Michaelis-Gutmann Bodies in a Healing Brain Infarct

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A case of Michaelis-Gutmann bodies in a healing brain infarct is described. Morphologically this was consistent with cerebral malacoplakia. There are only 6 previously reported cases of cerebral malacoplakia, and only 1 of them was a consequence of postpartum stroke. The histologic and ultrastructural features of the malacoplakic lesion are reported and compared with the previously reported cases. (Stroke 1987;18:947-950)

The accumulation of histiocytes containing Michaelis-Gutmann (MG) bodies is rare. MG bodies are calcified, laminated, periodic acid-Schiff (PAS)-positive inclusions that were first described by Michaelis and Gutmann in 1902. Malacoplakia usually involves the urinary bladder, but involvement of other sites has been reported. Cerebral malacoplakia seems to be very rare. In a search of the literature we located only 6 previously reported cases of cerebral malacoplakia. Most were in children in association with neonatal herpes infection, and 1 case was in a young woman who died as a consequence of postpartum stroke.

We report the histochemical and ultrastructural findings of MG bodies in a healing brain infarct. To the best of our knowledge, our 72-year-old patient is the oldest case of cerebral malacoplakia reported in the literature.

Report of a Case

A 72-year-old man was admitted to the hospital because of sudden onset of confusion and dysarthria. Past medical history included congestive heart failure and chronic atrial fibrillation. Physical examination on admission revealed a right central facial palsy. Laboratory findings were 80 mg% urea, 1.5 mg% creatinine, 10 mg% calcium, and 4.1 mg% phosphate; electrocardiogram showed atrial fibrillation. Chest x-ray examination displayed enlargement of the heart, mild pulmonary congestion, and a small pleural effusion. The electroencephalogram revealed slow wave activity in the left temporal region. The diagnosis of a thromboembolic event in the form of a cerebrovascular "accident" was made.

On the seventh day of hospitalization the patient began complaining of abdominal pain. Serum urea rose to 110 and creatinine to 2.4 mg%, while calcium and phosphate were 10.2 and 5.1 mg%, respectively (normal, 8.8-10 mg% and 2.5-4.5 mg%). Renal perfusion scan and an intravenous pyelogram were suggestive of an infarction of the left kidney.

After a few days, during which serum urea, calcium, and phosphate remained unchanged and there was no alteration in the neurologic state, his abdomen became distended, tympanic on percussion, and tender. The diagnosis of mesenteric thrombosis was considered. On the 34th day of hospitalization, during abdominal angiography, massive vomiting of coffee-ground material developed, followed by cardiac arrest unresponsive to resuscitation.

Necropsy Findings

The relevant gross necropsy findings were mural thrombi in both atrial appendages, pulmonary embolism and infarction, and occlusion of the left renal artery with renal infarction. There was also infarction in the left temporo-occipital region of the brain, but the supplying artery was not occluded.

The gastrointestinal tract did not reveal any abnormality except for erosive gastritis and coffee-ground material in the stomach. Histologic examination confirmed the infarction in the kidney and lungs without any calcification and a healing brain infarct of approximately 1 month's duration.

Microscopic and ultrastructural findings in the brain showed the margins of the necrotic zones to contain numerous histiocytes with small basophilic granules in a foamy cytoplasm (Figure 1). The granules were mostly 0.4-4μm in diameter. They showed concentric "targetoid" laminations at high magnification. The smaller granules and the MG bodies stained positive with von Kossa, PAS, and Alcian blue; application of Perl's Prussian blue stain failed to reveal iron.

Tissue for electron microscopy was obtained from formalin-fixed material. There were abundant histiocytes, which contained MG bodies (Figure 2) ranging in size from 1.2 to 4 μm in diameter. They had a dense, central mineralized core with radially arranged crystalline material. Some of the calcified bodies were limited by a membrane. A narrow, clear zone was present between the electron-dense central area and the limiting membrane (Figure 3).
Discussion

Brain infarction is one of the leading causes of death, and in our department is a major finding in at least 5% of all autopsies. Nevertheless, we have never seen malacoplakia in an area of brain infarction. There have been 6 previously reported cases of cerebral malacoplakia; 5 were in children with a background of herpes simplex infection and were dissimilar to our case. The sixth case had some features in common with the present case. Both involved an area of brain infarction and both showed, in addition to the typical MG bodies, smaller basophilic granules that contained calcium. Clinically the 2 patients developed renal failure during hospitalization.

Malacoplakia is characterized by the accumulation of histiocytes containing MG bodies, the origin of which is unresolved. Their occurrence in nervous tissue seems to be very rare. In experimental animals, calcification 0.4–1.0 μm in diameter, similar to MG bodies, was seen in axons between 30 minutes and 1 week after spinal cord trauma. Later, phagocytosis of the axonal profiles containing calcified bodies was observed. The ultrastructural picture is essentially similar to our case and also similar to the ultrastructural features of malacoplakia reported in the literature.

Histochemically the MG bodies in our case were PAS-, Alcian blue-, and von Kossa-positive. All the cases investigated by Stevens and McClure were consistently positive for the same stains, confirming the presence of neutral polysaccharides and an acidic non-sulfated polysaccharide. All the MG bodies also contained calcium and phosphate. MG bodies are an example of dystrophic calcification. Calcium salt deposition at sites of local tissue damage may be augmented by hyperphosphatemia that occurs in renal failure. Since our patient and the patient described by Blumberg et al had renal failure and transient hyperphosphatemia, it is possible that the mechanism of augmented dystrophic calcification might have played a role in the pathogenesis of cerebral malacoplakia in these cases.

Additional factors, such as infection or immunodeficiencies, have been raised as a pathogenetic mechanism of malacoplakia. These factors were not found in our patient although we cannot completely rule out an occult bacterial infection elsewhere.

In view of the present emphasis on the cytotoxicity of calcium, especially in relation to axonal degeneration, it is possible that calcification may play a role in determining the extent of cellular damage or in the conversion of a potentially reversible cell damage to an irreversible one presenting morphologically as a malacoplakia.
FIGURE 2. Michaelis-Gutmann (MG) bodies in the cytoplasm of the cells and extracellularly (×2,000).

FIGURE 3. A higher magnification of the Michaelis-Gutmann (MG) body, which is limited by a membrane (arrows) (×130,000).
References


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