Case reports

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Löffler's endocarditis

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The clinical, laboratory, and necropsy findings in a patient with massive eosinophilia and fatal cardiac failure are reported. Necropsy revealed partial obliteration of the lumen of the left ventricle with dense white thrombus, and fibrous infiltration of the myocardium. An additional finding, not hitherto described in Löffler's endocarditis, was massive enlargement of the mesenteric lymph nodes.

Case report

A 48-year-old male caucasian wool carder was admitted with a 4-month history of weight loss and epigastric pain. In the weeks before admission he was treated for ankle oedema, nocturia, and intermittent nocturnal

sweating. He felt increasingly tired and unwell with pain in the legs, neck, arms, and chest, and shortly before admission he developed diarrhoea and mild crampy abdominal pain.

On admission he looked unwell but was not in acute distress. The venous pressure was not raised and the

FIG. 1 Chest x-ray on admission (A) and one week before death (B).

blood pressure was 140/80 mmHg (18.6/10.6 kPa). The heart was not enlarged nor were there any thrills or murmurs. The peripheral pulses were intact. There were numerous splinter haemorrhages. The lung fields were normal. There was slight tenderness and guarding above and to the left of the umbilicus but the liver and spleen were not enlarged. The nervous system was intact and the optic fundi normal.

The peripheral blood contained leucocytes $59 \times 10^9/l$ of which 80 per cent were mature eosinophils: no blast forms were seen. The haemoglobin was 14.5 g/dl and the erythrocyte sedimentation rate was 20 mm in the first hour. Plasma proteins measured 63 g/l (albumin 30, globulin 33). The blood urea was 43 mg/100 ml (7.13 mmol/l) and the serum electrolytes were normal. Serum calcium was 9.2 mg/100 ml (2.3 mmol/l) and phosphorus 3.9 mg/100 ml (1.25 mmol/l). Serum alkaline phosphatase was 12.6 K A units. Though antibiotics had been withheld no pathogens could be cultured from blood, urine, or sputum. Of the cells in the sputum a third were eosinophils. The urine contained no sugar, albumin, or blood.

The chest x-ray was normal on admission (Fig. 1A) but the electrocardiogram showed non-specific inversion of the T wave in leads II, III, aVF, and V5 to 6 (Fig. 2A). The sternal marrow showed myeloid hyperplasia with increased eosinophils and eosinophil precursors: erythropoiesis was normoblastic and normal

megakaryocytes and platelets were seen. Occult blood was detected in the faeces but no parasites or ova were found despite diligent search. Serum was anticomplementary for *Taenia*, *Fasciola*, *Trichinella*, and hydatid disease. The Tine test was negative. Barium studies showed no abnormality of the large or small intestines. Achlorhydria was present.

For two weeks the patient had an intermittent low grade pyrexia, aching pains in the upper chest and shoulders, and diarrhoea. In the third week the evening temperature rose to 39.4°C , and an apical systolic murmur was noted. Blood cultures remained negative and there were fewer splinter haemorrhages. He became increasingly dyspnoeic and developed bilateral pulmonary crepitations and pleural effusions. He rapidly developed enlargement of the liver and spleen and the cardiac shadow became enlarged with distension of the pulmonary veins, basal septal lines, and bilateral pleural effusions (Fig. 1B). The electrocardiogram showed a QS pattern in V1 and V2 and pronounced diminution of the R waves in V3 and V4 (Fig. 2B). The voltage of the QRS complexes, other than V2 and V3, had fallen and the depth of T wave inversion in leads II, III, and aVF had increased. The cardiographic appearances were consistent with cardiomyopathy.

Clinically the patient fulfilled the criteria of Löffler's endocarditis. In addition to decongestive therapy, hydrocortisone 200 mg daily and ampicillin 2 g daily were administered. Within 24 hours the pyrexia disappeared, the dyspnoea diminished, and the leucocyte count fell from $32,400/\text{mm}^3$ (72% eosinophils) to $12,700/\text{mm}^3$, with virtual disappearance of circulating eosinophils (neutrophils 61%, lymphocytes 36%, monocytes 3%). Unfortunately the improvement in cardiac failure was short lived and four days after steroid therapy was started he collapsed suddenly. The cardiogram showed ventricular fibrillation. Electrical defibrillation resulted in asystole which proved unresponsive to intracardiac adrenaline and attempted endocardial pacing.

Necropsy report

The pericardial cavity contained 100 ml and each pleural cavity 1000 ml of clear fluid. The heart was enlarged, weighing 550 g. The apical third of the left ventricular cavity was obliterated by mural thrombus which also encroached considerably upon its middle third and extended up as a layer of homogeneous firm white material to surround the lower end of some of the chordae tendineae (Fig. 3). The valve ring was slightly dilated but the mitral valve cusps were normal. Only the base of the thrombus showed organization. Beneath the endocardium was a thin layer of fibrosis and the myocardium showed patches of fibrosis extending into areas unrelated to mural thrombus. The right ventricle was hypertrophied also and showed patchy fibrosis and a thinner and less extensive mural thrombus. The tricuspid and semilunar valves were normal and the atria contained no thrombus. The coronary arteries were normal.

Numerous sections from the heart were stained by the following methods: haematoxylin and eosin, P.A.S., Gram, Ziehl Neelsen, Gomori's silver, and Verhoeff's

FIG. 2 Selected electrocardiographic leads recorded on admission (A) mounted beside the same leads recorded one week before death (B).

FIG. 3 Section through the left ventricle showing the thick mural thrombus outlined by arrows.

FIG. 4 Enlarged mesenteric lymph nodes and adjacent small intestine.

elastin. The myocardium showed no recent necrosis but there had been widespread replacement of muscle fibres with fibrous tissue, some of which was old and some recent. In places this fibrosis extended into areas unrelated to the mural thrombus and elsewhere thrombus extended over normal myocardium. The myocardium showed no basophilic degeneration. No multiplication or fragmentation of elastic tissue was seen beneath the

mural thrombus. The base of the thrombus was invaded by capillaries, fibroblasts, and mononuclear cells, some containing haemosiderin, but most of it was pure thrombus in which fragments of nuclear material, but no red cells, persisted. No bacteria, fungi, or parasites could be found. Only one tiny interstitial focus of neutrophils and eosinophils was found in the myocardium. The main coronary arteries were histologically normal, but a

few small branches and a Thebesian vein contained organizing thrombi.

The mesenteric and peripancreatic lymph nodes formed a large mass in which the individual lymph nodes measured up to 3.5 cm in diameter (Fig. 4). They were discrete, with thin capsules, and the cut surface was fleshy in consistency and pale grey in colour, with numerous whitish dots and a few larger irregular opaque white areas. Histologically there was extensive oedema, and some recent necrosis with recognizable nuclear remnants, suggesting that the changes were fairly recent. Some necrotic areas showed a very pale peripheral zone and a central conglomeration of deeply eosinophilic material mixed with nuclear debris. The enlargement of the glands was caused almost solely by the recent necrosis and oedema, with no excess of neutrophils, only occasional eosinophils, and unusually few plasma cells. Fibrous tissue was only moderately increased and outside the necrotic areas germinal centres were retained. Staining by Gram, Ziehl Neelsen, P.A.S., and Gomori's silver method revealed no malignant cells, tubercle bacilli, fungi, parasites, or other aetiological agents. Lymph nodes elsewhere in the body were not enlarged.

No macroscopical changes were noted in the small intestine but histologically there were a few patchy fibrotic areas in the submucosa which were infiltrated in places with eosinophils and neutrophils. Occasional foci of epithelioid and giant cells, and a few dense clumps of eosinophils were found in the mucosa and submucosa. Special stains revealed no bacteria, fungi, or parasites. The lungs showed oedema, congestion, and some old apical pleural scars. The liver and spleen were congested but the other organs were normal.

Discussion

To date, approximately 90 cases of Löffler's endocarditis have been reported (Brockington and Olsen, 1973). The present case is the first reported from Ireland, but the cardiac pathology bears a striking resemblance to that in cases reported from Europe (Löffler, 1936), South Africa (Brink and Weber, 1963), and the United States (Hardy and Anderson, 1968; Roberts, Liegler, and Carbone, 1969; Rasche, Kelsch, and Weaver, 1973). The abnormal electrocardiogram, the evidence of micro-emboli, the insidious onset and inexorable progress of the cardiac failure, the lack of response to digitalis and the short-lived improvement produced by steroid therapy have been recorded and can be understood readily in the light of the necropsy findings in the heart. Though other cases of sudden death have been described, there have been few previous electrocardiographic recordings made at the time of death. Inability to pace the heart from the right ventricle following correction of ventricular fibrillation may have been caused by the presence of mural thrombus.

The aetiology of the condition remains obscure. The patient did not have eosinophilic leukaemia nor was the condition secondary to asthma, Hodgkin's disease, sarcoidosis, carcinoma, drugs, or detectable parasitic infection. The patient had never been to the tropics and none of the wool he worked with was from the tropics. The disappointing failure to isolate some infective or toxic agent before death was matched by the failure to find such an agent at necropsy. Nevertheless, the hitherto undescribed massive enlargement of the mesenteric lymph nodes and the microscopical lesions in the bowel arouse suspicion that some agent may have gained entry through the gastrointestinal tract. The rapid disappearance of circulating eosinophils in response to steroid therapy suggests that they represented an allergic response.

Brockington, Luzzato, and Osunkoya (1970) suggest that the endocardial damage may be related to the presence of very large numbers of circulating eosinophils. The unusual severity of the cardiac lesions in this case may have been related to the remarkably high eosinophil count. Recent major surveys (Roberts *et al.*, 1969; Brockington and Olsen, 1973) have put forward the attractive proposition that Löffler's endocarditis and endomyocardial fibrosis are probably the same disease at different phases of its evolution. Had the pathological process been less fulminant in this patient, enabling him to survive for several years, it seems likely from the distribution of the thrombus that the heart would have displayed the appearance of endomyocardial fibrosis.

The present case supports the view that the administration of steroids can produce temporary remission, but that unless given before severe cardiac failure supervenes therapy does not affect the outcome (Hardy and Anderson, 1968). Though it is tempting to withhold treatment until an aetiological diagnosis has been made, we believe that patients with severe eosinophilia and an abnormal electrocardiogram should receive steroids without delay.

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