Cerebral Nocardiosis Mimicking Multiple Brain Metastases in a Patient with Locally Advanced Non–Small-Cell Lung Cancer

Cathy Voide, MD, Stefan Zimmermann, MD,† Alex A. Adjei, MD, PhD,‡ Daniel C. Betticher, MD,† Reto Meuli, MD,§ Guy Prod'hom, MD,‖ Stefano Giulieri, MD,* and Solange Peters, MD, PhD¶*

CASE REPORT

A 66-year-old man, diagnosed with a right upper lobe adenocarcinoma invading the chest wall and mediastinum, cT4cN0cM0, underwent the first cycle of weekly cetuximab and 3-weekly cisplatin (100 mg/m^2)–docetaxel (85 mg/m^2). Concomitant medication included dexamethasone 8 mg twice daily for 3 days. The onset of delirium on day 21 of the second cycle of chemotherapy prompted a brain computed tomography scan and a brain magnetic resonance imaging scan (MRI; Fig. 1*A*). As the observed brain lesions were interpreted as central nervous system metastases, corticosteroid treatment with 12 mg per day of dexamethasone was initiated. Clinical deterioration motivated a subsequent brain MRI, performed after an 11-day interval (Fig. 1*B*). A stereotactic biopsy of one lesion was performed, followed by empiric antibiotic treatment of meropenem. A Ziehl-Neelsen (modified bleach) stain (Fig. 2*A*) of cerebral lesions aspirates and a Gram stain of the biopsy (Fig. 2*B*) showed filamentous bacteria, that were identified as *Nocardia farcinica*. Antibiotic treatment was switched to sulfamethoxazole-trimethoprim. Screening for human immunodeficiency virus showed a negative result. Thoracic computed tomography showed several new lesions suggestive of disseminated nocardiosis (Fig. 3). A follow-up MRI after 4 weeks of treatment showed no improvement in most of the brain lesions. Progressive clinical deterioration culminated in death 7 weeks after the diagnosis of cerebral nocardiosis.

*Infectious Diseases Department, Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland; †Oncology Department, Fribourg Hospital and Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne; Switzerland; ‡Roswell Park Cancer Institute, Buffalo, New York; §Radiology Department, ‖Microbiology Institute, and ¶Oncology Department, Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland.

Cathy Voide and Stefan Zimmermann as first authors and Stefano Giulieri and Solange Peters as senior authors contributed equally to this work.

Disclosure: The authors declare no conflict of interest.

Address for correspondence: Solange Peters, MD, PhD, Oncology Department Centre Hospitalier Universitaire Vaudois (CHUV), 1011 Lausanne, Switzerland. E-mail: Solange.Peters@chuv.ch

ISSN: 1556-0864/14/0903-0e24

DISCUSSION

Nocardia are branched aerobic, Gram-positive, weakly acid-fast bacteria that include more than 80 species.[1] *Nocardia spp* is ubiquitous in the environment and is acquired by direct inoculation or by inhalation. This bacteria is responsible for localized or disseminated opportunistic infections, with a subacute, chronic, or rarely acute course. The most common clinical manifestation in disseminated disease is pulmonary infection with hematogenous spread to the brain and/or the skin. Known risk factors for disseminated nocardiosis are cell-mediated immunodeficiencies such as solid organ transplantation, acquired immunodeficiency syndrome, systemic corticosteroid therapy, solid organ tumors, and hematologic malignancies.

Although most of the patients have risk factors, disseminated nocardiosis could be seen without underlying immunosuppression or illness in 15% of cases.[2] Brain lesions in a patient with a solid tumor should raise the possibility of a *Nocardia* infection besides metastases. A delay in the diagnosis of this infection may indeed be fatal as these bacteria are virulent, with a tendency to disseminate and to be resistant to the empiric antibiotic treatment of cerebral abscess. Stereotactic biopsy is crucial to make the diagnosis and to obtain the antibiotic susceptibility that is highly unpredictable.

Optimal management of cerebral nocardiosis is not defined. At least initially, combination antibiotic therapy including trimethoprim-sulfamethoxazole and either ceftriaxone or imipenem is advocated. Linezolid is an interesting alternative to trimethoprim-sulfamethoxazole pending *Nocardia* species identification and drug susceptibility. Therapy with an oral agent should be continued for at least 12 months.[1] Compared with pyogenic abscess, surgical drainage may be more often necessary, particularly if there are multiple lesions.[3]

Because of the propensity of locally advanced non–small-cell lung cancer to disseminate widely and early, often involving the central nervous system,[4,5] it is not surprising that our patient was initially erroneously diagnosed with cerebral metastatic relapse in the absence of symptoms of infection. A high level of suspicion is necessary to consider this diagnosis in patients presenting with new brain lesions who are deteriorating despite chemotherapy and steroids. Stereotactic aspiration plays a major role in diagnosing this infection.

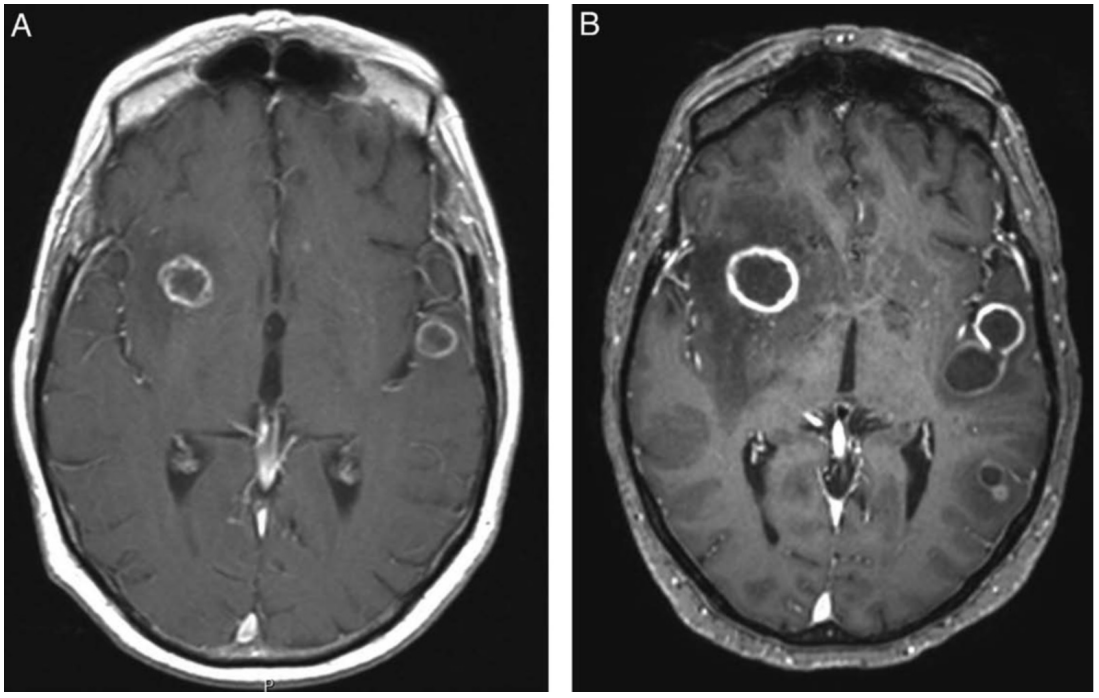

FIGURE 1. *A*, Two right hemispheric lesions and one left temporal lesion ranging in size from 12 to 15 mm, with annular peripheral enhancement. *B*, Significant progression in size and number of the multiple preexisting lesions, some with a bilobar shape, strongly suggestive of brain abscesses, involving both the supra- and infratentorial regions.

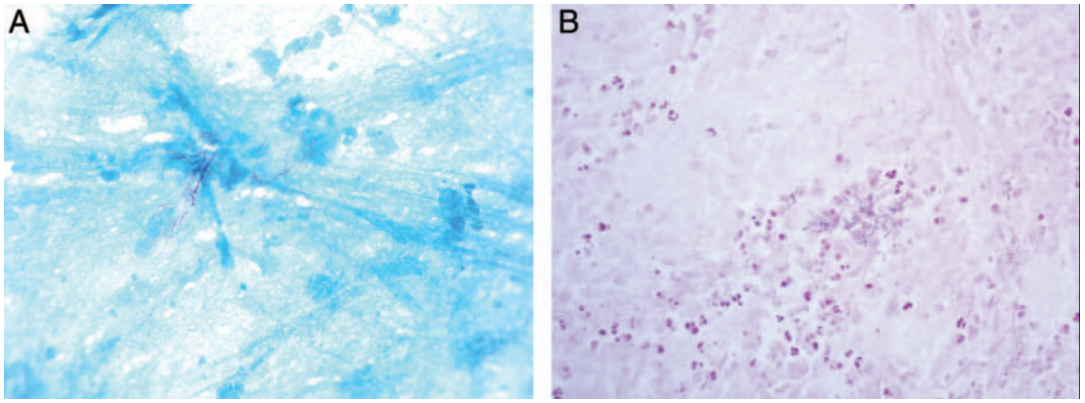

FIGURE 2. *A*, Acid-fast, bacillus-positive, branching filamentous bacteria identified as *Nocardia farcinica* strain. *B*, Gram stain of the biopsy showing an inflammatory process with multiple filamentous bacteria.

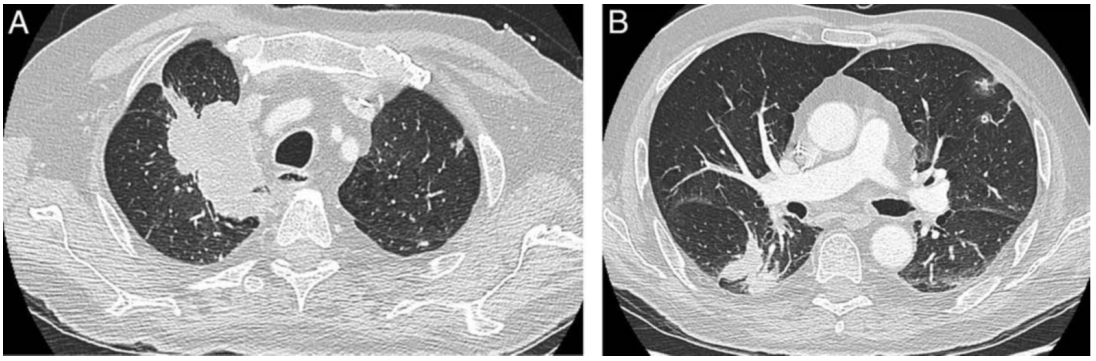

FIGURE 3. Thoracic computed tomography showed multiple left nodular lesions suggestive of pulmonary nocardiosis with hematogenous cerebral dissemination.

REFERENCES

1. Sorrel TC, Mitchell DH, Iredell JR, Chen SC. *Nocardia* Species. In: Mandell GL , Bennett JE, Dolin R. *Principles and practice of infectious diseases*. 7th Edition. New York, NY: Churchill Livingstone, 2010. Pp. 3199–3207.
2. Torres OH, Domingo P, Pericas R, Boiron P, Montiel JA, Vázquez G. Infection caused by Nocardia farcinica: case report and review. *Eur J Clin Microbiol Infect Dis* 2000;19:205–212.
3. Lee GY, Daniel RT, Brophy BP, Reilly PL. Surgical treatment of nocardial brain abscesses. *Neurosurgery* 2002;51:668–71; discussion 671.
4. Andre F, Grunenwald D, Pujol JL, et al. Patterns of relapse of N2 nonsmall-cell lung carcinoma patients treated with preoperative chemotherapy: should prophylactic cranial irradiation be reconsidered? *Cancer* 2001;91:2394–2400.
5. Cox JD, Scott CB, Byhardt RW, et al. Addition of chemotherapy to radiation therapy alters failure patterns by cell type within non-small cell carcinoma of lung (NSCCL): analysis of radiation therapy oncology group (RTOG) trials. *Int J Radiat Oncol Biol Phys* 1999;43: 505–509.