CASE STUDY

Systemic lupus erythematosus, eosinophilia and Löffler’s endocarditis. An unusual association


ABSTRACT: A 24-yr-old male, known since the age of 11 to have a nonerosive arthritis and later diagnosed as having systemic lupus erythematosus (SLE), developed subacute heart failure with diffuse lung infiltrates and died suddenly after having presented a moderate hyper eosinophilia for 6 months for which no other causes besides the SLE were found. A post mortem examination revealed Löffler’s endocarditis (endocarditis parietalis fibroplastica) with acute pulmonary capillaritis. This represents Löffler’s endocarditis in the setting of SLE. To the best of the authors’ knowledge, this association has not been reported before.


Löffler’s endocarditis [1] is characterized by an eosinophilic endomyocardial fibrosis and may occur in association with eosinophilia such as hypereosinophilic syndrome (HES), eosinophilic leukaemia, carcinoma, lymphoma, drug reactions, or parasites [2, 3]. Associations with the combination of pulmonary infiltrates and peripheral eosinophilia can be classified into two groups [4, 5]: 1) illnesses in which peripheral eosinophilia is a major component, either of known aetiology such as allergic bronchopulmonary aspergillosis, drug reactions (e.g. to nitrofurantoin, minocycline or many others), and certain parasitic infections or may be of unknown aetiology such as chronic eosinophilic pneumonia, hypereosinophilic syndrome, and Churg–Strauss syndrome; 2) illnesses in which peripheral eosinophilia occurs infrequently and is a minor component, such as infections (e.g. tuberculosis, brucellosis, histoplasmosis, etc.), neoplasms (e.g. Hodgkin’s disease) and immunological disorders (e.g. rheumatoid lung disease, sarcoidosis, etc.).

This report describes a young patient with nonerosive arthritis, later diagnosed as systemic lupus erythematosus (SLE). As the corticosteroid dose was tapered, a moderate eosinophilia became apparent. Within 6 months, diffuse interstitial lung disease and heart failure developed, and the patient died suddenly. At autopsy, typical Löffler’s endocarditis and an acute pulmonary capillaritis were found. Such an association makes a report on this case worthwhile because the association of SLE, eosinophilia and Löffler’s endocarditis has not hitherto been described.

Case report

A 24-yr-old-Caucasian male working as an informatician and who was a smoker of 10 cigarettes daily was transferred to the authors’ hospital with hypoxia and heart failure. He died suddenly within 2 days of admission.

Since the age of 11, he had suffered from polyarthritis. At the age of 15, human leukocyte antigen (HLA)-B27 and rheumatoid factor were found to be positive, and sulphasalazine was prescribed. At the age of 17, pleuritis and pericarditis, alopecia, skin lesions, photosensitivity, anaemia, lymphopenia, a positive antimicrobial antibody (ANA), a positive anti-deoxyribonucleic acid, and a positive leukocyte elastase (LE) test were found. The patient was treated with methylprednisolone (40 mg·day⁻¹), chloroquine (100 mg·day⁻¹), and piroxicam (20 mg·day⁻¹), with good functional results. At the age of 20, methylprednisolone was reduced to 4 mg·day⁻¹. Periangular vascular lesions appeared temporarily, eosinophilia rose to 400·mm⁻³ and the rheumatoid factor (RA-latex) was negative. At the age of 22, he had complaints of polyarthritis and precordial discomfort. Eosinophilia reached 570·mm⁻³, and circulating immune complexes were positive as well as the extractable nuclear antigen (ENA) (two positive bands, but negative for Sjögren syndrome A (SSA)/Ro, Sjögren syndrome B (SSB)/La, Serrata marcescens, ribonuclease-protein, and Jo1 antibodies). Urinalysis revealed the presence of microscopic haematuria (8–10 red blood cells per field).

At the age of 23 both the complaints and the periungual vasculitis worsened; the eosinophilia ranged 380–1250·mm⁻³. The urinalysis was normal with normal serum creatinine and urea. One year later, subacute diffuse interstitial lung infiltrates appeared with dry cough, haemoptysis and retrosternal discomfort but no fever. This led to a rapidly progressive respiratory failure (fig. 1). Five days before admission to the authors’ hospital, echocardiography revealed a minor pericardial effusion and a thickened heart
No ventricular thrombi were seen. Microbiological examinations of blood, sputum and urine were negative. The patient was empirically treated with low-molecular-weight heparin, antibiotics and 40 mg methylprednisolone. The arterial oxygen tension (\(P_{a,O_2}\)) was initially 8.4 kPa (63 mmHg) (room air), but dropped to 7.8 kPa (59 mmHg) on 2 L O\(_2\) min\(^{-1}\) and to 9.6 kPa (72 mmHg) on 4 L O\(_2\) min\(^{-1}\). The patient was referred to the authors' hospital.

On admission (day 1), he was pale, bilateral basal lung crackles were heard, the heart was hyperdynamic with a regular rhythm of 120 beats min\(^{-1}\), the blood pressure was 100/60 mmHg, the central venous pressure was clinically increasing and there was a positive hepatojugular reflux. A moderate anaemia was present, liver tests revealed some degree of disturbance (table 1). Serological investigation showed a positive ANA (homogenous staining pattern) and ENA, negative c- and p- anti-neutrophil cytoplasm antibody (ANCA), a negative RA-latex, the presence of circulating immune complexes, a low 50% haemolysing dose of complement (CH\(_{50}\)) of 230 U mL\(^{-1}\) and severe T\(_4\)-lymphopenia (79.2 mm\(^{-3}\)). Renal function was normal. Lung function showed a severe restrictive defect with a low carbon monoxide diffusing capacity (29% predicted). The \(P_{a,O_2}\) had improved to 13.3 kPa (100 mmHg) on 2 L O\(_2\) min\(^{-1}\).

When the medical history of this patient was revised with a nonerosive arthritis, pericarditis, a leucopenia of <4,000 mm\(^{-3}\) on more than two occasions and a lymphopenia of <1,500 mm\(^{-3}\) on more than two occasions, a positive LE test in December 1988, a positive anti-DNA antibody and an abnormal titre of ANA, the diagnosis of SLE was made based on the American Rheumatism Association classification [6]. Corticosteroids (methylprednisolone 40 mg i.v.) were continued and diuretics (furosemide 2 \(\times\) 40 mg i.v.) were added. On day 2 the patient’s condition was improved, \(P_{a,O_2}\) was 10.6 kPa (80 mmHg) on room air, and he even managed a visit to the hospital cafeteria with his family. The next morning (day 3) he explained to the nurse that he was feeling well. Fifteen minutes later, he was found dead in bed.

An autopsy was performed; an examination of the heart revealed Löffler’s endocarditis with a massive mural thrombosis of the left ventricle (fig. 2) and diffuse fibrous pericardial adhesions. The lung showed an acute pulmonary capillaritis (fig. 3) with a polynuclear infiltrate and multiple pleural adhesions. There were no signs of aryllymphoplasmocytic pneumonia, fibrosis or emboli. A centriflobular congestion of the liver was also found. Examination of the major abdominal vessels revealed no thrombi. No parasites were found at the autopsy.

Table 1. Results of the laboratory investigation before admission (-3, -2, -1 yrs; day -3), and on admission (day 1 and 2)

<table>
<thead>
<tr>
<th></th>
<th>-3 yrs</th>
<th>-2 yrs</th>
<th>-1 yr</th>
<th>Day -3</th>
<th>Day 1</th>
<th>Day 2</th>
</tr>
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<tbody>
<tr>
<td>Haemoglobin mg dL(^{-1})</td>
<td>14.0</td>
<td>14.7</td>
<td>12.6</td>
<td>11.4</td>
<td>10.0</td>
<td>0</td>
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<tr>
<td>Haematocrit</td>
<td>0.43</td>
<td>0.43</td>
<td>0.37</td>
<td>0.33</td>
<td>0.30</td>
<td>-</td>
</tr>
<tr>
<td>Thrombocytes (10^9) L(^{-1})</td>
<td>267</td>
<td>237</td>
<td>229</td>
<td>143</td>
<td>208</td>
<td>-</td>
</tr>
<tr>
<td>Leukocytes</td>
<td>5.6</td>
<td>7.8</td>
<td>5.0</td>
<td>8.4</td>
<td>7.4</td>
<td>-</td>
</tr>
<tr>
<td>Neutrophils %</td>
<td>75</td>
<td>82</td>
<td>48</td>
<td>76</td>
<td>92</td>
<td>-</td>
</tr>
<tr>
<td>Eosinophils %</td>
<td>7</td>
<td>7</td>
<td>24</td>
<td>11</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Lymphocytes %</td>
<td>11</td>
<td>7</td>
<td>24</td>
<td>7</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>GOT U L(^{-1})</td>
<td>6</td>
<td>14</td>
<td>13</td>
<td>-</td>
<td>204</td>
<td>227</td>
</tr>
<tr>
<td>GPT U L(^{-1})</td>
<td>5</td>
<td>1</td>
<td>6</td>
<td>-</td>
<td>349</td>
<td>546</td>
</tr>
<tr>
<td>(\gamma)GT U L(^{-1})</td>
<td>10</td>
<td>12</td>
<td>11</td>
<td>-</td>
<td>39</td>
<td>39</td>
</tr>
<tr>
<td>AP U L(^{-1})</td>
<td>94</td>
<td>133</td>
<td>121</td>
<td>-</td>
<td>130</td>
<td>148</td>
</tr>
<tr>
<td>PTT %</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>52.7</td>
<td>-</td>
</tr>
</tbody>
</table>

GOT: glutamate oxaloacetate transaminase; GPT: glutamate-pyruvate transaminase; \(\gamma\)GT: \(\gamma\)-glutamyl transpeptidase; AP: alkaline phosphatase; PTT: partial thromboplastin time.

Fig. 1. Chest radiograph showing patchy reticulo-micronodular infiltrates, increased heart size and obliteration of both costodiaphragmatic angles (note the electrode patch laterally of the right hilum).

Fig. 2. Opened left cardiac ventricle, showing massive mural thrombosis.
Cardiac involvement or Löffler's endocarditis is frequently seen in the hypereosinophilic syndrome [3], an idiopathic syndrome characterized by: 1) a persistent elevation in the total eosinophilic count (>1,500 mm$^{-3}$) for over 6 months or death within 6 months; 2) associated multiorgan damage; and 3) no detectable underlying causes for the eosinophilia [13]. The current patient did not meet criteria (1) or (3). The cardiac disease in the patient was speculated to be not directly due to SLE, but was secondary to the increase of eosinophils after the corticosteroids were tapered off. Indeed, eosinophils have been shown to be able to cause myocardial toxicity especially due to their cationic proteins [11, 14]. According to Roberts et al. [15], it is likely that Löffler's endocarditis, associated with other diseases, is due to the eosinophilia itself and not to an unrecognized underlying factor. In this respect Löffler's endocarditis has been reported in patients with variegated eosinophilic responses, whether they were secondary to drugs or to parasitic diseases [3, 15].

Animal models of hypereosinophilia caused by parasitic infection have demonstrated a cardiac dysfunction and accumulation of eosinophils in the myocardium, in addition to histological alterations leading to decreased myocardial compliance [16]. In the current patient, neither serological nor stool examination tests were carried out to exclude the presence of parasites because no clinical signs of parasitic infection were present; also, on autopsy, no parasitic infestation was found. In SLE, as in rheumatoid arthritis, marked eosinophilia has occasionally been described [17, 18]. However, to the best of the authors’ knowledge, no Löffler's endocarditis has been reported in this context.

At autopsy, the patient’s lung showed acute pulmonary capillaritis, with polymorphonuclear cell infiltration and multiple pleural adhesions. A variety of pulmonary parenchymal lesions have been described in SLE, ranging from acute lupus pneumonitis syndrome to a more chronic diffuse interstitial disease with subacute or recurrent infiltrates [19]. A microscopic examination of the patient’s lung revealed expansion of the interalveolar septa by polymorphonuclear cells, which caused capillary thromboses with necrosis and rupture of the alveolar septa (fig. 3). The alveolar lumens were filled with a fibrinous exudate. These lesions are typical for pulmonary capillaritis [20, 21]. This entity is not pathognomonic for SLE, and has been reported in Wegener's granulomatosis, microscopic polyarteritis, Goodpasture's syndrome, idiopathic pulmonary renal syndrome, Behçet syndrome, Henoch–Schönlein purpura, IgA nephropathy, antiphospholipid syndrome, progressive systemic sclerosis and phenytoin use [20]. In hypereosinophilia the presence of pulmonary capillaritis has not been described [20]. In the current case, the autopsy also demonstrated the presence of fibrinous pleural lesions. Pleural disease, i.e., adhesions, thickening or effusion, may be found.
at autopsy in up to 93% of the cases affected by SLE; however, clinically apparent disease is less frequent [19].

In conclusion, the patient, with an unrecognized systemic lupus erythematosus, died suddenly from a restrictive cardiomyopathy with intracavitary thrombosis and associated acute pulmonary capillaritis. These cardiac lesions were probably related the blood eosinophilia, and the latter was considered secondary or associated to systemic lupus erythematosus, as no other cause was detected.

References