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Case Report

Case Presentation of a Patient with Systemic Lupus Erythematous, A Tour through the More Unusual Presentations

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Abstract

We present the case of a 23 year old female with Systemic Lupus Erethematosus [SLE] from diagnosis followed for 7 years. She presented unusually, with acute autoimmune hepatitis that has not recurred. Subsequently she developed significant haematological involvement with complications of profound thrombocytopenia and neutropenia. Ultimately she developed a rare malignancy-namely CD8+ epidermotropic T-cell lymphoma. We discuss the complications of SLE and the development of the cutaneous T cell lymphoma.

Keywords: SLE: Systemic Lupus Erythematous; Autoimmune hepatitis; Haematological; Cutaneous T cell lymphoma

Case Presentation

A twenty three year old female with no past medical history was referred to the Rheumatology clinic in 2009 following an acute illness managed by the Hepatologists. She presented with jaundice and diarrhoea. She had no risk factors for acute hepatitis and was not taking any hepatotoxic medication. Her liver enzymes were significantly elevated, suggestive of acute hepatic injury. Her bloods showed Bilirubin 300umol/L (0-20), ALT 1500IU/L (10-35), ALP 150IU/L (35-104 INR 1.5 and Albumin was 35g/L (34-50). Further investigations demonstrated a strongly positive anti-nuclear antibody (titre >1:5120). Anti-smooth muscle and anti-mitochondrial antibodies were negative. IgG was elevated at 23.18g/L (7.0-16.0 g/L). HIV and Hepatitis B&C serology was negative for previous infection. Subsequently a liver biopsy demonstrated evidence of acute hepatitis, with associated portal and lobular inflammation. She was treated with a tapering dose of oral prednisolone in combination with Azathioprine 75mg daily. Shortly thereafter she developed a macular rash, arthralgia and alopecia with an associated thrombocytopenia and lymphopenia.

Further investigations revealed positive antibodies to Ro and double stranded DNA 208IU/ml (0-50). C3 was low at 0.77g/L (0.90-1.80). The ESR was elevated at 66mm/hr. The anti-phospholipid screen was negative with the exception of an IgM anti-cardiolipin antibody. A diagnosis of Systemic Lupus Erythematosus (SLE) was made with associated lupus hepatitis.

She responded well to the initial treatment for several months with evidence of both clinical and serological remission. In early 2010 she presented again with mucosal bleeding and a petechial rash. Profound pancytopenia was noted with a platelet count of 0 (150-400 $x10^9$/l), haemoglobin 54 (115-155 g/l) with positive direct antiglobulin test. This flare was complicated by a retinal haemorrhage resulting in central vision loss. She underwent a diagnostic Bone Marrow Aspirate and Trephine (BMAT) which demonstrated red cell aplasia with normal megakaryocytic suggesting peripheral destruction. She was treated with intravenous methyl prednisolone, Cyclophosphamide and Rituximab for lupus-related pancyopenia. After several weeks her blood counts normalized. Over the next four years she remained relatively well although she required annual Rituximab infusions predominantly for mild flares comprising of arthritis, rash and constitutional symptoms.

In late December 2014, she developed serositis manifesting as pleuritic chest pain (pleurisy). An echocardiogram demonstrated associated pericarditis with a small pericardial effusion noted. She was again treated with high dose intravenous corticosteroids and Rituximab and made a good clinical recovery.

She experienced a further flare in early 2016, characterized by fatigue, fever, anorexia, abdominal pain and diarrhoea. On admission, she was noted to be febrile at 40°C. Blood tests revealed pancytopenia with Haemoglobin 60 (115-155 g/l), neutrophils 0.03 (2-7.5x10^9/l) and platelets 35 (150-400x10^9/l). Ferritin was modestly elevated at 1038 (13-150 ug/l) in keeping with ongoing inflammatory response. Fibrinogen was raised and triglycerides were normal (going against macrophage activation syndrome). She underwent a BMAT which revealed a poorly cellular specimen. The early stages of her admission were complicated with heavy menstrual bleeding, epistaxis, and hemorrhoidal bleeding secondary to thrombocytopenia. Cross sectional imaging of the thorax, abdomen and pelvis found no evidence of lymphadenopathy. *E.coli* was isolated from blood cultures and she was diagnosed with neutropenic sepsis, felt to be secondary to acute cholecystitis. She was treated with broad spectrum antibiotics (ceftazidime and gentamicin) and concurrent Granulocyte-colony stimulating factor. The pancytopenia was managed with blood product support.

When the infection had been treated she was commenced on high dose IV corticosteroids, Rituximab, and intravenous immunoglobulin at a dose of 2g/kg for her lupus flare. She was discharged on a reducing course of oral prednisolone and there was evidence of ongoing bone marrow recovery evidenced by resolving pancytopenia.

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However, three weeks following discharge she reattended with abrupt onset widespread rash with pruritus. She reported recent sun exposure and a brief period of non-compliance with oral steroids. The rash appeared to be consistent with severe diffuse subacute cutaneous lupus erythematosus with features of erythematous papules and plaques. Furthermore there was evidence of longstanding subtle underlying livedo reticularis.

This was associated with a moderate recurrence of thrombocytopenia with platelets $66x10^9$/l. She was treated empirically with oral steroids restarted at a higher dose and made a good clinical improvement. The rash rapidly resolved and the platelet count had normalized with a week ($164x10^9$/l). A 4mm punch skin biopsy was performed with a sample taken from the lateral border of the right thigh.

The results of the biopsy revealed an epidermal centered lymphocytic infiltrate with abnormal nuclear morphism noted. Immunohistochemistry demonstrated that lymphocytes were $CD^{3+}CD^{8+}$ T cell predominant, with down regulation of CD5. It was felt that the morphological and immunohistochemical findings would be in keeping with active lupus erythematosus, but in view of the down regulation of CD5 expression, it is not possible to exclude a CD^{8+} epidermotropic T-cell lymphoma. Subsequent PCR confirmed a Clonal T cell expansion which was fully consistent with the diagnosis of CD^8 positive epidermotropic T cell lymphoma.

She was referred onwards to a specialist centre for assessment and ongoing management

Discussion/Conclusion

This case highlights the complexities and the complications associated with SLE. In addition, the unusual initial presentation with autoimmune hepatitis, severe pancytopenia with subsequent complications and the ultimate development of a rare T cell malignancy.

Autoimmune Hepatitis (AIH) is a form of chronic active hepatitis which in its original description of the disease was referred to as lupoid hepatitis [1]. The link with SLE is controversial but has not been completely disproven. In one series of 30 patients with new biopsy proven AIH 23.3% also fulfilled ACR criteria for SLE [2]. Suggesting that there is in fact an overlap seen in these conditions. In patients with SLE however, deranged LFT's are seen in 30-60% of patients but the cause is most often due to medications [especially NSAIDs], viral infections and increasingly Non Alcoholic Steatohepatitis [NASH] [1].

The prevalence of thrombocytopenia in SLE varies and has been reported in the literature from 7- 59.3% [3,4]. The cause is variable and broadly can be attributed to the disease itself, another concurrent disease or iatrogenic. There are three mechanisms; impaired production in the bone marrow, sequestration in the spleen and accelerated peripheral destruction, with the latter the most common [3]. Cutaneous lymphomas are rare with an estimated annual incidence of 1:100000 [5]. They are often a diagnostic challenge as they have a broad clinical presentation and management approach. Cutaneous T cells Lymphomas (CTCL) are much more common than B cell and represent approximately 75% of all primary cutaneous lymphomas [6]. Treatment for CTCL depends on the type and stage of the disease [6].

It is known that the rates of haematological malignancy are slightly higher in patients with SLE [7,8] but this is mostly an increased risk of Non-hodgkins Lymphoma and lung cancer in smokers.

Our case report highlights the complexities in the management of SLE a chronic autoimmune rheumatic disease with significant multi-system involvement. She experienced rare associations with her autoimmune hepatitis and also development of a T cell malignancy.

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