course in adults have been proposed: high creatinine levels at onset, proteinuria >1 g/24 h, arterial hypertension, extracapillary proliferation in renal biopsy, interstitial fibrosis and tubular atrophy.¹⁸

The overlapping of IgAV and SLE is rare and has not yet been clarified. SLE is mainly an immunocomplex-mediated disease and, although C1q, C'3, C'4 and IgG depositions are common, IgA deposition can also occur.²⁴ As IgAV is an IgA-mediated process, Beale *et al*²⁵ suggested that as high levels of IgA resulted from similar B-cell and T-cell abnormalities in IgAV and SLE, the cellular changes would be closely interrelated and could represent an integrated response to a variety of immunological stimuli. However, subtypes of IgA interfering in this

process were not mentioned. Some years later, Burden *et al*²⁶ found an association between the presence of IgA anticardiolipin antibodies, the development of cutaneous leucocytoclastic vasculitis and a high risk of thrombotic events in patients with SLE. Yet, further investigation is necessary to clarify a common underlying mechanism between these two diseases. Despite this, in the present case, the pathogenesis of IgAV was probably related to a previous upper respiratory tract infection, as the immunomodulator role of infectious antigens has already been demonstrated.⁶

Although IgAV is infrequent in adults, non-thrombocytopenic palpable purpura with multiorgan involvement should be considered as part of an expanded differential diagnosis. As renal involvement worsens the prognosis, prompt diagnosis and multidisciplinary intervention can help to manage these patients. On the contrary, it is important to note that patients with SLE can also develop other types of vasculitis, so a high level of clinical suspicion is mandatory whenever de novo leucocytoclastic vasculitis occurs.

Learning points

- ▶ IgA vasculitis (IgAV), formerly Henoch-Schönlein purpura, is rare in adults, but should be considered in a case of non-thrombocytopenic palpable purpura with multiorgan involvement.
- ▶ Renal involvement is the most important marker for IgAV prognosis, so early detection and management are mandatory.
- ▶ Patients with systemic lupus erythematosus can also develop other types of vasculitis, although the underlying mechanism has not yet been disclosed.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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