Nontuberculous Mycobacterial Infection of a Metastatic Brain Neoplasm in an Immunocompromised Patient

Ann A. Little, MD; Stephen S. Gebarski, MD; Mila Blaivas, MD, PhD

Background: Nontuberculous mycobacterial infections occur in immunocompromised patients but so rarely involve the central nervous system (CNS) that they may not be included in a differential diagnosis of CNS lesions in such patients.

Objective: To illustrate a putative mechanism for nontuberculous mycobacterial infection of the CNS via breakdown of the blood-brain barrier by metastatic neoplasm.

Results: A 56-year-old man who had undergone renal transplantation in February 2003 and was taking an immunosuppressive regimen of mycophenolate mofetil and cyclosporine was seen in the emergency department after a syncopal episode. Head computed tomography revealed a single focal occipital lesion with vasogenic edema. Hospital admission and further workup led to diagnosis of metastatic carcinoma infected with nontuberculous mycobacteria in the setting of a disseminated nontuberculous mycobacterial infection.

Conclusion: This case illustrates that breakdown of the blood-brain barrier by metastatic neoplasm may provide a route of access for a pathogen that is not normally seen in the CNS.

Arch Neurol. 2006;63:763-765

ONTUBERCULOUS MYCOBACTERIAL (NTM) infections with or without dissemination are well documented in immunocompromised patients and patients with lung disease, such as cystic fibrosis.¹² Nontuberculous mycobacteria are ubiquitous in the environment but rarely are sources of disease in immunocompetent individuals because of their low virulence. These infections usually manifest with localized involvement, such as cutaneous disease, pulmonary disease, lymphadenitis, skeletal disease, and foreign body infections. Cutaneous and pulmonary disease are most prevalent in patients who have undergone solid organ transplantation. Foreign body infections, such as venous catheter infections, are often seen in hematopoietic stem cell recipients.¹ A small percentage of cases may initially be seen with disseminated disease involving a number of organ systems. Disseminated disease is most often associated with the human immunodeficiency virus population, which represents a small but significant subset of NTM infections in any immunocompromised group examined.

Involvement of the central nervous system (CNS) by NTM is exceedingly rare under any circumstance. Recent reviews of CNS infections related to the immunocompromised state³⁴ mention tuberculous but not NTM infections. The literature contains only a few case reports of NTM infections of the CNS. These include focal lesions⁵⁻¹⁰ and diffuse involvement such as chronic meningitis.¹¹ We report a unique case of metastatic neoplasm infiltrated with NTM in an immunocompromised patient who had undergone a solid organ transplantation.

METHODS

A 56-year-old patient with a 40-pack-year history of tobacco use who had undergone renal transplantation in February 2003 was seen in the emergency department in January 2005 after a syncopal episode. A head computed tomographic (CT) scan revealed a single, approximately 2.5-cm, left occipital lesion with surrounding vasogenic edema, local mass effect, and nearby bone destruction (Figure 1A).

On hospital admission, immunosuppressive therapy consisted of mycophenolate mofetil, cyclosporine, and prednisone. Because of the vasogenic edema and mass effect, dexamethasone administration was initiated.

Initial physical examination revealed a cachectic appearance and an enlarged left supraclavicular lymph node. Neurological examination revealed a right homonymous hemianopsia. Laboratory studies on hospital admission were significant for microcytic ane-
Computed tomographic (CT) scan and magnetic resonance images (MRIs) of the brain of a 56-year-old man with nontuberculous mycobacterial infection of an adenocarcinoma metastatic to the left occipital lobe. A, Intravenous contrast-enhanced axial CT section through the occipital lobes displayed in the brain window shows an approximately 2.5-cm mixed attenuation mass (small arrow) with surrounding vasogenic edema (large arrow). B, T2-weighted axial MRI through the occipital lobes shows the mass lesion to contain a high-T2 material centrally surrounded with a peripheral low-T2 rim (small arrows), as can be seen with densely cellular neoplasm with a liquid necrotic core. Moderate local vasogenic edema is present as well as local bone involvement (large arrow). C, Intravenous contrast-enhanced, sagittal, T1-weighted MRI through the lesion also shows the local meningeal involvement (arrows) and bone destruction (arrowhead).

Our patient’s state of immunosuppression as a solid organ transplant recipient increased his risk for NTM infection. Doucette and Fishman searched MEDLINE for English language articles since 1966 documenting cases of nontuberculous mycobacterial infection. Our patient’s posttransplantation baseline value) levels.

Initial concern was for a metastatic process. Further workup included plain radiographs of the chest, chest CT, lumbar puncture, esophagogastroduodenoscopy, colonoscopy, open biopsy of the left supraclavicular lymph node, and magnetic resonance imaging of the brain. Chest CT revealed a noncalcified left lower lobe lung mass measuring 2.3 × 1.8 cm with speculated margins and a gas-filled center as well as multiple bilateral nodules measuring 2 to 3 mm in diameter scattered diffusely through the lungs with enlarged retroperitoneal lymph nodes. Colonscopy results were grossly normal. Esophagogastroduodenoscopy revealed normal-appearing nodular, edematous mucosa throughout the duodenum. Lumbar puncture findings were unrevealing (red blood cells, 0; white blood cells, 4 in tube 4; glucose level, 65 mg/dL [3.61 mmol/L]; protein level, 95 g/dL; cytologic examination results were negative for neoplasm; flow profile results were negative for lymphoma; acid-fast bacilli, bacterial, and fungal smears and culture results were negative). Sputum tuberculosis–polymerase chain reaction results were negative.

Magnetic resonance imaging of the brain was obtained to further characterize the lesion found on CT and to search for additional lesions. Magnetic resonance imaging showed an approximately 2.5-cm, solitary occipital lesion (Figure 1B and C). This mass lesion had a central fluid-like high–T2 signal component with restricted diffusion in this fluid, low-peripheral T2 signal showing heterogeneous pathological contrast enhancement, and local meningeal involvement. As was also shown on CT, the lesion demonstrated vasogenic edema, local mass effect, and erosion of the nearby occipital bone.

Tissue specimens from the supraclavicular lymph node, duodenum, and colon were filled with foamy macrophages. Sections of lymph node, duodenal biopsy specimen, and sputum were acid-fast bacilli positive and periodic acid–Schiff negative, consistent with disseminated NTM infection. (Mycobacterium tuberculosis polymerase chain reaction results were negative; purified protein derivative findings were nonreactive.)

Concern remained high for metastatic vs primary brain tumor because NTM so rarely cause focal lesions in the brain. Open brain biopsy was undertaken for definitive diagnosis. The surgical report of the occipital lesion described a focal mass extending to and invading the dura as well as eroding the overlying skull. Pathological examination of the occipital lesion tissue demonstrated both adenocarcinoma and NTM infection (Figure 2A and B). Clusters of foamy macrophages containing colonies of acid-fast bacilli were scattered throughout the neoplasm, associated with small numbers of neutrophils. The neoplasm itself contained no identifiable brain parenchyma and was consistent with metastatic carcinoma with a focal endocrine pattern. Immunoperoxidase staining for keratin cocktail was positive within the neoplastic cells. Staining for thyroid transcription factor 1 was negative in the neoplastic cell nuclei. The proliferation index approached 90% in some areas, as determined using Ki-67 staining.

Triplet-drug therapy was initiated in treatment of disseminated Mycobacterium avium-intracellulare complex infection. Whole brain radiation was carried out for palliative care of CNS metastasis. Given the lung lesion and smoking history, lung adenocarcinoma was a likely candidate for the primary neoplasm; however, the patient declined further diagnostic workup.
of NTM infection in patients who had undergone transplantation and identified reports of 183 solid organ transplantation cases complicated by NTM infection. Ninety-four of 183 solid organ transplantation cases were renal transplantations. In patients who had undergone renal transplantation, cutaneous NTM was most common, followed by disseminated disease (approximately one third of cases identified). Our patient had a disseminated NTM infection that appeared to be highly active based on dense infiltration of macrophages and profusely positive acid-fast bacilli staining throughout all tissues in which a biopsy was performed.

We postulate that the breakdown of the blood-brain barrier caused by metastatic neoplasm allowed an entry point for NTM infection to the CNS. The edema seen on imaging corresponds to abnormal capillary permeability consistent with disruption of the blood-brain barrier.12

Accepted for Publication: December 15, 2005.
Correspondence: Ann A. Little, MD, Department of Neurology, University of Michigan Medical Center, 1924 Taubman Center, 1500 E Medical Center Dr, Ann Arbor, MI 48109 (alitt@umich.edu).

Author Contributions: Study concept and design: Little and Gebarski. Acquisition of data: Little, Gebarski, and Blaivas. Analysis and interpretation of data: Little, Gebarski, and Blaivas. Drafting of the manuscript: Little and Gebarski. Critical revision of the manuscript for important intellectual content: Little, Gebarski, and Blaivas. Administrative, technical, and material support: Gebarski. Study supervision: Gebarski.

REFERENCES