Thorax 1984;**39**:70–71

Pulmonary malakoplakia

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Malakoplakia is an uncommon chronic inflammatory process of unknown aetiology. It was first described by Michaelis and Gutmann in 1902,[1] and in most reported cases the genitourinary tract has been affected in association with *Escherichia coli* infections.[2] Although malakoplakia has been described in other tissues, only three cases of pulmonary malakoplakia have so far been reported.[3 4]

When mucosal surfaces are affected malakoplakia appears as soft yellow brown plaques, but it may resemble an abscess when it is deep seated. The diagnosis is made by demonstrating certain characteristic histological features. By light microscopy two features are required for the diagnosis of malakoplakia. One is the characteristic von Hansemann histiocyte (fig 1). The second hallmark is the Michaelis-Gutmann (MG) body, which may be intracellular or extracellular. The MG body is round, about the size of a nucleus, and may appear lamellated (left hand inset, fig 1). By electron microscopy the MG body is seen to arise through mineralisation of cytoplasmic macrophagolysosomes (fig 2), and these in turn are formed in part by digested bacteria and by end products of degenerated host cells.

Case report

A 44 year old white man had received a cadaveric renal transplant for renal failure secondary to chronic glomerulonephritis of unknown aetiology. Twelve months after transplantation his maintenance immunosuppressive treatment consisted of prednisone 15 mg/day and azathioprine 175 mg/day. He felt well and there was no evidence of infection.

Eighteen months after transplantation he developed a perianal abscess. *E coli* sensitive to ampicillin was cultured from the lesion. There were no pulmonary symptoms at that time, and the chest radiograph was normal. Despite repeated surgical drainage and treatment with ampicillin the abscess persisted one year later. During this period cultures of drainage fluid consistently grew an ampicillin sensitive *E coli*, while cultures for anaerobes, mycobacteria, amoebae, and actinomycetes were negative.

Thirteen months after the perianal abscess first appeared, the patient developed cough, purulent sputum, and haemoptysis. The chest radiograph showed a cavitating nodular lesion 4 cm in diameter in the right lower lobe. Fibreoptic bronchoscopy showed a yellowish, friable mass projecting into the superior segment of the right lower lobe bronchus. Cultures of material from this lesion grew *E coli* sensitive to ampicillin. Examination of biopsy specimens taken via the bronchoscope showed the characteristic features of malakoplakia (fig 1). This prompted biopsy of the

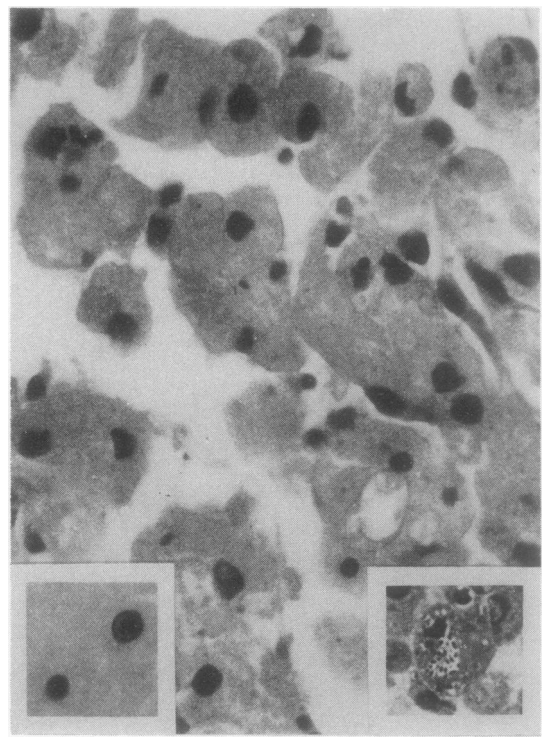

Fig 1 *Light microscopy of the endobronchial biopsy specimen: the characteristic von Hansemann histiocytes have finely granular or reticulated cytoplasm. (Haematoxylin and eosin, × 655.) The Michaelis-Gutmann bodies (left hand inset) are best demonstrated with a calcium stain. (von Kossa stain, × 655.) Intracellular bacilli (right hand inset) are readily identified in plastic embedded sections 1 μm thick. (Toluidine blue, × 712.)*

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Accepted 7 June 1983

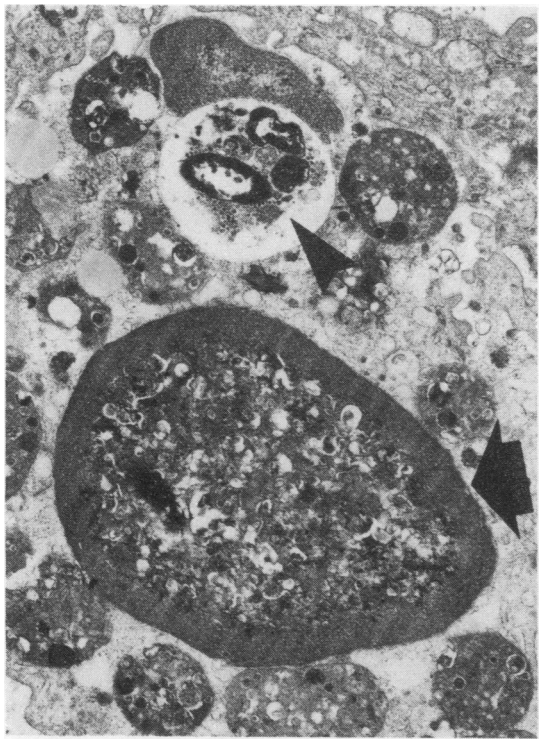

Fig 2 *Electron micrograph of the perianal lesion: a Michaelis-Gutmann (MG) body (arrow) is identified within a von Hansemann histiocyte, and three degenerating bacilli are seen within a membrane-bound phagolysosomal vacuole (arrowhead). Note the morphological similarity between the adjacent phagolysosomes and the centre of the MG body. (Uranyl acetate and lead citrate stain, × 9625.)*

perianal lesion, which also showed malakoplakia (fig 2). Repeated treatment with ampicillin had no effect on either the pulmonary or the perianal lesions.

Immunological and cell function studies were undertaken and the results of these have been reported in detail elsewhere.[5] The total white blood cell count was normal with a slight neutrophilia; the IgG level was slightly low, while IgA and IgM were normal. The total haemolytic complement and C3 and C4 activities were also normal. Circulating T lymphocyte numbers were normal, as was the proliferation of lymphocytes in response to non-specific mitogens. Chemotaxis and phagocytosis by the patient's circulating neutrophils and monocytes were normal; both these cell types, however, showed impaired in vitro killing of *Staphylococcus aureus* and *E coli*.

A two month therapeutic trial of bethanechol chloride was unsuccessful. Because it was felt that the bactericidal abnormality shown by the patient's monocytes and neutrophils might be secondary to or aggravated by the immunosuppressive drugs, the dose of azathioprine was reduced from 175 to 50 mg per day. Three months later the perianal lesions (present for two years) had cleared completely and the pulmonary lesions had also resolved. The in vitro bactericidal activity of the patient's neutrophils and monocytes had also returned to normal.

Discussion

The aetiology and pathogenesis of malakoplakia are unknown. Macrophage phagocytosis is normal in patients with malakoplakia, but there appears to be a defect in bactericidal activity of peripheral monocytes, tissue macrophages, and on occasion neutrophils.[5-8] *E coli* has been the infecting agent in most cases, but malakoplakia has also been reported in association with other organisms, including *Klebsiella*[6] and fungi.[9]

Treatment for malakoplakia has generally consisted of surgical drainage and antibiotics. One case in which an intracellular defect of cyclic nucleotides was found responded to treatment with the cholinergic agonist bethanechol chloride,[10] but the two month trial of this drug was ineffective in our case. Both the lesions and the associated in vitro defect in moncyte killing resolved on reduction of the long term immunosuppressive treatment. Apparently in some patients at least malakoplakia may result from an acquired phagocytic cell defect related to disease or drug induced immunosuppression.[4 5]

Malakoplakia probably is underdiagnosed, and probably has multiple causes. Chest physicians frequently have to investigate infection in the compromised host, and with an increased awareness of this interesting form of chronic infection wider application of the necessary histological and phagocytic cell function studies should permit more frequent recognition of malakoplakia when it affects the lungs.

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