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Pericarditis as initial clinical manifestation of systemic lupus erythematosus in a girl

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The most common diagnostic features of systemic lupus erythematosus (SLE) include mucocutaneous lesions, nephritis, arthritis and haematological disorder. Serositis in the form of pericarditis is an uncommon first-line clinical manifestation. We report on an 11-year-old Nigerian girl who presented recurrently with pericarditis as the initial clinical manifestation of SLE. Other diagnostic clinical features, namely malar rash and polyarthritis, evolved sequentially over time. Diagnostic laboratory features were lymphopenic leukopenia, a positive lupus erythematosus cell preparation and positive lupus anticoagulant tests. She responded well to non-steroidal anti-inflammatory and immunosuppressive therapy. Unexplained pericarditis in any child should warrant immediate screening for SLE.

Systemic lupus erythematosus (SLE) is a chronic, recurrent multi-systemic auto-immune disease characterised by the production of auto-antibodies that cause widespread tissue damage.[1] There is a strong genetic basis to the pathogenesis of SLE. Multiple abnormalities of both the innate and adaptive immune system may precede clinical presentation by many years.[2] In SLE certain histone post-translational modifications linked to apoptotic and non-apoptotic cell death cause activation of normally tolerant lymphocyte subpopulations.[3] The natural history of SLE remains unpredictable. Patients may present with many years' history of nonspecific symptoms that are frequently attributed to other diseases.[4-6] A strong index of suspicion is therefore critical in diagnosing SLE in populations where it is considered rare. The diagnosis requires the presence of at least 4 of 11 American College of Rheumatology (ACR) diagnostic criteria, but these criteria may occur serially or simultaneously.[7] Compared with renal, musculoskeletal and mucocutaneous features, pericarditis is an uncommon SLE clinical event,[8-11] and when it occurs, it is usually in association with the more common features. We report a rather unusual case of a Nigerian girl who presented initially with recurrent attacks of lupus pericarditis.

Case report

An 11-year-old girl was referred to us with a complaint of recurrent central chest pain of 3 months' duration with severe worsening over the past 2 weeks. Intermittent excruciating chest pain lasting a few minutes to an hour often radiated to the back and shoulder. There was associated chest heaviness and heartbeat awareness. She had responded poorly to several analgesics and antacids prescribed for the assumed diagnoses of peptic ulcer disease, reflux oesophagitis, gastritis and myocardial infarction in two different hospitals where she had earlier been taken for treatment.

She was neither pale nor cyanosed, but was in severe intermittent agonising chest pain. The jugular venous pressure was not elevated. The apex beat was located to the 4th intercostal space, mid-clavicular line; percussion suggested a normal area of cardiac dullness. There was neither pericardial nor pleural friction rub and no cardiac murmurs. There was no peripheral oedema, and neither finger nor toe clubbing. None of the joints was tender. Her weight, height, and body mass index at baseline were 40.0 kg, 156.0 cm, and 16.4 kg/m^2, respectively. The temperature, respiratory rate, pulse (regular and of good volume), blood pressure, and mean arterial pressure were 36.1°C, 26 cycles/min, 104 beats/min, 100/60 mmHg and 73 mmHg, respectively, at baseline. The results of investigations performed are summarised in Table I.

The provisional diagnosis was viral pericarditis. This was revised on the basis of results of subsequent investigations (Table I) to pericarditis probably due to SLE. The echocardiogram (ECHO) repeated at the 8th month revealed marked pericardial thickening (Fig. 1, a and b). Similar ECHO findings were found at 24 months.

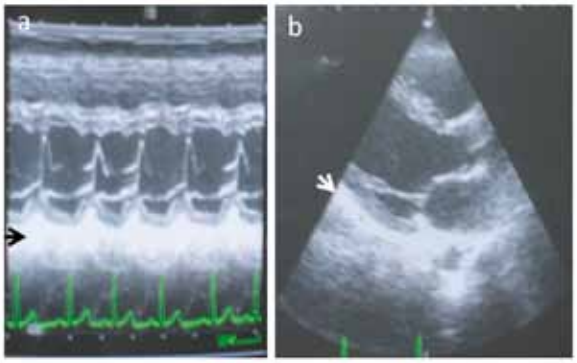

Fig. 1. M-mode (a) and 2D (b) echocardiographs done 8 months after diagnosis showing highly echogenic and thickened pericardium (arrows) as complication of the recurrent lupus pericarditis.

The patient improved remarkably following treatment with ibuprofen (30 mg/kg/d) for 3 months in addition to oral prednisolone (30 mg/m^2/d) for 4 weeks initially and thereafter tapered to 20 mg/m^2/48 h for 6 months and to 10 mg/m^2/48 h subsequently.

A malar rash developed after 12 months of follow-up, while arthritis involving the costochondrial, sacro-iliac and both knee joints occurred simultaneously after 17 months of follow-up. Ibuprofen (30

TABLE I. RESULTS OF SOME INVESTIGATIONS PERFORMED

Investigations	Results
Haematological findings	
Haematocrit (N=5), %	33.0 - 43.0
White blood cell count (N=5) ($\times 10^9$/l)	2.65 - 3.15 (normal 4 - 10)
Platelet count (N=5) ($\times 10^9$/l)	220 - 233 (normal 150 - 400)
Lupus erythematosus cell preparation	Positive
Partial thromboplastin time et kaolin (PTTk) (s)	51.2 (normal 35 - 40)
PTTk with mixing test experiment (s)	Positive; PTTk 48.0 (normal 35 - 40)
Erythrocyte sedimentation rate (mm/h)	14.0 (normal <5)
Baseline electrocardiogram	
Rhythm and heart rate	Sinus, 100 beats/min
QRS complex	Normal
PR interval, s	0.16 (normal 0.12 - 0.16)
ST segment	Elevated in all leads
T wave	Normal direction
Pathological Q wave	None
Electrocardiogram at 8th month	Normal
Baseline echocardiogram	
M-mode/two-dimensional	Normal cardiac chambers and myocardial contractility; highly echogenic pericardium with mild pericardial effusion
Colour Doppler	No regurgitation across the valves
Echocardiogram at 8th month*	
M-mode/two-dimensional	Thickened pericardium with effusion antero-posteriorly (Fig. 1); LVM† and LVM index were 147.62 g (normal 26.5 - 149.1)[12] and 44.43 g/m$^{2.7}$ (normal 13.06 - 44.88),[12] respectively
Colour Doppler	Left ventricular ejection fraction was 54.26% (normal 64.0 - 83.0)
Urine sediments	Normal
Proteinuria	3.2 mg/m^2/h (normal <4)
Baseline eGFR‡, ml/min/1.73 m^2	107

*Similar echocardiogram findings at 2 years.
†Left ventricular mass. The normal reference values for the LVM and LVM index are from reference 12.
‡Estimated glomerular filtration rate.

mg/kg/d) was then re-introduced for 3 months while prednisolone was escalated to 20 mg/m^2/48 h for 4 weeks; her current maintenance prednisolone is 10 mg/m^2/48 h. Azathioprine (1 mg/kg/d) was given for 2 years.

The final diagnosis was lupus pericarditis, the case having satisfied 5 of 11 ACR diagnostic criteria for SLE. These were pericarditis, malar rash, polyarthritis, and a positive mixing test experiment indicating presence of a lupus anticoagulant (anti-phospholipid antibody subtype), a positive LE cell test and persistent lymphopenic leukopenia (1.29 - 1.30$\times 10^9$/l). At the time of writing, she had been been followed up for 32 months and maintained remission for 15 months on the above medications. At the last clinic visit, all clinical problems had resolved and her abnormal haematological profile had normalised.

Discussion

Anti-DNA antibodies such as anti-nucleosomal, anti-double-stranded DNA, and other auto-antibodies that are synthesised in SLE owing to loss of tolerance by the T and B lymphocytes form immune complexes that provoke inflammatory reactions within tissues and organs, leading to structural damage and disturbance of function. Cardiac damage in SLE is therefore the result of the inflammatory reaction caused by some of these auto-antibodies. Pericarditis and/or myocarditis are frequently and significantly associated with anti-ribonucleoprotein antibodies such as anti-Ro/SS-A (Sjögren's syndrome A nuclear antigen) and anti-La/SS-B (Sjögren's syndrome B nuclear antigen) antibodies that are directed against cardiac structures in childhood SLE.[13] Similarly, lupus pericarditis has been associated with elevated pericardial fluid levels of helper T cells (CD4+), natural killer cells and inflammatory cytokines, namely interleukins (IL-1β, IL-6, IL-10), tumour necrosis factor alpha (TNF-α) and interferon-ɣ.[14]

Compared with the frequency of other diagnostic clinical features of SLE, namely lupus nephritis (81.0 - 100.0%),[6,11] mucocutaneous lesions (68.0 - 70.0%)[5,10] and arthritis (65.4 - 91.0%),[5,6,11] lupus pericarditis (7.7 - 40.0%) is a rare clinical event in children, as is neuropsychiatric lupus (7.7 - 36.4%).[5,6,11] The rarity of pericarditis among other diagnostic clinical ACR criteria led to the clinical delay in this patient. Rheumatic fever was not entertained as a diagnosis because clinical, electrocardiographic and ECHO features in the child were not supportive. Lupus pericarditis rarely occurs in isolation without the other well-known diagnostic features of SLE.[6,11,15] In this patient, pericarditis was curiously the sole clinical presentation for more than 12 months before some of the more common diagnostic criteria, namely malar rash and arthritis, supervened sequentially over a period of 12 - 17 months.

Misdiagnosis is a common phenomenon in SLE.[6,10,16] In one series, all patients were initially misdiagnosed, with malaria accounting for 36.4% of all misdiagnoses.[6] Unless there is a deliberate effort to routinely screen for SLE in populations where it is considered rare, its diagnosis will continue to be missed. That this patient was variously misdiagnosed and treated for acute gastritis, myocardial infarction, and reflux oesophagitis attests to this fact.

Although pericarditis was the initial sole clinical presentation in this patient, subsequent echocardiographic assessment revealed subclinical myocardial hypokinesia (left ventricular ejection fraction 54.26%), possibly due to lupus myocarditis.

The patient has demonstrated remarkable clinical and laboratory improvement, but careful follow-up and routine cardiovascular screening is required because of the persistent myocardial hypokinesia. This is particularly important for early intervention in order to avoid heart failure. The fact that lupus anticoagulant is a strong risk factor for thrombosis in SLE[17] suggests the possibility of a future thrombotic event such as myocardial ischaemia in our patient, since she was positive on lupus anticoagulant testing. Although the latter normalised following treatment, the test still needs to be performed regularly for early detection of the reappearance of the lupus anticoagulant so that definitive therapy can be started to avoid a coronary thrombotic event. Routine treatment with antimalarials (hydroxychloroquine or chloroquine) has been reported to be protective against thrombosis, and is associated with increased survival in SLE patients who are positive for lupus anticoagulant.[18,19] It is concluded that long before other diagnostic features, pericarditis may be the sole and initial clinical manifestation of SLE in a child. Unexplained pericarditis in any child should therefore warrant immediate screening for SLE.

Lupus pericarditis rarely occurs without the other well-known diagnostic features of SLE.

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