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Prostatic Malacoplakia
An Ultrastructural and Immunohistochemical Study

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A case of malacoplakia of the prostatic gland associated with postatic nodular hyperplasia from a 69 years old man was presented, and its light and electron microscopic and immunohistochemical features were discussed along with its pathogenesis. This lesion was incidentally found in a transurethral prostatectomy specimen, and consisted of large number of epithelioid cells in which were typical cytoplasmic inclusions known as Michaelis-Gutmann bodies. Ultrastructurally, these inclusions showed a dense, central calcified bodies of various developmental stages. Immunohistochemical study using antilysosomal antibody revealed no lysosomal activity. Based on these findings, we could suspect that main problem for this development of malacoplakia is altered intracellular digestion process of foreign biologic materials.

Key Words: *Malacoplakia, prostate, ultrastructure, immunohistochemistry.*

INTRODUCTION

Malacoplakia is a rare and quite peculiar form of granulomatous lesion, predominantly occurring in the genito-urinary system. It was first described by Michaelis and Gutmann in 1902 and subsequently designated as malacoplakia by von Hansemann in 1903. Thereafter more than 200 cases of this lesion have been described and studied with refined techniques including electron microscopy and immunohistochemistry to understand its pathogenesis. The majority of this lesion occurs in the urinary tract, especially urinary bladder (Smith, 1965; McClurg et al., 1973; Lewin et al., 1974; Thorning and Racko, 1975) but more recently, lesions involving other organs have been described. These organs include testes (Shaba and Black, 1971), epididymis (Green, 1968), prostate (Hoffmann and Garvido, 1964: McClure, 1979; Goldman, 1965), kidney (Miller and Finck, 1970), colon (Terner and Lattes, 1965; Ranchod and Kahn, 1972; Joyeuse et al., 1977), stomach Nakabayashi et al., 1978) and many other organs. In a review of the literature, less than 20 cases of prostatic malacoplakia were found. With this rarity of this lesion, we felt that it could be justified to report an additional case of prostatic malacoplakia with ultrastructural and immunohistochemical studies on its currently accepted pathogenesis.

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CASE REPORT

A 69-year-old male patient presented with a history of increasing difficulty of urination, frequency and nocturia for 6 years. There had been two episodes of acute urinary retention that was relieved by catheter insertion. Otherwise, there was nothing relevant in the past medical history except a mild maturity-onset diabetes mellitus which was controlled by diet only. Clinical examination revealed and enlarged prostate and transurethral resection was performed. The

removed prostatic fragments weighed 49 gm in toto. Closed examination disclosed multiple small spongy nodules of usual benign hyperplasia of the prostate and a small poorly defined round yellow brown area of 0.3 cm diameter.

Microscopically, the main histopathologic features of prostate represented nodular hyperplasia. The area corresponding to grossly yellow brown and soft portion was composed of epithelioid cells, lymphocytes and a few neutrophils, the former comprising by far the largest component of cells (Fig. 1). Numerous Michaelis-Gutmann bodies of 2 to 7 um in diameter were present within the cytoplasm of epithelioid cells. These inclusions were mineralized, PAS-positive, darkly black with von Kossa's stain, and reacted weakly with Perls' stain (Fig. 2). In addition, there were sharply circumscribed intracytoplasmic bodies that were not so intensely calcified, but positive in PAS and weakly reactive to Prussian blue stain.

Electron microscopy confirmed the presence of Michaelis-Gutmann bodies with apparently different stages of its development.

Most of epithelioid cells had one or two nuclei that contained evenly dispersed chromatin and prominent nucleoli. As a result of the initial fixation in 10% neutral formaldehyde solution, many of the subcellular components were poorly preserved. However, a few well preserved mitochondria, rough and smooth endo-

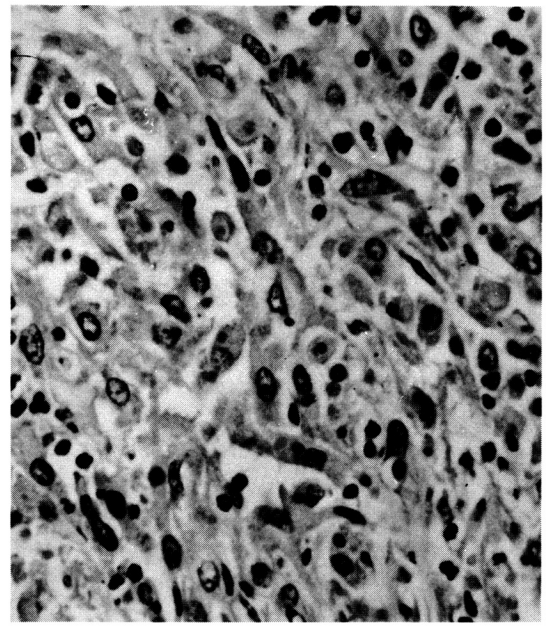

Fig. 2. PAS-positive granules of different sizes and densities within macrophages. PAS, x400.

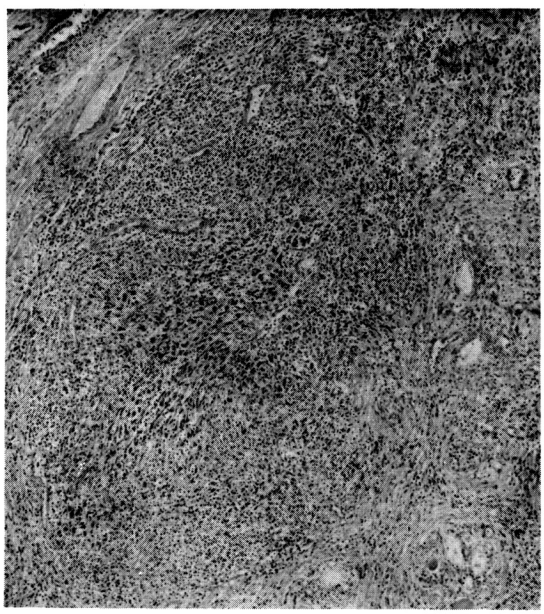

Fig. 1. Granulomas consisted of epithelioid cells which contain Michaelis-Gutmann bodies. H&E, x100.

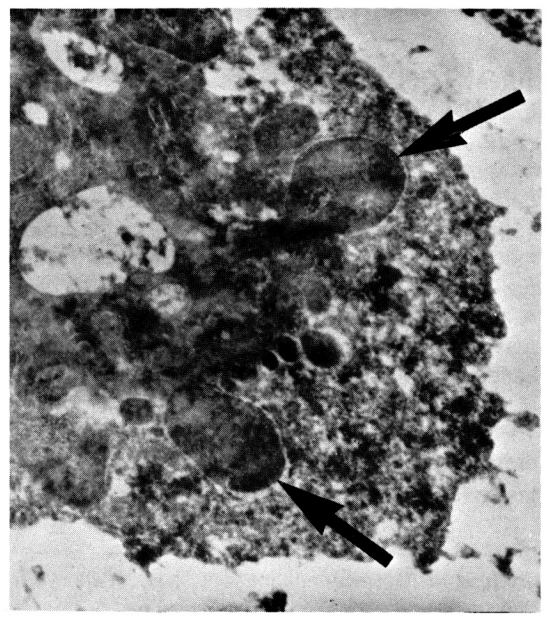

Fig. 3. Many phagolysosomes (arrow) within the cytoplasm of histiocytes. x9,800.

plasmic reticulums were remained. Strikingly prominent were numerous phagolysosomes that varied greatly in size and were filled with granular materials. These phagolysosomes were lined by a single limiting membrane, and the Michaelis-Gutmann bodies appeared to develop within the phagolysosomes. The earliest visible change appeared by homogenization of the intraphagolysosomal structures probably due to digestion of ingested material, (Fig. 3) followed further by calcification to produce irregular electron-dense amorphous mass. In the intermediate stage of development, the Michaelis-Gutmann bodies became a larger round and more electron dense masses (Fig. 4). In the late stage, growth of Michaelis-Gutmann bodies underwent concenric layering of calcium phosphate crystals to produce the typical concentrically laminated calcospherules corresponding to ones seen on light microscopy (Fig. 5, 6).

Immunoperoxidase method (the peroxidase-antiperoxidase complex and antilysosomal antibody) revealed no lysosomal activity of epithelioid cells.

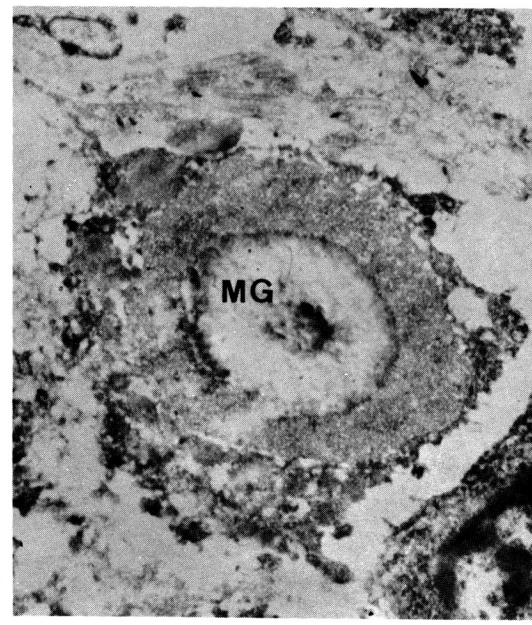

Fig. 5. The late stage in the development of Michaelis-Gutmann body (MG) with distinct lamination. x9,800.

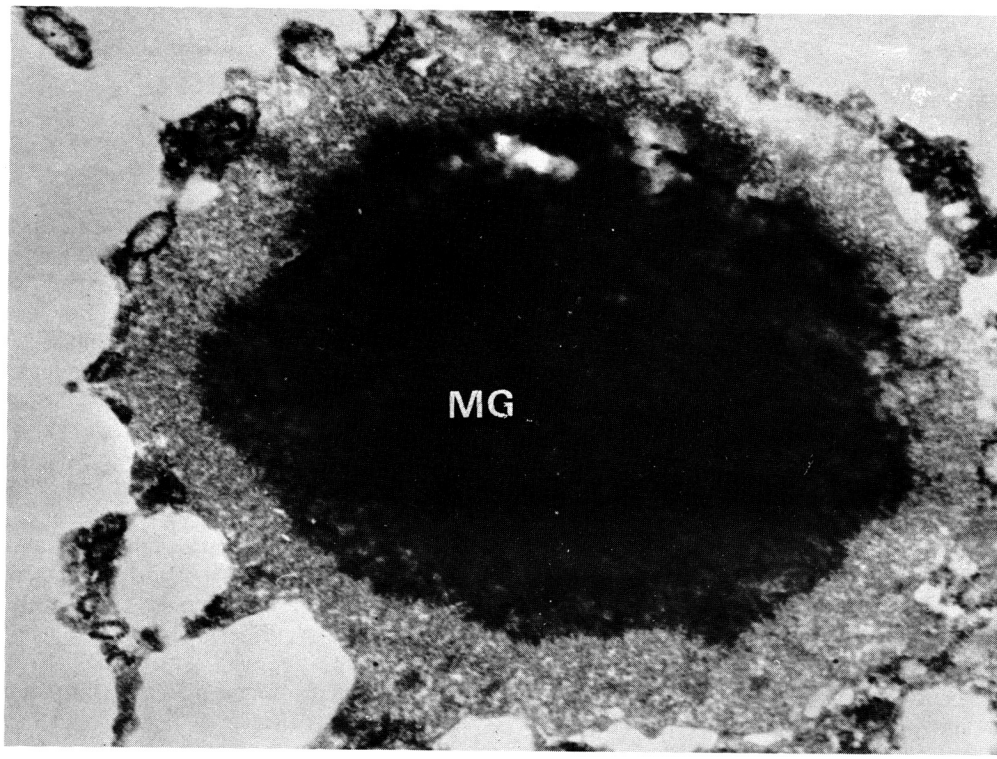

Fig. 4. Michaelis-Gutmann body (MG) composed of central electron-dense core and outer granular rim. x22,400.

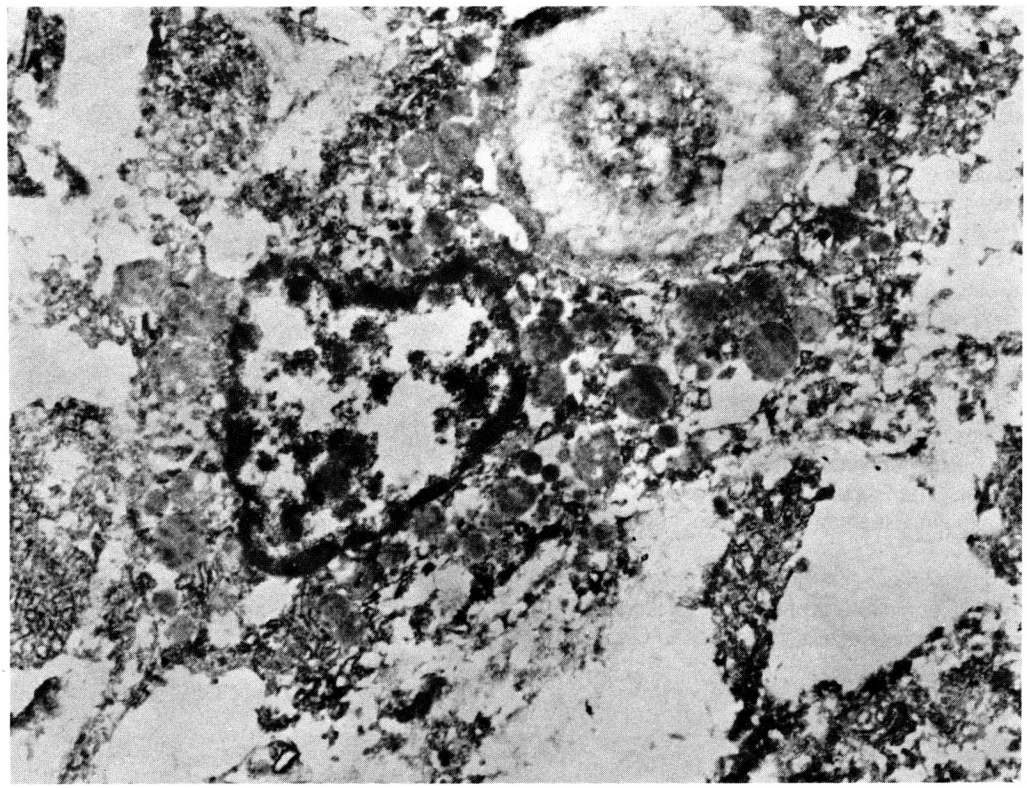

Fig.6. Same stage of malacoplakia with fig. 5. x9,800.

DISCUSSION

Malacoplakia is an uncommon condition characterized by an infiltrate of epithelioid cells containing large intracytoplasmic inclusions and concentrically laminated, siderocalcific spherules, known as Michaelis-Gutmann bodies. So far, less than 200 cases have been reported in the literature, and among these, prostatic malacoplakia comprises the one tenth of cases.

Although malacoplakia has been known for over 60 years and its pathology has been well defined, numerous postulations about its etiology and pathogenesis have been presented despite more refined techniques in the form of immunohistochemical as well as tissue culture and electron microscopic studies. Histochemical and clinical studies have suggested that malacoplakia has an infectioous origin (McClure, 1979; Terner and Lattes, 1965). This suggestion has been supported by electron microscope (McClurg et al., 1973; Lewin et al., 1974). Lewin et al. (1976) stated that the main cause of this disease might be the incomplete bacterial degradation which could be identified in various stages of degradation process by electron microscopic studies, and postulated that phagocytized bacteria are incorporated but incompletely digested in the phogolysosomes of macrophages. Additional comments on these findings were that these bacterial remnants persisted as dense amorphous aggregates and fragmented membranous structures which later appeared to become encrusted with calcium phosphate crystals to form the laminated Michaelis-Gutmann bodies (Lewin et al., 1976). The plausible biochemical explanation about these morphological sequences was proposed by Thorning and Vracko (1975). They postulated that the main problem is the retardation of intravacuolar digestion of ingested materials which might be due to impaired digestion process within the epithelioid cells, especially defect in acidification of

phagolysosomal vacuolation. Since intravacuolar acidification can be blocked by exposure of cells to carbonic anhydrase inhibitors, they have considered the possibility that malacoplakia may, in some instances, be caused by the administration of drugs that have the capacity to inhibit carbonic anhydrase activity such as sulfonamide. Although biochemical aproach of detailed stage-based evaluation of phagolysosomes and Michaelis-Gutmann bodies for the present case is not so easy due to prior fixation to formalin, the previous electron microscopic findings, in general, well matched our observation.

As to the informations about the types of specific organism that may cause Michaelis-Gutmann bodies which we are deeply concerned with, E. coli and Klebsiella have been described as the most frequently detectable organisms, especially in patients with altered immune status. In our case, E. coli was also detected in urine culture, but specific underlying diseases that were known to be the cause of immune alteration were not evaluated, only leaving mere speculation on the possible role of various drugs given to this patient during his frequent urinary retention.

Immunohistochemical study, using the antilysosomal antibody by PAP technic showed no positive lysosomal activity which was quite contrast with that of Charpentier's result (Charpentier et al., 1983). The rational explanation for this different result remains unclarified, but the age of these lesions might explain complete degradation of phagolysosomal element, with which no antigenic activity remains to interact with antibodies. Assumption of the possibility that impaired lysosomal activity might be an important contributing factor to produce intracytoplasmic inclusions should be supported with demonstration of bacterial structures in various stages of indigestion.

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