Malakoplakia in Kidney Transplant Recipients

By Kanza Haq

Malakoplakia is derived from Greek words, meaning “soft plaque.” It is a rare, chronic, granulomatous disease that was first reported in 1902 by Leonor Michaelis and Carl Gutmann. Malakoplakia was initially thought to exclusively involve the urogenital tract, but it can affect any organ of the body and has been reported in the gastrointestinal tract, brain, bones, adrenal glands, lymph nodes, lungs, skin, and other organs (1). Most patients affected by malakoplakia have associated conditions characterized by some degree of immunosuppression, and it has been described in patients with solid organ transplant and kidney transplantation in particular. Other risk factors include recurrent urinary tract infections (UTIs), autoimmune diseases requiring steroid use, chronic systemic diseases, neoplasia, chemotherapy, alcohol abuse, and poorly controlled diabetes (2). Although it is more commonly seen in kidney transplant recipients, there are reported cases of malakoplakia in patients with liver, cardiac, and hematopoietic stem cell transplantation as well (3–5). Kidney transplant malakoplakia cannot only involve alloergic parenchyma; it has also been reported in extra-renal sites (e.g., ureter, bladder, gastrointestinal tract, skin, submandibular gland, testicles, and prostate) (6–8).

Clinical features

Previous reports in kidney transplant recipients suggest a higher prevalence of malakoplakia in women and in patients with recurrent Escherichia coli UTI (8, 9). Following transplantation, the onset of malakoplakia has been reported within months and up to 1 decade or more later. Clinical presentation is very variable; it usually manifests as chronic dysfunction of the allograft, recurrent UTIs, or renal mass. E. coli is the predominant microorganism identified in most cases, although other organisms have been implicated, such as Klebsiella, Proteus, Citrobacter, Corynebacterium, and Aerobacter species (8–10).

Pathogenesis

The pathogenesis of malakoplakia is not well understood but thought to involve reduced levels of cyclic guanosine monophosphate (cGMP) in mononuclear cells, causing impaired lysosome function and intracellular lysis of phagocytosed bacteria (11). This leads to persistence of infection, and the granulomatous reaction generates the appearance of soft, yellowish nodules and plaques on gross examination. (Imaging and diagnostic features are elucidated in Table 1.)

Treatment/prognosis

Data about the therapeutic approaches to treat malakoplakia are limited, but the mainstay of treatment in transplant patients is reduction in immunosuppression and long-term antibiotics. Antibiotics having intracellular penetration are recommended, but ideal treatment duration still remains unclear. Treatment time of a few weeks to months has been described in previous reports with variable outcomes (8–10). The cholesterinogenic bethanecoxol has also been used with antibiotics to improve intracellular killing of the organisms by increasing cGMP levels. Some cases are refractory to antibiotoic treatment and ultimately require surgical management. Prognosis of malakoplakia has improved over time, likely due to use of appropriate antibiotics and minimization of immunosuppressive regimens. The mortality rate has decreased, but non-recovery of renal function leading to graft failure is still seen (8–10). An important caveat is to consider graft rejection risk while reducing immunosuppression, especially in the early posttransplant period.

Conclusion

It is important to consider malakoplakia in the differential diagnosis for allograft dysfunction with a history of recurrent UTI or a mass in kidney transplant patients. Recognition and understanding of malakoplakia are important because it is a pathologic condition that has not been well studied and can contribute to loss of graft function and morbidity. More high-quality data are needed to elucidate treatment options for malakoplakia and to better understand long-term sequelae and its implications on prognosis.

Kanza Haq, MD, is with the Division of Nephrology, Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD.

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References


Table 1. Imaging and diagnostic features in malakoplakia

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<thead>
<tr>
<th>Imaging features</th>
<th>Diagnosis features</th>
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<td>Computed tomography</td>
<td>Poorly defined low signal intensity nodules related to the presence of calcium and iron in the Michaelis-Gutmann bodies (15); findings in a previous report of increased uptake on a gallium scan and decreased uptake on dimercaptosuccinic acid (DMSA) in the involved area (16)</td>
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<td>Magnetic resonance imaging</td>
<td>Graft biopsy is required to establish the diagnosis and for timely treatment decisions. Pathogonomic biopsy findings are histocytes with granular cytoplasm (von Hanssenn cells) and targetoid intra-cytoplasmic Periodic acid-Schiff (PAS)-positive inclusions, called Michaelis-Gutmann bodies (2) (Figures 1 and 2)</td>
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<td>Michaelis-Gutmann bodies are derived from remnants of partially phagocytosed bacteria with iron and calcium deposits. Identification sometimes may require special stains, such as the von Kossa stain for calcium and the Prussian blue stain for iron.</td>
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