Case Report

Systemic lupus erythematosus, eosinophilic vasculitis and acalculous cholecystitis

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Introduction

Patients with atypical features of a common disease often pose diagnostic challenges, as they may have two distinct disease entities, a rare manifestation of the common illness, or even a new syndrome. We describe a case of a 30-year-old woman with what we feel was a rare acute presentation of systemic lupus erythematosus (SLE), with hyper eosinophilia, acalculous cholecystitis and biopsy proven eosinophilic vasculitis affecting the kidney, responding successfully to immunomodulatory therapy to date.

Case

A 30-year-old woman presented with a 5 day history of fever, diarrhoea and vomiting. Closer questioning revealed a 6 week history of fatigue and flitting polyarthralgia involving wrists, hands and feet. There was no past medical history of note, in particular no respiratory tract illnesses and no history of allergy. She took no prescribed or over the counter medications. On examination she was unwell, pyrexial (39.9 °C) and markedly intravascularly deplete, although her limbs were oedematous. There were no cutaneous, nail-fold or joint abnormalities present. A sinus tachycardia of 126 bpm was present, blood pressure was 122/55 mmHg and heart sounds were normal. Oxygen saturation was normal on air, and examination of the respiratory system was unremarkable. There was local tenderness in the right upper quadrant but the abdomen was soft.

Initial investigations showed acute renal failure, mild hepatic dysfunction in an obstructive pattern, a low albumin, and deranged clotting with low platelets [Na 130 mmol/l, K 3.7 mmol/l, Ur 18.9 mmol/l, Cr 323 μmol/l, bilirubin 62 μmol/l (<20), Aspartate amino transferase (AST) 40 U/l (<40), Alkaline phosphatase (ALP) 213 U/l (30–135), albumin 33 g/l (36–42), Prothrombin time (PT) 18.6 s (12.5–15.5), Activated Partial Thromboplastin Time (APTT) 46.9 s (25.0–37.0), platelets 51 × 10^9/l]. The blood count was normal but the differential white cell count showed a relative (19.7%) and absolute eosinophilia (1.9 × 10^9/l).

Arterial blood gases showed adequate oxygenation on air with no evidence of acidosis (pH 7.45, pO2 16.4 kPa, pCO2 3.3 kPa, standard bicarbonate 22 mmol/l, base excess −4 mmol/l). Urinalysis revealed moderate amounts of blood and bilirubin, and a trace of protein. Bloods taken 4 h after admission showed a further derangement of clotting factors, a drop in platelet count to 9 × 10^9/l, a drop in haemoglobin (13.1 g/dl to 9.2 g/dl) and raised d-dimers > 2 mg/l (<0.5 g/l). She was resuscitated with fluids, fresh frozen plasma, platelets and high-dose broad spectrum antibiotics, but despite this, she rapidly deteriorated and required intensive care for 12 h after admission, with full ventilatory, inotropic, nutritional and renal support. Ultrasound examination of the abdomen showed a 13 mm thick-walled oedematous gall bladder with no dilatation of the common bile duct or intrahepatic ducts. The liver, spleen, pancreas and renal tract had normal appearances. She was judged unfit for theatre and so percutaneous drainage of the gall bladder was performed under ultrasound guidance 3 days later when her consumptive coagulopathy had stabilized. This revealed clear yellow fluid which proved sterile on culture. Tests for hepatitis A, B and C, HIV1 and 2, leptospirosis, legionnaires disease and tuberculosis were negative. Repeated examination for bacterial infection...
(blood, urine, sputum, stool, pleural aspirate, ascitic tap and cervical swab) and parastic infection were all negative. Serology, however, revealed a polyclonally raised serum ImmunoglobulinG, positive anti-nuclear antibody at 1:200 titre, positive double-stranded DNA (dsDNA) antibodies (Farr assay) at 28 iu/ml and low C3 and C4 levels. Antibodies to neutrophil cytoplasmic antigens, myeloperoxidase (MPO) and proteinase 3 (PR3), and glomerular basement membrane were negative. The eosinophilia persisted with levels as high as $10.5 \times 10^9$/l (48.1% of total white blood cell).

By day 10, although other parameters had stabilized, her liver enzymes became increasingly deranged with an obstructive pattern, peaking at a bilirubin of 156 $\mu$mol/l, ALP 1572 U/l, AST 47 U/l, and she was transferred to a tertiary liver unit for assessment. Following transfer, she was successfully weaned from ventilatory and inotropic support. She then underwent percutaneous ultrasound guided renal biopsy that revealed severe concentric vasculitis involving medium-sized vessels and also changes consistent with acute tubular necrosis. The glomeruli were normal. Thus, a diagnosis of eosinophilic systemic vasculitis was made according to biopsy results. She was promptly treated with three consecutive pulses of methylprednisolone (1 g/24 h) and after the third dose her renal function improved such that she did not require further renal replacement therapy.

She continued to make progress and was discharged after 27 days in hospital with normal renal function, a mild normocytic anaemia, a normal eosinophil count and improving liver enzymes (bilirubin 32 $\mu$mol/l, ALT 45 U/l, ALP 744 U/l), having had no further treatment for the cholecystitis other than systemic immunosuppression. Over the next 4 months she remained well clinically, and her steroid regime was slowly reduced. She did, however, continue to exhibit fluctuating derangements of liver function, now mainly a transaminasaemia (for example, bilirubin 7 $\mu$mol/l, ALP 200 U/l, ALT 100 U/l, glutamyl transpeptidase (GGT) 256 U/l) and therefore went on to liver biopsy. This showed normal architecture with no evidence of inflammation or fibrosis and no evidence of vasculitis. Shortly after this time the titre of dsDNA antibodies rose, she developed positive Ro-antibodies, and was commenced on azathioprine (see Figure 1). Over the subsequent 2 years, her condition evolved to meet the American College of Rheumatology classification criteria of SLE, with arthritis, rash, anti-cardiolipin antibodies, anti-dsDNA antibodies, and persisting renal abnormalities (protein leak averaging 1 g/24 h). Serological activity fluctuated, but she managed to be maintained on just azathioprine (150 mg) for immunosuppression. However, 5 years from presentation, she suffered a clinical relapse with nephrotic proteinuria and fluid overload. She was started on high dose steroids and diuretics. The azathioprine was stopped because of leukopenia and mycophenolate mofetil (MMF) substituted in its place, which achieved good control with no further relapse. A renal biopsy was performed which showed a diffuse lupus glomerulonephritis of predominantly mesangiocapillary pattern with active and sclerosing lesions. After 18 months of MMF, her dsDNA result was negative. Subsequently, she suffered no further relapses and was able to stop MMF, with a reducing dose of prednisolone.

**Fig. 1.** Graph illustrating changes in IgE and anti-dsDNA levels with time. Prednisolone was started early in treatment and continued, almost constantly, at different doses. However, azathioprine and mycophenolate mofetil were added at different points.
Acute acalculous cholecystitis unrelated to vasculitis has itself been uncommonly described, usually in relation to debilitated hospitalised patients. Its pathogenetic mechanism is unknown.

Liver disease thought to be directly related to SLE is more commonly recognized, usually manifesting as biochemical abnormalities of hepatic function in between 20–55% of patients. A more severe spectrum of disease – acute hepatitis to frank liver failure – is uncommon [10]. Finally, there were some highly unusual immunological features in this case. The patient had evidence of IgG antinuclear antibodies and double stranded DNA antibodies from disease outset, and from the time of first measurement, evidence of classical pathway complement consumption also. The dsDNA antibodies became weakly positive again in September 1998 after the acute illness, and over the subsequent 6 months the serology developed into that of classical lupus with strongly positive dsDNA antibodies, anti-Ro antibodies and very low C3 and C4 levels. At one point she also developed anti-cardiolipin antibodies (13 GPL). The striking combination of eosinophilia and raised IgE seen in the acute phase is suggestive of either an allergic response to an unknown inciting antigen, or possibly reflects disordered immune regulation. Both the eosinophilia and raised serum IgE levels responded to immunosuppression in the acute illness. IgE levels rose again in October 1998 as the dose of steroids was reduced, accompanied by other immunological change suggestive of disease activity (increase in dsDNA antibody levels, complement consumption, development of anti-Ro antibodies), as well as derangement of liver enzymes, although not at this time by an eosinophilia. Both serum IgE and IgM fell markedly to the point where they became barely detectable, presumably in response to the addition of azathioprine (see Figure 1) as no other treatment changes took place during this time, other than the addition of calcium and vitamin D3 for bone protection.

In summary, we describe a case of a 30-year-old woman with a rare acute presentation of SLE, with hyperesoinophilia, acalculous cholecystitis and biopsy proven eosinophilic vasculitis affecting the kidney, responding successfully to immunomodulatory therapy to date.

Conflict of interest statement. None declared.

References


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