Malacoplakia of the cranium and cerebrum in a human immunodeficiency virus–infected man

Case report

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Malacoplakia is a rare chronic inflammatory disease associated with infection and immunosuppression, and very few occurrences have been reported in the cerebrum. The authors describe the case of a 41-year-old man with advanced human immunodeficiency virus (HIV) infection who presented with a very aggressive malacoplakia lesion that had extended through the scalp, temporalis muscle, skull bone, and deep through the dura mater into the superior sagittal sinus and adjacent brain. Pathological examination revealed sheets of histiocytes invading these structures, and macrophages containing numerous round bodies known as Michaelis–Guttmann bodies, pathognomonic for malacoplakia. Because of the rarity of this phenomenon, appropriate treatment and management of malacoplakia are speculative. A complete resection of the lesion, antibiotic therapy, and treatment of his underlying HIV infection had a salutary effect, with the patient faring well more than 9 months postoperatively.

KEY WORDS • malacoplakia • intracranial mass lesion • human immunodeficiency virus

Abbreviations used in this paper: CNS = central nervous system; CSF = cerebrospinal fluid; CT = computerized tomography; HIV = human immunodeficiency virus; MR = magnetic resonance; PCR = polymerase chain reaction; PML = progressive multifocal leukoencephalopathy.
A local incision and drainage of this presumed abscess revealed gross purulence, and the wound was left open and packed with iodoform gauze. Examination of bacterial, fungal, and mycobacterial cultures from this material demonstrated no growth. After this, a defect in the underlying skull was palpated, prompting the need for an axial CT scan that revealed a 4-cm osteolytic lesion in the right frontoparietal skull, a hyperdense epidural fluid collection, and a low-density lesion within the right frontal lobe surrounded by vasogenic edema (Fig. 1 left). Subsequent MR imaging revealed a right frontal lobe lesion involving the scalp and skull, with intracranial extension (Fig. 1 right). Chest radiography and CT scanning revealed a right lower lobe cavitary lesion with hilar adenopathy.

Operation. After intubation, transbronchial biopsy sampling of the cavitary lesion was performed. A bicoronal incision was then modified to accommodate the scalp mass and provide exposure of the underlying calvarial defect. The lesion, which lay immediately under the subcutaneous layer of the scalp and infiltrated the galea aponeurotica and right temporalis muscle, was soft, fleshy, relatively avascular, and yellowish-gray. Deep in the scalp, it infiltrated the bone peristium, circumscribing a 4- to 5-cm defect in the calvarial bone and dura mater, extending to, and in some places infiltrating, the pial layer overlying the cerebral cortex. Medially, it invaded the right lateral wall of the superior sagittal sinus. We performed an en bloc excision of the scalp component and the underlying bone, maintaining a 10-mm margin around the edge of the osseous defect. The intracranial component was excised piecemeal. The superior sagittal sinus was ligated where the lesion infiltrated it, and this component was removed as well. Blood loss was 5500 ml, and a single episode of hypotension to 60/20 mm Hg was successfully treated with fluid and blood product replacement. Subgaleal undermining of the adjacent scalp allowed a primary, tensionless closure.

Postoperative Course. Postoperatively, the patient’s course was stable and CT scanning revealed complete resection of the lesion (Fig. 2). The patient was discharged on postoperative Day 8.

Histopathological Examination. Examination of the endobronchial biopsy specimen of the cavitary lung lesion revealed reactive squamous metaplasia with submucosal proliferation of macrophages. Calcium staining revealed Michaelis–Guttmann bodies, consistent with a diagnosis of malacoplakia.

Analysis of surgical specimens revealed sheets of histiocytes and macrophages penetrating through the calvaria, dura, and into the brain parenchyma. Within the cytoplasm of the macrophages, patchy pale-blue round bodies consistent with Michaelis–Guttmann bodies were found, again indicative of malacoplakia (Fig. 3 upper). Calcium staining also revealed Michaelis–Guttmann bodies were found (Fig. 3 lower). Gomori-methenamine-silver stain of frozen section tissue showed scattered intracytoplasmic coc-
cobacillary forms suggestive of bacteria that were Gram positive. Special stains for fungal, acid-fast and modified acid-fast organisms, and spirochetes were negative, as were cultures for bacterial, fungal, and mycobacterial organisms, on both the endobronchial and cranial surgical specimens.

**Discussion**

Patients infected with HIV are at risk for both opportunistic infections and malignancies of the CNS, and the extent of immunosuppression determines the likelihood of an opportunistic infection. For example, PML, toxoplasmosis, and cryptococcosis usually occur in patients with CD4 counts of less than 50 to 100 cells/mm$^3$. Diseases of the CNS may be focal or diffuse in these patients. Focal brain lesions are typically the result of bacterial or fungal infection, toxoplasmosis, CNS lymphoma, or PML. Cryptococcal and cytomegalovirus infections usually present in a diffuse fashion, although focal presentations have been reported. Mycobacterial infections may present as either a focal or diffuse process.

Brain abscess, with peripheral uniform ring contrast enhancement and surrounding brain edema, may occur in intravenous substance abusers with endocarditis and embolic phenomena involving the CNS. Septic emboli due to endocarditis and infections such as those with nocardia species, mycobacteria, and the endemic mycoses may cause both CNS and lung involvement in susceptible hosts. Both tuberculomas and invasive aspergillosis are rare but have been reported. The incidence of toxoplasmosis has declined with the widespread use of prophylactic medications, such as trimethoprim/sulfamethoxazole. On CT and MR imaging, toxoplasmosis appears as multiple rounded hypodense lesions with ring enhancement and surrounding edema. The incidence of primary CNS lymphoma in individuals with HIV infection is much higher than in the general population and is usually associated with latent Epstein–Barr virus infection, which can be detected using PCR testing of the CSF. These lesions may be solitary or multiple and are typically periventricular. A human polyomavirus, the JC virus, is associated with PML. Patients with PML typically present with rapidly progressive focal neurological deficits without signs of increased intracranial pressure. Clinical findings are often more severe than suggested by the CT-documented hypodense, nonenhancing lesions of the cerebral white matter. Testing with PCR has been used to amplify JC virus DNA in the CSF.

A trend toward noninvasive diagnosis of brain lesions in patients with HIV infection via blood serology, CSF PCR assays, and empiric antimicrobial treatment is prevalent. Positive serology for toxoplasmosis with characteristic CT or MR imaging findings usually prompts treatment for toxoplasmosis, and biopsy sampling may be pursued only if empiric treatment is unsuccessful. Neurological symptoms associated with PML may improve after initiation of antiretroviral therapy. Patients harboring small focal lesions without significant mass effect in a surgically inaccessible location may be candidates for this approach; however, those

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**Fig. 3.** Upper: Photomicrograph of brain tissue showing Michaelis–Guttmann bodies within the cytoplasm of macrophages (arrows). H & E, original magnification × 400. Lower: Von Kossa (calcium) stain of brain tissue showing Michaelis–Guttmann bodies (arrow). Original magnification × 200.

**Fig. 4.** Axial CT scan obtained 6 months after initial surgery, showing repair of the cranial defect with custom-fabricated implant and no recurrence of contrast-enhancing lesion.
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presenting with a more extensive lesion and mass effect and violation of the scalp and calvaria, such as in the present case, may require surgical exploration to debride the lesion, decompress the brain, and reconstruct the calvarial and scalp layers.

Malacoplakia, in our case, was diagnosed by the histopathological examination of the lung and cranial biopsy specimens. This is a rare chronic inflammatory process that most commonly affects the genitourinary tract and can be difficult to distinguish clinically from a neoplastic process. It is an inflammatory response to an infectious process that develops as the result of dysfunctional lysosomes within macrophages that either fail to kill ingested intracellular organisms or are effective at killing but fail to eliminate the resulting end products. Immuno logical abnormalities may play a role, as a significant proportion of reported cases occur in individuals with immunocompromised systems, including those with acquired immunodeficiency syndrome, autoimmune thyroiditis, lupus erythematosus, tuberculosis, sarcoidosis, malignancy, diabetes mellitus, and alcoholism.

The organism isolated in most cases of malacoplakia is E. coli although other pathogens have been reported. In patients with HIV, pulmonary lesions caused by Rhodococcus equi, a Gram-positive opportunistic infection usually associated with horses and livestock, predominate; this is germane to this particular case, as the patient cared for livestock. Gram-positive organisms were seen on special stains of brain tissue obtained in this case, but the cultures were not fruitful.

Given its rarity, no trials exist that compare the efficacy of various treatments for malacoplakia. Based on a literature review, Van der Voort, et al., formulated some general treatment guidelines, which may be summarized as follows: if possible, stop or reverse immunosuppression; excise the lesion; and administer an antibiotic agent with good intracellular penetration and effectiveness. Most successful treatments have included a quinolone antibiotic agent is still the recommendation. No data exist regarding the appropriate treatment duration or route of antibiotic administration. The patient presented here underwent complete excision of the brain lesion but not the lung lesion. He underwent a 3-month course of ciprofloxacin and trimethoprim/sulfamethoxazole postoperatively, along with combination antiretroviral therapy, including zidovudine, lamivudine, and lopinavir/ritonavir, on which he will remain indefinitely. An axial CT scan obtained 6 months after surgery showed no recurrence of the disease (Fig. 4), and the cranial bone defect was reconstructed using a custom-fabricated implant without untoward event. Serial CT scanning was performed to monitor the status of the lung lesion, which had nearly resolved at 9 months. At 9 months, the patient was clinically stable without evidence of disease recurrence, and the incisions were healed.

Conclusions

Malacoplakia, an uncommon inflammatory condition associated with bacterial pathogens, occurs in immunocompromised individuals and rarely involves the cerebral cortex and adjacent tissues. In the present case, resection, antibiotic therapy, and optimization of the patient’s immune status were effective strategies in achieving a good outcome.

References


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