Systemic lupus erythematosus simulating Henoch Schonlein purpura

M N Lucas[1], **S Dias**[2]

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Introduction

Systemic lupus erythematosus (SLE) in children is a multisystem autoimmune disease with a great variability in presentation and course. The diagnosis of SLE is based on clinical and laboratory features consistent with this illness[1].

Case report

A 3 ½ year old boy presented to ward 6B, General Hospital, Kalutara on 22nd August, 2006, with fever, rash and swelling of lower limbs of 8 months duration. Fever occurred only in the evening and was not associated with chills. There was an erythematous, maculo-papular rash on the trunk and lower limbs, appearing with the onset of fever and disappearing when the fever subsided. This was associated with mild pruritis. Residual pigmentation was present. Periarticular tender swellings around both ankle joints were noted on admission. The swellings were seen to extend up to the knee joints at times of fever and rash. They were painful and he refused to walk during these episodes. He developed a single episode of palpable purpura symmetrically involving the buttocks and extensor surfaces of the lower limbs while in the ward. This was characteristic of Henoch Schonlein purpura (HSP) and was associated with painful swelling of both lower limbs. It settled spontaneously within a few hours. Similar episodes had also occurred at home.

Eyelid and facial swelling were observed 1 month prior to development of above symptoms and were attributed to an allergic reaction. Blood stained stools were noted on and off for three weeks, 1 month back. He was known to be constipated. He was the product of a non-consanguineous marriage and had a normal birth and developmental history. There was no family history of a similar illness.

[1]*Paediatric Registrar,* [2]*Consultant Paediatrician, General Hospital, Kalutara.*

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On examination, he was an uncooperative, miserable child. His height was 95cm (10th centile for age) and weight was 16 kg (50th centile for age). He was pale, anicteric, had angular stomatitis but no oral ulcers. A periarticular swelling was seen to involve both ankle joints. Movements were not restricted and neither erythema nor warmth was seen except during an episode of rash. Generalised lymphadenopathy with discrete, non-tender, firm nodes <2cm in diameter, predominantly involving the cervical area, was present. An ejection systolic murmur was heard over the left sternal edge. Rest of the cardiovascular system was normal. The respiratory system was normal. The liver was palpable 3 cm below the costal margin. It was firm, smooth and non-tender. Spleen was not palpable. An anal fissure was present. No neurological deficits were found.

The child was very well in between the episodes of rash and lower limb swelling and the lymphadenopathy and hepatomegaly regressed while in the ward. Systemic onset juvenile idiopathic arthritis (SOJIA), HSP, SLE, Kawasaki disease, other vasculitis and malignancy were considered in the differential diagnosis.

The following are the results of investigations done on admission. The haemoglobin (Hb) level was 7.9 g%, the white blood cell (WBC) count 10.8 x 10^9/l (N 72%, L 27%) and the platelet count (PC) 267 x 10^9/l. The erythrocyte sedimentation rate (ESR) was 147 mm in the 1st hour whilst the C-reactive protein (CRP) was 48 mg/l. The SGOT was 52 U/ and the SGPT 13 U/L. The blood urea was 13 mg%, the serum sodium 138 mmol/l and the serum potassium 3.5 mmol/l. The urine full report was normal. The peripheral blood film showed normocytic normochromic red cells, hypochromic microcytic red cells, rouleaux formation, neutrophil leucocytosis, adequate platelets and an absence of blast cells. An ultrasound scan of the abdomen did not reveal any abnormality.

Further tests were carried out six days later, on 28th August. Hb level was 9.5 g%, WBC

count 10.9 x 10^9/l (N 62%, L34%), PC 345 x 10^9/l, ESR 143 mm in the 1st hour and CRP 12 mg/l. Serum ferritin was 45 ng/ml (normal range 20–400 ng/ml) and serum iron 58.4 µg/dl (normal range 59-158 µg/dl). Mantoux test was negative. Slit lamp examination of the eye showed no evidence of anterior uveitis. Bilateral diffuse inflammatory shadows were found on chest x-ray. X-ray of ankle joint was normal. The 2D echocardiogram was normal. Skin biopsy, done during an episode of palpable purpura, showed leucocytoclastic vasculitis with moderate perivascular infiltrate of neutrophils and lymphocytes with involvement of the vessel walls (characteristic of HSP). Lymph node biopsy showed reactive lymph nodes with no evidence of lymphoma.

Although the palpable purpura, pertiarticular swelling and leucocytoclastic vasculitis were characteristic of HSP, the persistently high ESR led us to investigate further. Anti nuclear antibody (ANA) was >1/80 titre. This was repeated and confirmed. Double stranded DNA (Ds DNA) was positive with >1/10 titre. Rheumatoid factor was positive with 1/320 titre. Complement levels showed a normal C3 level of 107 mg/dl (normal range 55-120 mg/dl) and reduced C4 level of 9.8 mg/dl (normal range 20-50 mg/dl). Immunoglobulin (Ig) levels revealed a hyperimmunoglobulinaemia with IgG 2798.2 mg/dl (normal range 569-1597 mg/dl), IgA 158.4 mg/dl (normal range 55-152 mg/dl) and IgM 105.1mg/dl (normal range 22-100 mg/dl). Considering these investigation results, a diagnosis of SLE was made.

He was treated as moderate SLE with prednisolone 0.5 mg/kg/day i.e 7.5 mg daily with ibuprofen 10 mg/kg 8 hourly. A good response was seen, with complete resolution of symptoms and fall in ESR to 66 mm 1st hour in one week and 53 mm 1st hour, 3 weeks after starting treatment.

Discussion

The incidence of SLE varies significantly in different populations. Paediatric data suggest that the incidence of SLE, with onset before 19 years of age, is probably between 6 and 18.9 cases per 100,000 in white females. Incidence rates are higher in Southeast and South Asia[1]. The male to female ratio is 1:4.4[2,3]. Mean age of diagnosis is 12 years[1]. The recent 5 year survival rate has been reported to be as high as 100%, with the 10 year survival rates as high as 86%[4]. Most patients have at least four of the American College of Rheumatology Classification Criteria for SLE at the time of diagnosis (table 1)[5].

Table 1
American College of Rheumatology Classification Criteria for SLE

1. Malar rash	
2. Discoid rash	
3. Photosensitivity	
4. Oral ulcers	Usually painless, observed by physician.
5. Arthritis	Non-erosive, involving 2 or more peripheral joints, characterized by tenderness, swelling or effusion.
6. Serositis	Pleuritis or pericarditis.
7. Renal disorder	Persistent proteinuria > 0.5g/day or cellular casts.
8. Neurologic disorder	Seizures / psychosis
9. Haematological disorder	Haemolytic anaemia with reticulocytosis or leucopenia <4 x 10^9 /l on 2 or more occasions or lymphopenia <1.5 x 10^9 /l on 2 or more occasions or thrombocytopenia <100 x 10^9 /l.
10. Immunologic disorder	Positive LE cell preparation or anti DNA antibody in abnormal titre or presence of Sm nuclear antigen or false positive serologic test for syphilis.
11. Antinuclear antibody	An abnormal titre by immunofluoresence

Children with SLE frequently present with systemic constitutional symptoms such as fever, diffuse hair loss, weight loss and evidence of diffuse inflammation such as lymphadenopathy and hepato-splenomegaly and these manifestations are seen throughout the disease. Skin, musculoskeletal and renal systems are the most common organ systems involved in paediatric SLE (pSLE). Important treatment decisions are made mainly on evidence of major organ involvement i.e. immunosuppression is advocated in cases with nephritis, neuro-psychiatric disease, vasculitis and severe hematologic disease[1.,6]. Gastrointestinal disease, myositis and myocarditis are rare in children. Most SLE patients have musculoskeletal involvement, mainly arthritis, arthralgia or tenosynovitis. The arthritis seen in pSLE is commonly a painful, symmetric polyarthritis affecting both

large and small joints with reduced range of movement[1].

Skin involvement is reported in 50-80% of patients at the time of diagnosis. Malar rash, photosentitive skin rash, vasculitic rash, palmar/plantar erythema, Raynauds phenomenon, annular erythema, discoid lupus and lupus profundus are seen. True vascultic rash is seen in 10-20% of children and includes ulceration, nodules and even palpable purpura. Patients with C4 deficiency often present with cutaneous lesions that are resistant to therapy[1]. Leucocytoclastic vasculitis is a histopathological description of immune complex-mediated inflammation of small and medium-sized arteries to the skin. This initially produces polymorphonuclear infiltration with the release of vasoactive amines and lysozymes, resulting in increased vascular permeability, oedema and polymorph lysis with nuclear debris. There is a later stage in which mononuclear infiltration occurs. Leucocytoclastic vasculitis is predominantly seen in HSP but can also occur secondarily to a number of conditions, including rheumatoid arthritis, SLE, sarcoidosis, malignancy, drugs and infection[7].

Most patients have initial neuro-psychiatric signs and symptoms within the first year of diagnosis of SLE. Headache is the most common manifestation and a true lupus headache is refractory to treatment. It is frequently seen in association with more severe CNS involvement including organic brain syndrome and psychosis. Psychosis is seen in 30-50% in those with neuro-psychiatric involvement. Cognitive dysfunction, seen in 20–57%, ranges from poor school performance to frank coma. Cerebrovascular disease is associated with antiphospholipid antibodies. Seizures are seen in 10-40% of the paediatric cases[1].

Lupus nephritis has been reported in 29-80% of paediatric cases. Renal disease is manifested within the first year after diagnosis in 90% of the cases. Renal biopsy is warranted at the time of initial presentation in patients with an active urine sediment or abnormal renal function. Hypertension is found in one third of paediatric lupus patients before starting steroid treatment. Factors associated with adverse renal outcome include class IV, initial evidence of nephrotic syndrome and non-white ethnicity[1].

Anaemia, thrombocytopenia and leucopenia are seen in 50-70% of patients. The most common anaemia is a normochromic normocytic anaemia, which when persistent, usually becomes a microcytic hypochromic anaemia. Coombs test is positive in 30-40% of patients but less than 10% have overt haemolysis. Thrombocytopenia is seen in 15% of paediatric patients at presentation.. Leucopenia is seen in 20-40% of cases of pSLE. Coagulation abnormalities are common is pSLE and lupus anticoagulant (LAC) is positive in 20-30% of cases. These patients have as increased risk of developing deep vein thrombosis and cerebral vein thrombosis[1].

Most common form of cardiac involvement is pericarditis and pericardial effusion[1]. Pulmonary involvement is common in pSLE and occurs in 25-75% of cases. The clinical spectrum includes pleuritis, pneumonitis, infectious pneumonia, pulmonary hemorrhage, pneumothorax and pulmonary hypertension. The most common manifestation is pleuritis. Severity can range from asymptomatic to life threatening involvement[1]. Gastrointestinal involvement occurs in 20-40% of patients. Abdominal pain can result from peritoneal inflammation, vasculitis, pancreatitis, malabsorption, pseudo obstruction, paralytic ileus or enteritis[1]. Splenomegaly occurs in 20-30% of paediatric cases and reflects generalized inflammatory state. Functional asplenia is common and increases the risk of sepsis. Hepatomegaly occurs in 40-50% of patients and up to 25% have abnormal liver function tests. Markedly abnormal liver function tests are seen in lupoid hepatitis[1]. The thyroid is the most commonly involved endocrine gland and both hyper and hypothyroidism are seen. Delayed puberty is also commonly seen[1].

Investigations help to evaluate inflammatory activity, disease activity, organ involvement and function. Raised ESR is a nonspecific measure of inflammatory activity but CRP is often normal in active SLE. If the CRP is raised, the presence of an infection should be sought[8]. Low level of complement components (C3, C4 and CH50) are found in most patients with active renal disease and is found to correlate with the severity of lupus nephritis[8]. The hallmark of SLE is the production of autoantibodies directed against histone, non-histone, RNA-binding, cytoplasmin and nuclear proteins. Anti nuclear antibodies are seen up to 100% of patients and is considered positive if >1/80 titre. Anti-DNA antibodies are seen in 60-70% patients and have a high specificity. It is also known to correlate with severity of lupus nephritis. Rheumatoid factor

is seen in 12–29% of patients[1]. The 3 most reliable measures of disease activity are ESR, DsDNA and reduced C3 and C4 levels [6].
The severity of disease is categorized as mild, moderate or severe based on constitutional symptoms and the degree of visceral involvement. A diagnosis of mild SLE is made when there is cutaneous or joint involvement in the absence of constitutional symptoms. Moderate SLE comprises mild inflammation in other organs with or without constitutional symptoms. A diagnosis of severe SLE is made when there is severe inflammation e.g. severe renal, neuro-psychiatric, pulmonary or cardiac involvement, severe haemolytic anaemia or thrombocytopenia[8].

Mild SLE may not need immunosuppressant drugs. Arthralgia, mild serositis and fever can often be controlled with paracetamol and non-steroidal anti inflammatory drugs (NSAIDs). Rash may respond to topical steroids. Antimalarials, mepacrine and dapsone can be used in severe cutaneous SLE[8]. Immunosuppression with prednisolone is indicated if the patient has significant constitutional symptoms (high measures of disease activity) or evidence of visceral involvement or when treatment with NSAIDs and antimalarials fail[7]. Nephritis, vasculitis, neuro-psychosis and blood dyscrasias are indications for immunosuppression[6]. Corticosteroids can be given together with NSAIDs and chloroquine. The starting dose should aim to suppress disease activity. In patients with mild to moderate disease, the initial dose is 0.5mg/kg/day and for severe inflammation it is 1.0–1.5 mg/kg/day with the dose taken once daily in the morning. Once remission is achieved, the dose is slowly reduced by 10 mg/day over 2-3 months, and thereafter more gradually, as rapid steroid withdrawal can lead to disease relapse. Remission should be confirmed clinically and serologically before stopping treatment[7]. Azathioprine has a role as a steroid sparing agent in moderate to severe SLE[8]. Treatment with high dose steroids and cytotoxic drugs are more effective in controlling severe disease than steroids used alone[9,10]. Plasma exchange is also effective for management of acute flares of SLE[11].

Complications of SLE such as infection, hypertension, thrombosis and coronary artery disease occur as a result of the disease as well as therapy. Use of antibiotics and antihypertensives has contributed significantly to reduce mortality. Additional therapy, such as anti-platelet drugs, anticoagulants, anti-epileptics, antidepressants, hypolipidaemics and anti-anginals may be indicated for complications [7].

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