Löffler's endocarditis in childhood

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A 5-year-old girl with Löffler's endocarditis died in congestive heart failure. Necropsy showed extensive mural thrombosis within the heart chambers, myocardial and cerebral necrosis, pulmonary arterial thrombosis, and pronounced eosinophilic infiltration in heart, lungs, spleen, liver, and lymph nodes.

A 5-year-old girl with hepatosplenomegaly and eosinophilic leucocytosis died in congestive heart failure. Morphologically, extensive mural thrombi compromised the lumen of the right and left ventricles, while the liver, spleen, and lymph nodes were infiltrated by mature eosinophil leucocytes. These clinicopathological findings, while consistent with Löffler's endocarditis (Löffler, 1936), differed from reported cases by reason of the recent vascular fibrin thrombi, the acute and organizing myocardial necrosis, and the absence of myocardial fibrosis in our case. Clinically and pathologically, Löffler's endocarditis, endomyocardial disease with eosinophilia (Robert, Liegler, and Carbone, 1969), disseminated eosinophilic collagen disease (Odeberg, 1965), and mature eosinophilic leukaemia (Benvenisti and Ultmann, 1969) are so similar they may be considered as entities of a disease-spectrum.

We are reporting this unusual example of Löffler's endocarditis because the clinical disease was brief (1 month) and the acute pathological changes may offer a clue to the pathogenesis of the endomyocardial fibrosis occurring in this entity. It invites speculation as to a possible relation between Löffler's endocarditis and the endomyocardial fibrosis of Davies.

Case report
A 5-year-old white girl had intermittent abdominal pain, vomiting, and loose stools for 8 days in 1969. Her symptoms were temporarily relieved by antacid and antispasmodic therapy, but recurred, accompanied by a fever of 39.4°C and a leucocytosis of 90,000, with 87 per cent eosinophils.

She was admitted to her community hospital and a chest radiograph, upper gastrointestinal series, and a cholecystogram were normal. Her eosinophilic leucocytosis continued, with white blood cell counts up to 180,000/mm³. Bone marrow aspiration disclosed a myeloid-erythroid ratio of 20:1; the predominant cells were eosinophilic myelocytes, metamyelocytes, and mature eosinophils. Stools were negative for ova and parasites. Because of continued symptoms and eosinophilia, she was admitted to the Mott Children's Hospital, The University of Michigan Medical Center, later in the same month.

Past history
The child had had her DPT inoculations, rubella, and oral polio vaccines. A tuberculin skin test had been negative 4 months previously. She had had erythema multiforme during the previous winter and contact dermatitis in the following spring.

Physical examination
The child was pale and irritable with a temperature of 36.7°C, a regular pulse of 140/min, and respiratory rate of 32/min. Her lungs were clear. The spleen was palpable 2 cm below the left costal margin and the liver extended 5 cm below the right. The abdomen was mildly tender, but flaccid. Lymph nodes were not palpable, and the neurological examination was normal.

Laboratory studies
Haemoglobin was 8.1 g/100 ml, the haematocrit 22.5 per cent, and the platelet count 195,000/mm³. The white blood cell count was 152,000/mm³, with 8 segmented neutrophils, 1 neutrophil band-form, 5 lymphocytes, 83 eosinophils, 2 eosinophil band-forms, and 1 eosinophil myelocyte per 100 cells. Serum creatinine, uric acid, bilirubin, alkaline phosphatase, and blood urea nitrogen were normal. Serum glutamic oxalacetic transaminase was 80 units (normal 40 units). An LE preparation was negative. Total serum proteins, protein electrophoresis, and immune globulins were normal. A prothrombin time was 61.2 seconds (normal control 12 seconds). The direct Coombs' test was +.

A chest radiograph taken on the second day in hospital showed mild generalized cardiomegaly, pulmonary vascular congestion, and widespread linear opacities concentrated in the lung bases. The electrocardiogram showed nonspecific myocardial changes.

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The child remained afebrile throughout her admission. She became confused, restless, and dyspneic on the second hospital day. At 30° elevation, the neck veins were distended; digitalis, antibiotic, and corticosteroid therapy were started. She lapsed into coma and died on the third day, after an illness spanning only 25 days.

**Necropsy** The child measured 114 cm in length and weighed 18 kg. The heart weighed 150 g; both ventricles were dilated and contained mural thrombi. Thrombi covered the entire endocardium of the left ventricle from the posterior portion of the mitral valve ring to the apex, sparing only the superior one-half of the ventricular septum (see Fig.). The yellowish-tan thrombi filled the apex of the ventricle, enclosed the papillary muscles, and reduced the lumen of the left ventricle to a diameter of 2–3 cm. Thrombi adhered to patchy areas of the right ventricular endocardium. Two glistening polypoid thrombi were attached to the right atrial endocardium.

Focal firm yellow streaks interrupted the deep red myocardium of the right and left ventricles.

Histologically, the thrombi consisted of exuberant fibrin, abundant eosinophils, eosinophilic crystals, and necrotic debris. A palisade of epithelioid histiocytes formed an interface between the thrombus and the myocardium. The cytoplasm of numerous histiocytes contained tan, granular pigment. Many recent fibrin thrombi occluded the arterioles and venules within the myocardial. Focal and extensive areas of recent and partially organized necrosis were scattered through the myocardium, both adjacent to the mural thrombi and within the heart muscle. A Movat's pentachrome stain disclosed increased acid mucopolysaccharide in the subendothelial connective tissue and myocardial interstitium adjacent to the necrotic areas.

The combined weight of the lungs was 500 g. They were red and congested except for the left upper lobe, which contained a 2 × 2 cm wedge-shaped infarct corresponding to the distribution of an artery occluded by a friable, white thrombus 2 cm in length. Alveolar walls and alveoli contained abundant eosinophils and a few macrophages. Fibrin thrombi occluded several pulmonary arterioles and venules.

Recent triangular, nodular infarcts were present in the spleen; its venules and capillaries contained recent fibrin thrombi. In focal areas, recent fibrin thrombi occupied the sinusoids of the liver. Similar thrombi occluded renal and cerebral arterioles and venules. There was an associated focal proliferative glomerulitis and recent necrosis in the thalamus and cerebellum.

In addition to the cardiac and pulmonary infiltrates, mature eosinophils occupied the pericapilar adipose tissue, capsules, and subcapsular sinuses of lymph nodes, the red pulp of the spleen, and the portal spaces of the liver. No myelocytes or blast cells were present. The bone marrow showed hyperplasia of the eosinophil series with orderly maturation; megakaryocytes were abundant. A thorough search disclosed no parasites.

**Discussion**

Over 40 cases of Löffler's endocarditis have been reported (Weiss-Carmine, 1957; Roberts et al., 1969). The disease predominates in young men; its duration is usually less than 2 years. Patients have a blood eosinophilia, and nearly all die in congestive heart failure. The hearts are heavy, and the right or the left ventricle, or both, usually contain mural thrombi which cover a thick fibrotic endocardium. Most reported patients have had myocardial, as well as endocardial, fibrosis. Tissue eosinophilia is variable, ranging from dense to sparse. Over half of the patients have had inflammatory necrosis or thickening of blood vessels.

Two features of the present case are noteworthy. The sex and age of our subject are unusual. Though we have located 9 cases of idiopathic eosinophilia in children under 12 years of age (Thomsen and Plumb, 1939; Friedman, Wolman, and Tyner, 1944;
Gross, Hellweg, and Lambers, 1955; Engfeldt and Zetterström, 1956; Bentley et al., 1961; Oehme and Stave, 1962; Panoff, 1962; Odeberg, 1965), all have been in boys. Furthermore, only one case of Engfeldt and Zetterström was clinically and morphologically similar to ours.

The acuteness of the histopathological changes in our case is another unusual feature. Though necrosis was also observed in the reported cases, it was almost always accompanied — even in children — by myocardial and endocardial fibrosis (Engfeldt and Zetterström, 1956). Perhaps the fresh vascular thrombi in our case provide a clue to the pathogenesis of the myocardial fibrosis, vascular changes, and membranous glomerulopathy observed by Roberts et al. (1969) in some examples of Löfler’s endocarditis.

The macroscopical findings in our subject’s heart bear a striking resemblance to those reported in endomyocardial fibrosis by Davies (1960). The distribution of mural thrombi (left ventricular inflow tract, left and right ventricular apices; sparing of the superior left ventricular septum), and areas of organizing myocardial necrosis in our case are identical to similar areas described by Davies and by Connor et al. (1968) in endomyocardial fibrosis. Our finding of myocardial necrosis associated with vascular thrombi may validate the suggestion of Connor et al. (1968) that such areas result from small myocardial infarcts. A subendothelial interstitium rich in acid mucopolysaccharides was observed in our case and in the hearts reported as endomyocardial fibrosis; however, such areas in endomyocardial fibrosis are focal rather than generalized, and the presence of acid mucopolysaccharides was interpreted by Connor et al. as being the primary manifestation of cardiac injury. We believe the increased interstitial acid mucopolysaccharides in our case are the result of — not the cause of — endocardial damage precipitated by the occlusive fibrin thrombi.

The cause of Löfler’s endocarditis remains unknown. Because of the eosinophilia, Hardy and Anderson (1968), Cline (1969), and Roberts et al. (1969) suggest an allergic, hypersensitivity, or autoimmune phenomenon. The latter authors postulate that eosinophilia represents a high degree of allergy displayed by the host, and that the disappearance of eosinophilia indicates containment or elimination of the allergic stimulus. Even after the eosinophilia subsides, the resulting endomyocardial scar, if extensive, may compromise cardiac function (Roberts et al., 1969). Since the eosinophil is attracted by, and can phagocytose, antigen—antibody complexes, but not antigen or antibody alone, and since extracts of eosinophils can antagonize the biological effects of serotonin, bradykinin, and histamine (Cline, 1969), such a hypothesis is reasonable. The agent or agents, however, responsible for inducing such hypersensitivity remains obscure, as does the precise mechanism of production of the severe cardiac changes.

References


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