EOSINOPHILIC XANTHOMATOUS GRANULOMA WITH HONEYCOMB LUNGS

BY

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[WITH PHOTOGRAVURE PLATE]

The precise nature of the Hand–Schüller–Christian syndrome is unknown. Originally it was thought that the various pathological changes were specific, and that they were due to abnormal intracellular lipoid metabolism (Thannhauser, 1940). More recently it has been realized that the disease is probably a phase in a generalized disorder of the reticulo-endothelial system, and that it has certain features in common with eosinophilic granuloma of bone. The following case is reported as an example of the transition between these two diseases, and because, in addition to the recognized bony and pituitary manifestations, it shows pulmonary infiltration and polycystic, or honeycomb, lungs. So far as is known, no similar case has been reported from this country, and the occurrence of the disease in a subject of the patient's age is unique.

Case History

A boot-repairer aged 56 was admitted in September, 1948. In 1942 he had begun to notice breathlessness on exertion, and this symptom progressed slowly until his admission. In 1942 a radiograph of the chest showed diffuse pulmonary shadows, and he was treated for a short time in a sanatorium. A single specimen of sputum was alleged to contain tubercle bacilli, but this finding was not confirmed. In 1944 he had a fracture of the right femur, which occurred without local injury whilst he was sawing wood. Radiographs at this time showed a cyst of the femur at the site of fracture, but the fracture united in four months and no further investigations were undertaken. Nine months before admission there was a return of pain over the old fracture. In February, 1948, he suddenly began to suffer from excessive thirst and, soon after, from the passage of large quantities of urine. His thirst was such that he would often drink 20 pints (11.36 litres) of fluid daily. These symptoms were partially controlled by a proprietary pituitary snuff. Before the onset of these symptoms he had suffered from no serious illness. One of his sisters had died from pulmonary tuberculosis.

On examination he was seen to be a thin, normally proportioned man. There was no rash or abnormal pigmentation, and hair distribution was normal. Scattered rhonchi were heard over both lungs. The heart was normal; the blood pressure was 120/88. The liver and spleen were not palpable. A thickening of the right femur was palpable over the site of the old fracture. The nervous system was normal. There was no exophthalmos or any lymph-node enlargement.

Investigations.—A blood count showed Hb, 104%; red cells, 4,700,000; white cells, 10,000 (eosinophils 1%); sedimentation rate, 32 mm. in 1 hour (Westergren). Plasma proteins, total 7.8 g. per 100 ml. (albumin 5.6 g., globulin 2.2 g.). Serum cholesterol, 235 mg. per 100 ml. Serum calcium, 10.1 mg. per 100 ml. Serum alkaline phosphatase, 12 K.-A. units. The Wassermann reaction was negative. Vital capacity, 2,850 ml. (63% of normal). The hypertonic saline infusion test (Carter and Robbins, 1947) confirmed the presence of true diabetes insipidus.

Radiological examination showed a cystic area in the right femur immediately below the united fracture (Plate, Fig. 1). There was a generalized reticulation associated with miliary mottling through both lung fields (Fig. 2). The reticulation formed small annular shadows about 0.5 cm. in diameter. Tomography confirmed the presence of small cystic areas in the lungs. There was no enlargement of the mediastinal glands. The skull showed irregular translucencies resembling exaggerated venous channels rather than lipoid deposits. The pituitary fossa was normal. The remainder of the skeleton was normal.

Biopsy of the right femoral cyst was made on material obtained from a small incision on the outer side of the thigh. Histologically the sections showed vascular granulation tissue with a cellular exudate. The cells were almost all eosinophilic granulocytes, but some lymphocytes and large mononuclear cells were present. No foam cells or lipoid-containing macrophages were seen. The appearances were typical of eosinophilic granuloma of bone.

Treatment.—The diabetes insipidus was controlled by the injection of 10 units (0.5 ml.) of "pitressin tannate" once or twice daily. In November, 1948, a course of deep *x*-ray therapy was given to the right femur. There was complete relief of pain in the leg after the third day of treatment. In December, 1948, deep *x*-ray therapy was given to the pituitary fossa and then to the lungs. This produced no improvement in symptoms. The patient was last seen in March, 1949, when he stated that there had been no change in his breathlessness, and the dose of pitressin required to control the diabetes insipidus was the same. Radiographs of the chest and femur showed no change two and a half months after completion of radiotherapy.

Discussion

The term "eosinophilic granuloma of bone" was first used by Lichtenstein and Jaffe (1940) to denote a localized granulomatous condition of bone containing large numbers of eosinophilic granulocytes and giving rise to areas of cystic rarefaction. Otani and Ehrlich (1940) described similar cases earlier in the same year under the title of "solitary granuloma of bone." They found lipophages in biopsy material from one of their cases, but dismissed the possibility that the bony lesions were local manifestations of Hand–Schüller–Christian disease on the grounds that none of their seven cases showed evidence of generalized disease.

Previously, however, Fraser (1935) had reported four cases of the same condition as "skeletal lipoid granulomatosis" and had described the pathological changes as taking place in three stages—namely, endothelial-cell proliferation, eosinophilic infiltration, and lipoid storage. More recently it has become apparent that the local bony granulomata may be merely a part of a generalized disorder affecting the skeleton and viscera, and that other generalized reticuloses—namely, the Hand–Schüller–Christian disease and the acute reticulosis of infancy sometimes called the Letterer–Siwe disease (Abt and Denenholz, 1936)—may give rise to bony changes radiologically and histologically identical with those of eosinophilic granuloma. For these reasons it has been postulated that eosinophilic granuloma, Hand–Schüller–Christian disease, and Letterer–Siwe disease are all variants of a common pathological disorder (Wallgren, 1940; Farber, 1941; Mallory, 1942; Jaffe and Lichtenstein, 1944). Thus Mallory (1942) found all grades of transition between the three disorders and concluded that in infancy the disease was manifest as the rapidly fatal Letterer–Siwe disease, later in childhood as the Hand–Schüller–Christian disease, and in older children or adults as eosinophilic granuloma.

Jaffe and Lichtenstein (1944) considered that the three disorders "represented a peculiar inflammatory reaction to some, as yet, unknown agent of infection," the distinctive histological features in a given case depending on the duration of the disease. In their opinion the presence of fibrosis and lipoid-containing macrophages is merely indicative of chronicity. The increasing number of recorded cases which do not fall accurately into any one category, but which show features of all three diseases, has fully confirmed this view. It seems correct to regard eosinophilic granuloma as being a reticulosis with bony localization rather than a specific disease of bone.

As it is now accepted that these disorders are but phases of the same disease, it would be an advantage to have a single name to embrace the important features of all three. To avoid confusion in terminology Thannhauser (1947) suggested the name of "eosinophilic xanthomatous granuloma" as being descriptive of the main histological features. Until further knowledge is forthcoming on the aetiology of the disease this name should be adopted for the type of case described in this paper. The present case shows evidence of pulmonary, pituitary, and bony disease, and it is to be assumed that all three organs are affected by the same pathological process. The biopsy material from the bone showed granulation tissue and eosinophilic infiltration, and although lipophages were absent from this section it is probable, by analogy with other reported cases, that they may exist elsewhere.

That pulmonary infiltration occurs in eosinophilic xanthomatous granuloma has been recognized since Rowland (1928) described the case of a child aged 2 years who died from pulmonary fibrosis secondary to xanthomatosis. Since then many cases have been reported, and the recorded cases have been reviewed by Thannhauser (1940), Versiani *et al.* (1944), Weinstein *et al.* (1947), Ponseti (1948), Oswald and Parkinson (1949), and Schafer (1949). Oswald and Parkinson reported a case in which the granuloma gave rise to diffuse small cysts throughout both lungs, and they were able to find three similar cases in the literature. A similar case was reported by Schafer (1949). The case reported here shows the characteristic radiological changes of honeycomb lungs and is a further example of cystic pulmonary changes occurring in a more chronic phase of the disorder.

To clarify the protean manifestations of this disease it is suggested that eosinophilic xanthomatous granuloma should be regarded as a generalized disease of unknown aetiology, occurring in an acute or chronic form. In the acute variety, which occurs in infancy and early childhood, there is progressive infiltration of the skin, bones, lymph nodes, and viscera, leading to early death. The chronic variety, occurring in older children and adults, may present in a complete or an incomplete form. In the complete form there is pituitary, bony, and pulmonary disease, with possibly other visceral manifestations. In the incomplete forms, which are not uncommon, pulmonary, pituitary, and bony lesions occur either singly or in any combination. Thus, when the bony symptoms predominate the disease will be regarded as "eosinophilic granuloma of bone," and when the pituitary alone is affected it presents as diabetes insipidus.

It is the relation of the chronic form of this disease to pulmonary disorders that is particularly emphasized, for the possibility that lung fibrosis and cyst formation may be the sole manifestation of eosinophilic xanthomatous granuloma must be considered. It seems likely that such cases will arise, and confirmation of this concept is to be found in the association of pituitary disorders, transient or permanent, with honeycomb lungs (Oswald and Parkinson, 1949). Pathological evidence on this point is difficult to obtain, as in the chronic phase of the disease fibrosis obscures the histological picture. Further histological studies on this subject will be published elsewhere (Cunningham and Parkinson, in the press).

The response to irradiation therapy in eosinophilic xanthomatous granuloma is variable. In most instances the bony lesions respond symptomatically, and sometimes there is radiological improvement. The effect of irradiation on the pituitary and pulmonary disease is occasionally beneficial but usually without effect (Currens and Popp, 1943; Weinstein *et al.*, 1947; Ponseti, 1948). The present case had complete relief of pain in the femur, but the diabetes insipidus and the respiratory symptoms were unaffected; there were no radiological changes following treatment.

A final point of interest in this case is the age of the patient. The oldest case previously reported was that of a man aged 50 (Versiani *et al.*, 1944).

Summary

A case of eosinophilic granuloma of bone in a man aged 56 is described. The patient also had diabetes insipidus and honeycomb lungs.

Irradiation therapy relieved the pain of the bony lesion but did not affect the pituitary or pulmonary disease.

The name "eosinophilic xanthomatous granuloma" should be used to include the three diseases commonly known as the Hand–Schüller–Christian disease, Letterer–Siwe disease, and eosinophilic granuloma of bone.

The occurrence of pulmonary manifestations in this disease is discussed.

I wish to thank Dr. Neville Oswald for permission to publish this case, and Mr. Norman K. Harrison, of the Department of Medical Photography, St. Bartholomew's Hospital, for the photographs.

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ACUTE PNEUMONITIS IN A BERYLLIUM-WORKER

BY

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[WITH PHOTOGRAVURE PLATE]

The following case of acute bronchiolo-alveolitis is thought to be due to working in an atmosphere containing beryllium dust. It is believed to be the first acute case to be reported in this country.

Beryllium was discovered in 1797 by Vauquelin, who called it glucinum, owing to the sweet taste of its salts. It is a brittle steel-grey metal that is soluble in acids, and occurs chiefly as beryl, the double silicate of beryllium and aluminium ($Be_3Al_2(SiO_3)_6$). Phenacite (Be_2SiO_4) and chrysoberyl ($Be_2Si_2O_4$) also occur.

During the 1939–45 war beryllium was used in increasing quantities as an important component of certain alloys and for the production of phosphors for fluorescent lighting and gas mantles. The exact compositions of fluorescent mixtures for the manufacture of strip lighting are trade secrets, but they usually contain varying proportions of beryllium, zinc, manganese, and silica.

J. C. HARLAND AND F. D'ABREU: LUMBO-DORSAL SYMPATHECTOMY IN SEVERE HYPERTENSION

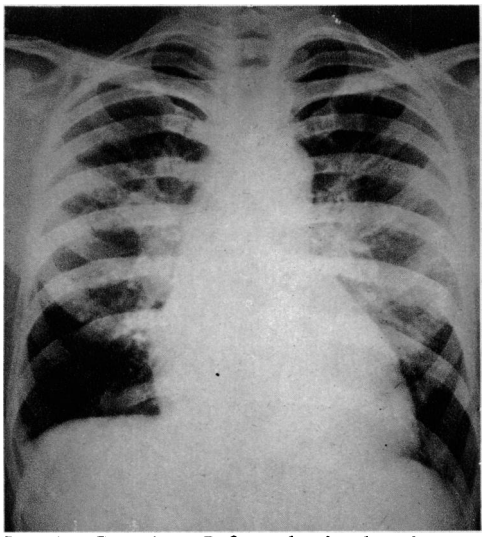

FIG. 1.—Case 1. Before lumbo-dorsal sympathectomy. Considerable cardiac enlargement and pulmonary engorgement.

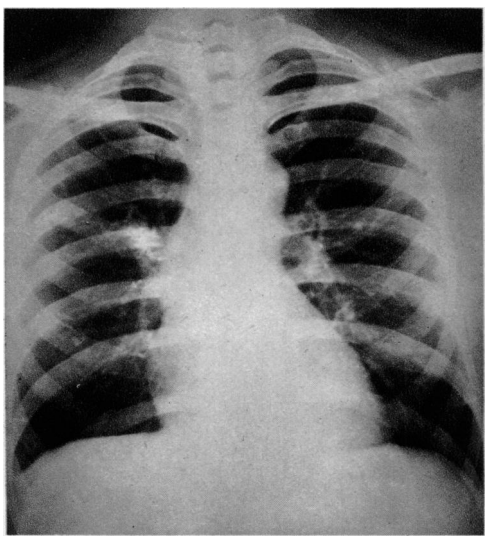

FIG. 2.—Case 1. Two months after sympathectomy. Heart size has decreased and there is no pulmonary engorgement.

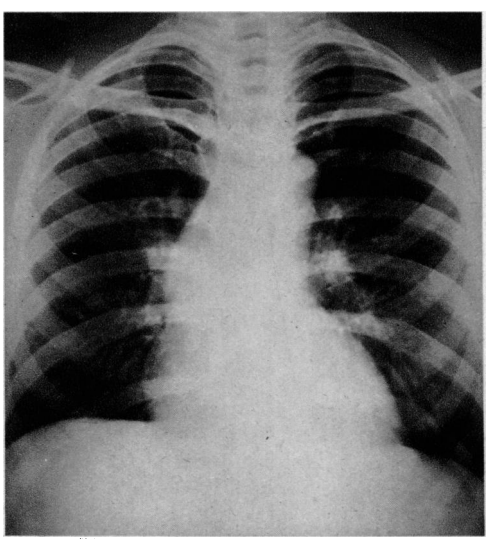

FIG. 3.—Case 1. Eighteen months after sympathectomy. Heart still smaller than before operation, and still no pulmonary engorgement.

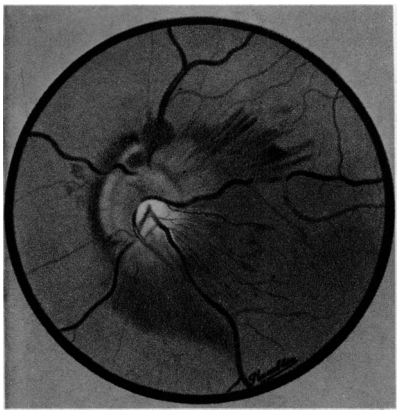

FIG. 4.—Case 5. Malignant hypertension. Left fundus before sympathectomy; showing papilloedema and numerous haemorrhages.

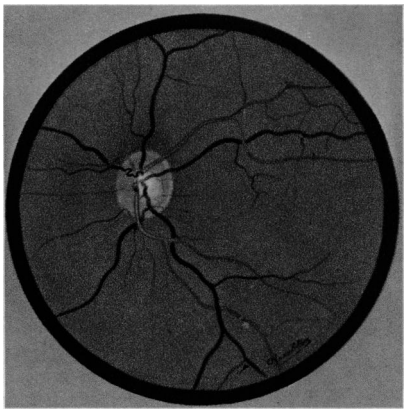

FIG. 5.—Case 5. Left fundus seven months after sympathectomy. Normal appearance.

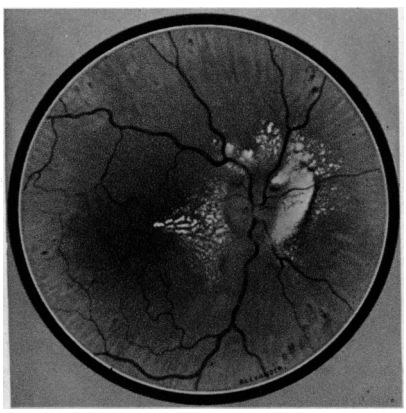

FIG. 6.—Case 6. Malignant hypertension. Right fundus before sympathectomy; papilloedema, a haemorrhage, numerous exudates, and considerable arterial spasm.

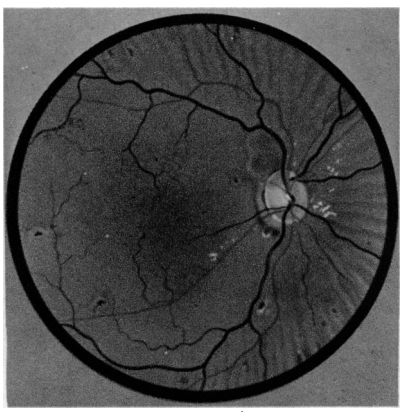

FIG. 7.—Case 6. Right fundus nine months after sympathectomy. Papilloedema has disappeared, and only a few small old exudates remain. Some areas of retinal degeneration and some branches of retinal artery in spasm.

T. PARKINSON: EOSINOPHILIC XANTHOMATOUS GRANULOMA WITH HONEYCOMB LUNGS

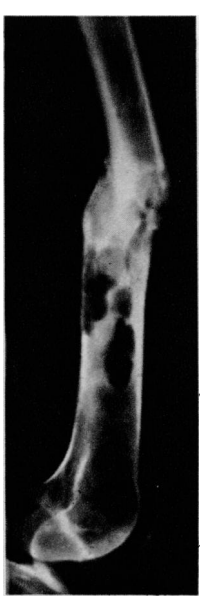

FIG. 1.—Cystic rarefaction in right femur below old fracture.

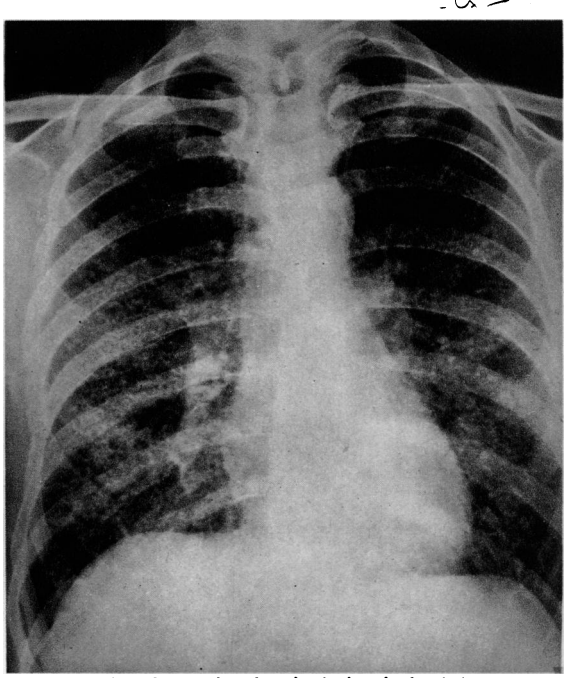

FIG. 2.—Generalized reticulation in both lungs.