Histiocytosis X characterized by marked elevation of serum alkaline phosphatase and rapid destructive changes in the lung parenchyma

P.B. Hansen

ABSTRACT: A 23 yr old man was admitted suspected of having a liver disease because of marked elevation of the serum alkaline phosphatase. A biopsy of the liver was without cholestasis. A skin biopsy of a papule was compatible with eosinophilic granuloma. Over a few months the patient developed severe restrictive lung disease. The elevation of the serum alkaline phosphatase was probably due to diffuse bone affection.

Histiocytosis X is, in all probability, a disorder of immune regulation and most likely caused by proliferation of histiocytes [1]. The disease includes unifocal eosinophilic granuloma, multifocal eosinophilic granuloma (Hand-Schüller-Christian syndrome) and diffuse histiocytosis X (Letterer-Siewe's disease) [2]. A description is given in the following of a young man with multifocal eosinophilic granuloma, who suffered from progressive involvement of the lungs with misleading elevation of his serum alkaline phosphatase.

An otherwise healthy man of 23 yrs was admitted to hospital suspected of suffering from a disease of the liver. Tests had shown an erythrocyte sedimentation rate of 71 mm in the first hour, a serum alkaline phosphatase of 2,435 U·l⁻¹ (normal 50 to 275 U·l⁻¹), a serum aminotransferase AST of 70 U·l⁻¹ (normal 10 to 40 U·l⁻¹), a normal bilirubin and a normal prothrombin time. His only complaint was of fatigue and mild dyspnoea on exertion. A spirometry test carried out immediately prior to admission was normal. The general condition of the patient was good. The only abnormal findings were numerous erythematous papules of 2 to 10 mm in diameter in his trunk and a few necrotic ulcers of a similar size on the palate. The elevation of his serum alkaline phosphatase persisted, reaching a maximum of 3,700 U·l⁻¹.

An X-ray of the chest revealed multiple bilateral fine nodules. The hilar and mediastinal lymph nodes were not enlarged. Ultrasound scanning of the liver was normal, including the porta hepatitis. A biopsy of the liver only showed nonspecific reactive changes; there was no cholestasis. There was slight inflammation of some of the portal tracts, with a predominance of eosinophils. Skin biopsy of a papule demonstrated histocyte proliferation, granuloma with multinucleated giant cells and eosinophilic infiltration. The characteristic histopathologic lesions were compatible with eosinophilic granuloma. A biopsy of the lip was normal.

X-rays of the bones were normal. A bone scan did not show any focal lesions, although diffusely increased activity was present. During the following months the patient developed marked symptoms of diabetes insipidus with a urine volume of 12–14 l per day. The diagnosis was confirmed by a dehydration test, and the urine volume could be reduced to roughly 2 l per day by treatment with desmopressin. CT scanning of both the pituitary gland and hypothalamus was normal.

The patient suffered progressive shortness of breath during the next few months. An X-ray of the chest at this time revealed cysts and hilar adenopathy in addition to the multiple nodules. A repeat spirometry test - 10 months after the first - demonstrated severely decreased vital capacity (VC, 1.4 l).

The patient was successfully treated with 40 mg of prednisolone daily, and has since been able to resume work. The erythrocyte sedimentation rate has become normal (4 mm·h⁻¹) and the serum alkaline phosphatase has fallen to 799 U·l⁻¹.

Discussion

Biopsy of the skin lesions confirmed the diagnosis in this patient, as it does in the majority of cases of histiocytosis X. The marked elevation of the serum alkaline phosphatase was most probably due to bone affection.
affection, despite the fact that no osteolytic lesions could be demonstrated by bone scanning. This has not been reported previously, but is in agreement with the observation that histiocytosis X cells possess the ability to secrete interleukin 1 and prostaglandin E-2 in vitro, properties which can induce bone resorption [3]. Diabetes insipidus and the lung symptoms have been described earlier in connection with multifocal eosinophilic granuloma. Less than 10% of these patients develop respiratory failure due to interstitial fibrosis and die from pulmonary disease [4].

References