Case Report

Adult-onset Still’s disease associated with collapsing glomerulopathy

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Abstract
A young woman of African descent presented with fevers, arthralgia, lymphadenopathy and a skin rash. Modest proteinuria was also noted. The clinical picture suggested an acute HIV sero-conversion illness, and a renal biopsy showed a collapsing glomerulopathy compatible with that diagnosis. However, HIV serology proved persistently negative and a diagnosis of Adult Still’s disease was subsequently made (by Yamaguchi criteria). Following steroid treatment, the patient’s fever abated and her inflammatory markers returned to normal. Collapsing glomerulopathy is a rare but important complication of Adult Still’s disease. Immunosuppressive treatment may be effective in improving renal outcome.

Keywords: Adult Still’s disease; collapsing glomerulopathy

Background

In the mid-1970s, focal segmental sclerosing glomerular lesions (‘collapsing glomerulopathy’) were first described in association with human immunodeficiency virus (HIV) infection [1]. It was later recognized that this lesion could occur in the absence of HIV infection, and it has, subsequently, been identified in association with intravenous heroin use, parvovirus B19 infection, hepatitis C, high-dose pamidronate therapy and in sickle cell anaemia [2].

Clinically, collapsing glomerulopathy differs from other forms of segmental sclerosing glomerulopathy being associated with a striking black racial preponderance and a generally poorer renal prognosis [2]. Many consider that it should be recognized as a separate diagnostic entity. The association between collapsing glomerulopathy and Adult-onset Still’s disease (AOSD) is not well described. We present the case of a young lady with AOSD-associated collapsing glomerulopathy, acute renal failure, rhabdomyolysis and possible polymyositis.

Case report

An 18-year-old student of African descent presented to her local hospital with a 3-week history of general malaise, weight loss, night sweats and recent-onset migratory large joint oligo-arthritis. She had experienced an episode of acute renal failure the previous year attributed to rhabdomyolysis from which she had made a good recovery but had failed to attend to with subsequent follow-up. She denied any risk factors for HIV infection. There was no history of recent foreign travel. Apart from occasional non-steroidal anti-inflammatory use, she was not taking any regular medications.

On examination, we noted a fever of 40°C and a resting sinus tachycardia of 120 beats/min. Blood pressure and respiratory rate were within normal limits. Proximal muscle weakness of the hip and shoulder girdle was noted, but no muscle wasting or tenderness. Submandibular and axillary lymphadenopathy were noted. Skin examination was normal although the patient did describe a skin rash prior to hospital admission. There were small bilateral knee effusions, evidence of joint-line tenderness and decreased range of movement, limited by pain.

Initial laboratory tests showed a microcytic anaemia with haemoglobin of 11.1 g/dL and a mean corpuscular volume of 66 fl. Haemoglobin electrophoresis revealed alpha thalassaemia trait. Renal function was within normal limits (creatinine 76 μmol/L). The creatine kinase level was elevated at 2217 U/L, as was ferritin at 11 68 mg/L. The C-reactive protein (CRP) level was elevated at 220 mg/dL. Blood tests for malaria, sickle cell disease and thyroid dysfunction were negative. An autoimmune screen for antinuclear antibodies, anti-double-stranded DNA, rheumatoid factor, anti-neutrophil cytoplasmic antibodies and antibodies to extractable nuclear antigens was negative. Complements C3 and C4 were normal. Serum protein electrophoresis revealed a polyclonal increase in IgG only. Serology for HIV, Epstein Barr virus, human T-lymphotropic virus, hepatitis B and C, anti-streptolysin O titres and parvovirus were all negative as was a urine toxicology screen. Multiple blood cultures were sterile. Joint aspiration was unsuccessful due
AOSD associated with collapsing glomerulopathy

Fig. 1. Collapsing glomerulopathy. Silver stain showing collapse of the glomerular capillaries and acute tubular damage.

to the very small size of the effusions. A chest radiograph showed clear lung fields and a computed tomography scan of the thorax, abdomen and pelvis identified axillary and submandibular lymphadenopathy but no other abnormality. Trans-thoracic echocardiography was also normal. A spot urine protein/creatinine ratio was 190 mg/mmol.

A renal biopsy was performed which showed evidence of collapsing glomerulopathy, with a moderate amount of chronic renal damage (Figure 1). Mixed tubular changes including enlargement, thyroidization, granular cytoplasm and atrophy, with a slight chronic inflammatory infiltrate, were observed. Staining for IgG, IgM, IgA and myoglobin was negative.

Treatment was commenced with oral prednisolone 1 mg/kg/day and an angiotensin-converting enzyme inhibitor, which resulted in prompt clinical improvement (Figure 2). The patient was discharged on a reducing dose of steroids with normal blood parameters.

Discussion

Our patient displayed the typical features of AOSD—quotidian fevers, an evanescent rash, generalized arthralgia and laboratory features reflecting non-specific heightened levels of immune activity. Although not a part of the diagnostic criteria, the particularly high serum ferritin, often disproportionate to the CRP, is a well-recognized feature of AOSD.

There are two sets of diagnostic criteria for AOSD [3,4] (Table 1). The Yamaguchi criteria require the presence of five or more criteria, of which at least two are major, yielding 96% sensitivity and 92% specificity.

The association between AOSD and inflammatory polymyositis is less well recognized [5]. As the patient’s CK and myalgia improved remarkably with the onset of steroids, EMG and muscle biopsy were not done to confirm the presumptive diagnosis of polymyositis. Our patient also had the clinical and laboratory manifestations of rhabdomyolysis. Rhabdomyolysis may also be a feature of AOSD and has previously been reported [6].

Renal manifestations occur in ~25% of cases of AOSD. These include haemolytic uraemic syndrome, thrombotic thrombocytopenic purpura, mesangioproliferative glomerulonephritis and amyloidosis. Collapsing glomerulopathy is a rare association with just three other reports in the literature [7–9]. Pathologically, collapsing glomerulopathy is characterized by effacement of podocyte foot processes, swelling or disappearance of primary processes and loss of the actin-based cytoskeleton. The underlying GBM is wrinkled and folded with sub-occlusion of capillary lumens. A dense lymphocytic infiltrate is often seen within the interstitium, and extensive tubulo-interstitial disease is often present.

The pathogenic trigger for collapsing glomerulopathy in AOSD (as for other associations) has yet to be defined. The resemblance of AOSD to an acute viral illness has led to speculation that, in genetically predisposed individuals, a viral trigger leads to AOSD. An association between collapsing glomerulopathy and viral illnesses (classically parvovirus B19 infection) has also been reported. It is therefore plausible that AOSD associated with CG may represent a systemic reaction to a virus in genetically susceptible individuals [10].

Therapeutic strategies for AOSD include use of a variety of immunosuppressants including corticosteroids, mycophenolate mofetil and intravenous immunoglobulin. In refractory cases of AOSD, biologic agents (anti-TNF α, anti-IL-1 and anti-IL-6) have been used with success [8].

Data on renal outcome in AOSD-associated collapsing glomerulopathy are limited, but remission of the underlying condition with immunosuppression may ameliorate the course of the renal disease. Previous case reports of AOSD-associated collapsing glomerulopathy all describe renal remission [7–9]. With increasing recognition of this disease association, the true incidence and prognosis will become clearer.

Our patient made a marked improvement with oral prednisolone at 1 mg/kg/day. Her symptoms and subsequently serologic markers normalized within 2 weeks.

Conflict of interest statement. None declared.

Table 1. Diagnostic criteria for Adult Still’s disease.

| Cush criteria | Yamaguchi
|----------------|----------------|
| Requires all of the following | Major criteria |
| Fever > 39°C | Fever > 39°C |
| Arthralgia or arthritis | Arthralgia/arthritis > 2 weeks |
| Rheumatoid factor < 1:80 | Typical rash |
| ANA < 1:100 | WBC count > 10 000 with |
| | 80% PMNs |
| In addition, two of the following | Minor criteria |
| WBC count > 15 000 | Sore throat |
| Still’s rash | Lymphadenopathy |
| Pleuritis or pericarditis | Increased LFTs |
| Hepatomegaly, splenomegaly | Negative rheumatoid factor |
| or lymphadenopathy | and ANA |

Clinical manifestations of AOSD
Fig. 2. Clinical response to treatment with corticosteroids (arrow indicates initiation of treatment).

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