

## Systemic lupus erythematosus in children: a case report and review

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### SUMMARY

A 12-year-old Papua New Guinean female presented initially with nonspecific clinical symptoms, fever of unknown origin and anaemia. She subsequently developed multisystem disease involving the respiratory, gastrointestinal, central nervous, musculoskeletal and cutaneous systems. She was diagnosed to have systemic lupus erythematosus (SLE) and started on treatment. Unfortunately the patient defaulted from follow-up after treatment, which covered seven months only, to present with acute respiratory distress from which she died within 24 hours. A relevant literature review with the clinical features of systemic lupus erythematosus in children is described.

### Introduction

Systemic lupus erythematosus (SLE) is a chronic multisystem autoimmune disease that characteristically involves many organ systems and is associated with serological aberrations, particularly the presence of antinuclear antibodies. SLE is primarily a disease of young adult women; about 15% of cases begin during childhood. The manifestations are protean and virtually any organ system can be involved. Cases of SLE have been reported before in Papua New Guinea (1,2). Here we describe a 12-year-old female who presented initially with nonspecific clinical features but subsequently developed multisystemic features of SLE. A brief review of the literature is presented with a description of the clinical features of SLE in children.

### Case Report

A 12-year-old Papua New Guinean female from Giri-Bogia, Madang was admitted to Madang General Hospital (MGH) because of persistent fever, fatigue, anorexia, weight loss and skin changes of four weeks duration. In addition, she developed painless ulceration on the lips and buccal mucosa a few days before

admission. She had been treated previously at the outpatient department with chloroquine, Fefol and albendazole. However, symptoms persisted and at outpatients she was commenced on daily Imferon injections because of anaemia at a haemoglobin (Hb) level of 6.7 g/dl. After Imferon injection she developed generalized joint pain, high fever and facial swelling. There was no history of joint swelling, cough, shortness of breath or night sweats. The girl was the first born in the family and had no previous hospitalization. There was no history of drug allergy.

On examination, she was pale, had a pulse rate of 100/minute, temperature of 37.7°C and blood pressure of 110/80 mmHg and weighed 38 kg. She had dark skin with facial puffiness and hypopigmentation over the malar regions. There were no petechiae. There were tender cervical lymph nodes on the left. The tongue and mouth showed ulcerations. Her joints especially her knees and hips were tender but not swollen. Examination of the respiratory, cardiovascular and central nervous systems did not reveal any abnormality.

The initial clinical assessment was anaemia with a drug reaction, probably from the

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Imferon injection. The possibilities of connective tissue disorder – perhaps systemic lupus erythematosus – and pulmonary tuberculosis were considered.

Full blood examination showed an Hb level of 8.2 g/dl. The peripheral film showed normocytic, normochromic morphology. Her white cell count (WCC) was 5200/ $\mu$ l with a differential count of neutrophils 59%, lymphocytes 41% and a platelet count of 100,000/ $\mu$ l. The erythrocyte sedimentation rate (ESR) was initially 32 mm/hour and later increased to 63 mm/hour.

The test for lupus erythematosus (LE) cells was negative. The direct Coombs' test was positive for warm agglutination and the Venereal Disease Research Laboratories (VDRL) test was reactive. A blood slide for malaria parasites and the hepatitis B surface antigen test were both negative. She was treated initially on the ward with intravenous chloramphenicol, intramuscular quinine and oral Fansidar.

When the child's initial symptoms were not improving and skin changes became prominent, the patient was strongly considered a case of SLE and prednisolone was commenced.

On day 8 of admission she developed respiratory distress and wheezing and was still spiking a temperature.

Nebulized salbutamol was commenced as well as antituberculous treatment. Chest X-ray showed nonspecific infiltrative patchy opacities on both lung fields. Two weeks after admission she had joint swellings and tenderness. Aspirin was included in the treatment at this stage.

There was considerable improvement over the next 2 weeks and antituberculous treatment was stopped except for isoniazid (INAH) prophylaxis because of her prednisolone treatment.

She was discharged home 5 weeks after admission.

The patient was readmitted within 72 hours of discharge with nausea and vomiting. She

was noticed to have increasing jaundice and had tender hepatomegaly. Her serum bilirubin was raised to 142 mmol/l and her liver enzymes were elevated: SGOT (AST) 826 IU and SGPT (ALT) 161 IU. Electrolytes and urea were normal. She was commenced on intravenous 4.3% dextrose/saline, intravenous vitamin K and amoxycillin and gentamicin. Isoniazid prophylaxis was stopped but prednisolone continued. Her clinical signs significantly improved over the next two weeks and liver function tests improved (AST 248 and ALT 155).

At the beginning of the third month from first admission she complained of headache and later became confused and disorientated, talking nonsense. She had other neuropsychiatric manifestations with auditory and visual hallucinations and emotional lability.

Following consultation with a senior colleague and a psychiatrist, haloperidol was added to the treatment. After two weeks on this medication she became completely depressed and refused to talk. Amitriptyline was added to the treatment and the child was later referred to a psychiatrist at the Port Moresby General Hospital (PMGH). Her clinical condition was reported to have improved over the next two to three weeks on haloperidol and the child was sent back to Madang.

Unfortunately the patient was not brought back for follow-up and only presented with an acute respiratory emergency 5 months after discharge from PMGH. She was cyanosed and in severe respiratory distress and pneumonia was considered. She was commenced on intravenous amoxycillin, gentamicin and intranasal oxygen. She died within 24 hours in the Intensive Care Unit of MGH. Postmortem examination was refused by the parents.

## Discussion

This patient presented with fever of unknown origin and a multisystem manifestation of arthralgia, anaemia, weight loss and skin rash. The possibility of drug reaction was raised as she had had Imferon before admission. A history of fever, weight

loss and the development of cough and respiratory distress made pulmonary tuberculosis another diagnostic possibility. Haematological malignancy was also considered with the history of arthralgia, anaemia and weight loss. However, the protean manifestations of fever, weight loss, and involvement of the skin, buccal mucosa, joints and the respiratory, hepatobiliary and central nervous systems fulfilled many of the diagnostic criteria for systemic lupus erythematosus. SLE is a chronic prototypical multisystemic autoimmune disease. Its manifestations are protean and virtually any organ system can be involved. The disease has previously been reported from PNG (1,2) and is seen more frequently in coastal than highlands Papua New Guinea (3).

SLE is extremely rare under 5 years of age and is reported to be primarily a disease of young adult women though about 15% of cases begin during childhood (4,5). The clinical features of paediatric SLE have previously been summarized according to the frequency of symptoms during the course of disease (6). Clearly defined criteria for the diagnosis of SLE have been formulated by the American Rheumatism Association (Table 1) (7). Our patient quite clearly had constitutional (fever), cutaneous (malar rash), musculoskeletal (arthritis), cardiopulmonary (pneumonia), neuropsychiatric (psychosis) and haematological (thrombocytopenia) features. She had more than 4 of the diagnostic criteria. The LE cell was negative though this is known to be present in about 76% of affected people (8).

The best screening test for SLE is the fluorescent antinuclear antibody (FANA) test. Up to 97% of patients with SLE have positive antinuclear antibodies (ANA) at some point in their illness (not necessarily at diagnosis). In a patient like ours with characteristic signs and symptoms, a FANA test may serve to confirm the diagnosis of SLE (9).

Other antibodies considered to be more specific for the diagnosis of SLE include those against native DNA and the extractable nuclear antigen Sm. The finding of low C3 and positive anti-native DNA is 100% specific for SLE. In our setting, we do not have facilities for ANA or anti-native DNA. Our patient's positive VDRL test is explained by the fact that

some patients with SLE develop antibodies against phospholipids, including cardiolipin (the substrate in many reagin tests), which can result in a false positive VDRL test (9). It is assumed that nearly all children with SLE have some evidence of renal involvement such as abnormal urine sediment, proteinuria and renal function changes (10). There is an area of controversy as to whether children with SLE should undergo renal biopsy. Biopsy can reveal a spectrum of renal pathology ranging from normal kidney to mesangial nephritis and glomerulonephritis (11). Our patient had only a trace of protein in the urine even with subsequent urine examinations and biopsy was not done.

Our patient's mild thrombocytopenia of 100,000/ $\mu$ l is compatible with SLE as antiphospholipid antibodies are associated with thrombocytopenia as well as thrombocytosis (12).

The clinical jaundice, tender hepatomegaly and elevated liver enzymes are all consistent with hepatic involvement in SLE. Erythrocyte sedimentation rate and other acute phase reactants are usually elevated in SLE.

The later presentation of neuropsychiatric manifestations of headache, disorientation and emotional lability is interesting as it appeared just as the jaundice was clearing and a differential diagnosis of hepatic failure was considered. Lupus cerebritis, as the neurological manifestations of SLE are sometimes referred to, implies an inflammatory aetiology of central nervous system (CNS) disease. An organic brain syndrome with progressive disorientation and intellectual deterioration is seen in severe cases. Less common are cranial and peripheral neuropathies and chorea (12). Although behavioural disturbance has been described with long-term use of steroids, high-dose corticosteroids (prednisolone 2 mg/kg) should be considered in the management of affected patients with the following:

- Lupus crises (widespread acute multisystem vasculitic involvement)
- Worsening CNS disease (in conjunction with antiepileptic and psychotropic medications)

**TABLE 1**

## CLINICAL FEATURES OF SYSTEMIC LUPUS ERYTHEMATOSUS

<b>Organ system</b>	<b>ARA criteria for classifying SLE*</b>	<b>Other features</b>
<b>Constitutional</b>		Fever, weight loss, malaise, anorexia
<b>Cutaneous</b>	1) Malar rash 2) Discoid rash 3) Photosensitivity 4) Oral/nasopharyngeal ulcers	Alopecia Raynaud's phenomenon Other rashes: subacute cutaneous LE, urticaria, bullous lesions, vasculitis, panniculitis
<b>Musculoskeletal</b>	5) Nonerosive arthritis	Arthralgia/myalgia Myositis Ligamentous laxity Avascular necrosis of bone
<b>Cardiopulmonary</b>	6) Pleuritis Pericarditis	Pleural effusions Myocarditis Pneumonitis Verrucous endocarditis Interstitial fibrosis Pulmonary hypertension
<b>Renal</b>	7) Proteinuria (>500 mg/24 hour) Cylinduria	Nephrotic syndrome Celluria Renal insufficiency Renal failure
<b>Neurological</b>	8) Psychosis Seizures	Organic brain syndrome Cranial nerve abnormalities Peripheral neuropathies Cerebellar signs
<b>Gastrointestinal</b>		Serositis Ascites Vasculitis (bleeding/perforation) Pancreatitis Elevated levels of liver enzymes

*Continued next page*

**TABLE 1** (continued)

CLINICAL FEATURES OF SYSTEMIC LUPUS ERYTHEMATOSUS

<b>Organ system</b>	<b>ARA criteria for classifying SLE*</b>	<b>Other features</b>
<b>Haematological</b>	9) Haemolytic anaemia Leukopenia (<4000/ $\mu$ l) Lymphopenia (<1500/ $\mu$ l) Thrombocytopenia (<100,000/ $\mu$ l)	Anaemia of chronic disease Lupus anticoagulant Thrombosis Splenomegaly Lymphadenopathy
<b>Other systems</b>		Sicca complex Conjunctivitis/episcleritis
<b>Laboratory</b>	10) ANA 11) Anti-dsDNA Anti-Sm False-positive VDRL LE preparation	

ARA = American Rheumatism Association

SLE = systemic lupus erythematosus

LE = lupus erythematosus

ANA = antinuclear antibodies

ds DNA = double-stranded native DNA

Sm = extractable nuclear antigen

VDRL = Venereal Disease Research Laboratories test for syphilis

\*Any combination of 4 manifestations listed as American Rheumatism Association criteria meets the 1982 revised ARA guidelines for classifying SLE; one or more features from within each bracket are considered as one manifestation

- Acute haemolytic anaemia
- Severe lupus nephritis
- Acute pleuropulmonary disease (eg lupus pleuritis, pneumonitis).

In acute life-threatening disease, measures such as high doses of drugs including intravenous pulses of corticosteroids may be warranted. Pulse therapy with methylprednisolone appeared to work well in a severe lupus patient who had had a long course of corticosteroid therapy (13). One of the current topics in the treatment of SLE is intermittent intravenous cyclophosphamide therapy, which is effective even for the steroid-resistant patients with severe lupus nephritis, at least for a short term (14). Whilst the widening

use of cytotoxic agents promises to continue to decrease the mortality from SLE (15), close and careful follow-up is always required.

The prognosis for patients with SLE has improved in the last 20 years. Survival rates at 10 years in excess of 85% have been reported. However, it is not clear whether the improved outcome is a function of aggressive treatment with corticosteroids and/or immunosuppressive agents (16). Unfortunately, our patient defaulted from follow-up after treatment which covered 7 months.

In conclusion, this case illustrates the protean manifestations of SLE with involvement of CNS, hepatic, pulmonary, mucocutaneous and haematological systems.

She appeared to respond to treatment but was lost to follow-up, and died in respiratory crisis. Patient and family education and counselling are crucial aspects of management in order to prevent such a loss after long-term and inter-departmental involvement in management.

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