Malakoplakia of the adrenal gland

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SUMMARY The clinical and pathological features of a case of malakoplakia of the adrenal gland occurring in a woman with Escherichia coli infection are described. This lesion mimicked a neoplasm, the true diagnosis only being revealed by histological examination. The light and electron microscopic features are described and it is suggested that malakoplakia is due to an abnormal macrophage response to E coli infection.

Until recently malakoplakia was thought to occur only in the urinary tract, but during the last two decades it has been reported in many sites, including the prostate, testis and epididymis, stomach, small intestine, appendix, colon, omentum, retroperitoneum, lymph nodes, vagina, broad ligament, endometrium, skin, lung, and bone. We describe here an example of malakoplakia of the adrenal gland, this being, to the best of our knowledge, the second documented case and the first to be reported in an adult.

Case report

A 68-year-old diabetic woman was admitted to the Manchester Royal Infirmary in March 1979 with complaints of general malaise and intermittent rigors. On examination she was febrile and confused, and a firm, fixed, slightly tender mass was palpable in the left hypochondrium. There were no other abnormal physical findings. Investigations showed a haemoglobin concentration of 8.7 g/dl and a white cell count of 15 \times 10^9/l (15 000/mm^3) with 90% neutrophils. An intravenous pyelogram showed a small contracted, poorly functioning, left kidney. A whole-body scan showed that the left adrenal gland was enlarged, probably by tumour, and that there was a collection of pus in the left pararenal area.

While in hospital the patient developed an enlarging abscess of the anterior chest wall which was separate from the collection of pus in the left pararenal area and which was drained of 500 ml of pus; E coli was cultured from the pus and this organism was also found on both blood and urine culture. Despite treatment with ampicillin and metronidazole the patient continued to have pyrexial episodes and therefore the left kidney and adrenal was explored. At operation a collection of pus was found near the upper pole of the kidney and the adrenal was enlarged. A left nephrectomy and adrenalectomy was performed. E coli was cultured from the pus obtained at operation.

After the operation her chest and abdominal wounds healed slowly but when antibiotic treatment was discontinued, pyrexial episodes returned. Further treatment with gentamicin produced slow improvement and she was discharged in July 1979 on a regimen of long-term amoxycillin. At follow-up four months after discharge she was well and her surgical wounds were healing.

PATHOLOGY

The resected specimen consisted of the left kidney and adrenal gland embedded in fat (Fig. 1). The kidney measured 7 x 4 x 2 cm and weighed 64 g. Its external surface was irregular and scarred and on section the normal architecture was obliterated, the renal parenchyma appearing firm and whitish-grey in all areas. The renal pelvis and upper part of the ureter appeared normal.

The adrenal gland was easily separated from the kidney and was considerably enlarged, measuring, together with some adherent periadrenal tissue, 4.8 x 4.2 x 3 cm. The gland appeared to be largely replaced by firm whitish tissue although a peripheral rim of apparently normal cortex was present around this tumour-like mass.

HISTOLOGICAL FINDINGS

The kidney showed severe chronic pyelonephritis with scarring and glomerular loss, periglomerular fibrosis, tubular atrophy, interstitial mononuclear cell infiltration, and interstitial fibrosis. In addition, particularly towards the hilum, there were large nodular collections of histiocytic cells surrounded by bands of fibrous tissue. The adrenal gland was

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largely replaced by a confluent infiltrate of similar histiocytic cells (Fig. 2), though there was a narrow peripheral rim of residual cortical tissue. No adrenal medullary tissue could be identified. All the histiocytic cells, both in kidney and adrenal, had abundant, coarsely granular, eosinophilic cytoplasm and small uniform nuclei showing no pleomorphism or mitotic activity. Their cytoplasm was PAS-positive after diastase digestion: fat staining with Oil Red 0 showed fine cytoplasmic lipid droplets. In addition, many cells contained round or concentrically laminated inclusions of the Michaelis-Gutmann type which stained strongly with von Kossa (Fig. 3): some also gave a positive reaction with a Perls’ stain. A few of the calciospherites were in extracellular sites. Admixed with the histiocytes were small numbers of neutrophil polymorphonuclear leucocytes, lymphocytes, and plasma cells. No bacteria could be seen on Gram’s stain.

ELECTRON MICROSCOPY
Formalin-fixed tissue was used for plastic-embedded sections and electron microscopy, and although tissue preservation was not optimal all sections examined showed histiocytic cells containing numerous phagolysosomes (Fig. 4). These cells ranged in size from 0.4 to 15 μm and contained, at the ultrastructural level, a variety of material including bacterial remnants, partially intact erythrocytes, electron-dense spherical bodies, vacuoles, and concentric whorled membranes (Fig. 5). Degenerate bacteria could be identified singly and, occasionally, in clumps within phagolysosomes and were sometimes in continuity with membrane profiles. Numerous Michaelis-Gutmann bodies were

Fig. 1 Adrenal gland replaced by tumour-like malakoplakic tissue and shrunken kidney, embedded in perinephric fat.

Fig. 2 Malakoplakic histiocytes with abundant coarsely granular cytoplasm and uniform nuclei. Haematoxylin and eosin × 650.
present in various stages of development (Figs. 6 and 7). In the earliest stages these consisted of electron-dense punctate or needle-shaped crystalline deposits on amorphous material within phagolysosomes. In the later stages of development these had acquired a dense central core, and many had also developed concentric lamellar rings of crystalline material around the core. Residual phagolysosomal structures were present as dense bodies and membrane profiles around the rim of some well formed Michaelis-Gutmann bodies.

Discussion

Only one previous example of adrenal malakoplakia has been described, this being in a six-week-old infant with concomitant colonic malakoplakia. In our case the kidney was also affected but the adrenal...
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Fig. 5  Electron micrograph of a giant phagolysosome within a histiocyte. A group of degenerate bacteria showing partial destruction of their cell walls and clumping and loss of cytoplasm are in the lower half. × 38 000.

Fig. 6  Formation of an early Michaelis-Gutmann body with needle-like crystalline deposition on amorphous material within a phagolysosome. × 38 000.
lesion appeared to have arisen independently, for there was no continuity between the two malakoplakic lesions, the kidney and adrenal being easily separable. Adrenal malakoplakia can mimic a neoplasm not only on radiological scanning but also at surgical exploration and on gross pathological examination, this being, in fact, the presumptive diagnosis in this case before histological examination. Histologically, however, the lack of pleomorphism and of mitotic activity indicates the non-neoplastic nature of the lesion while the typical appearance of the histiocytic cells and the presence of Michaelis-Gutmann bodies readily indicate the true diagnosis.

It would be generally agreed that the finding of Michaelis-Gutmann bodies is a necessary prerequisite for the diagnosis of malakoplakia, but it cannot be claimed that these calciospherites are specific to this condition for their occurrence has also been described in normal uroepithelium, non-specific giant cell cystitis, renal medullary calcinosis, and calcified aortic valves.

The nature of malakoplakia is not yet fully understood but the demonstration of intracellular bacteria with the ultrastructural characteristics of coliform organisms, the frequent association with urinary tract E coli infections, the response of some cases to antibiotic treatment, and the experimental production of malakoplakia using crude endotoxin-antigen complex of E coli have all tended to implicate Gram-negative enteric bacilli as the aetiological agent in this condition: certainly the patient described here, who had a proven E coli infection, would fit in well with this hypothesis.

Nevertheless, although E coli infections are common, malakoplakia is rare, and there must be additional factors in the pathogenesis of this condition. It has been suggested that the development of malakoplakia is dependent upon an altered immunological status, a defect in monocyte function, infection with an unusual strain of E coli, an unusually massive release of bacterial glycolipid, or altered macrophage function. It is probable that the last of these suggested factors is of the greatest importance for the presence of partially-degraded bacteria within phagolysosomes suggests that the macrophages are unable to phagocytose organisms completely. The products of incomplete digestion persist as amorphous electron-dense aggregates and phospholipid membranes within engorged phagolysomes, and it is the later deposition of calcium that gives rise to the characteristic Michaelis-Gutmann bodies. Whether, how-
ever, malakoplakia is a specific disease entity or merely a variant form of non-specific inflammatory response still remains enigmatic.

References


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