# Syncope on steroids

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An 83-year-old white woman sought medical attention because of a three-day history of slurred speech and an episode of syncope. Her medical history included long-standing rheumatoid arthritis treated with prednisone for the past five years (60 mg/day at presentation). In addition, cyclosporin (200 mg/day) had been started 16 months earlier for necrotizing scleritis.

For four to five months before admission, the patient complained of feeling unsteady on her feet. Six weeks before hospitalization, she presented to the emergency department with transient right leg weakness. Her presentation was felt to be consistent with an anterior cerebral artery transient ischemic attack, and she was started on acetylsalicylic acid. One week before admission, the patient experienced occasional hemoptysis, fevers, chills and night sweats. Shortly thereafter, she developed slurred speech and presyncopal symptoms. She was sent to the emergency department after a syncopal event in her family doctor's office. No seizure activity was noted.

She was known to be an articulate, independent woman, and she denied any previous cardiovascular history or stroke. As well, there was no history of respiratory disease, and she denied ever having a tuberculosis skin test, despite a familial history of pulmonary tuberculosis in her sister at age 20 years. She was a smoker of 35 years, and there was no history of recent travel.

On examination, the patient was not in acute distress. Her blood pressure was 170/80 mmHg, heart rate was regular at 120 beats/min, respiratory rate was 20 breaths/min and oxygen saturation was 96% breathing room air. Her oral temperature was 39.2°C. Head and neck, and cardiovascular examinations were normal, respiratory examination revealed inspiratory crackles at the left base, and abdominal examina-

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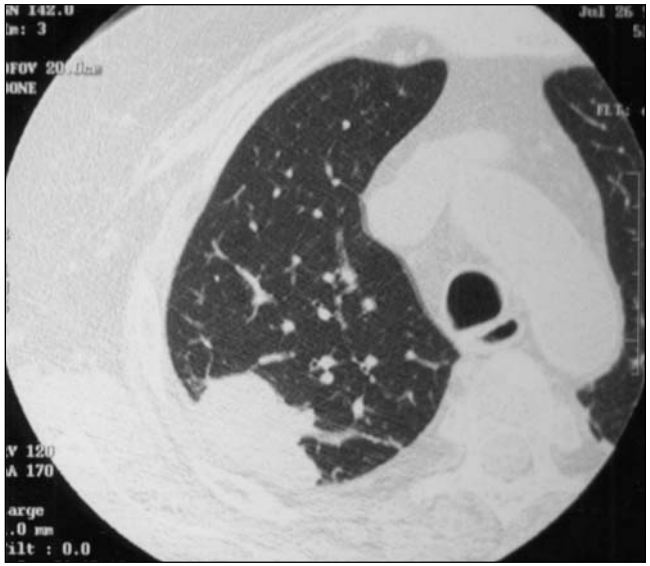

**Figure 1)** *Chest computed tomography image of the soft tissue mass in the posterior aspect of the right upper lobe abutting the chest wall without obvious extension*

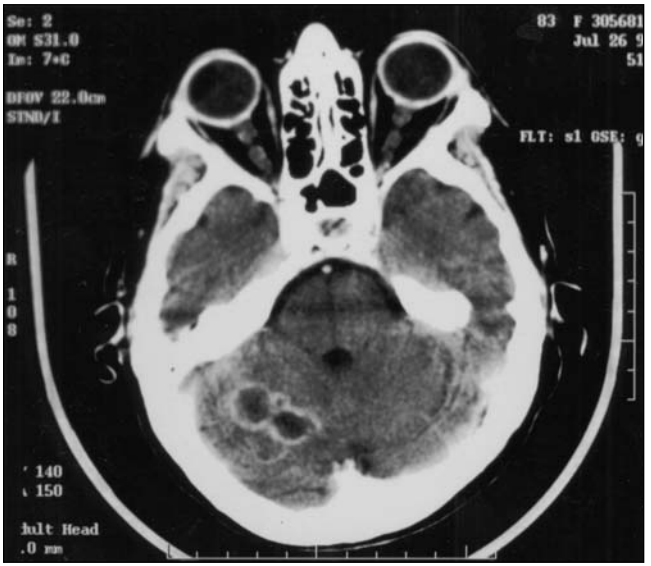


**Figure 2)** *A contrast cranial computed tomography scan demonstrating a large ring enhancing, multiloculated cystic lesion in the right cerebellar hemisphere. No mass effect is seen*

tion was unremarkable. Neurologically, the patient was alert and oriented, but her speech was slurred. Cranial nerve examination was normal. Motor, reflex and sensory examinations were also normal, with no focal signs. Cerebellar examination was remarkable for past-pointing and intention tremor on finger-nose testing, as well as dysdiadocokinesia, both localized to the left side. In addition, she leaned to the left on gait testing. There were peripheral joint findings consistent with rheumatoid arthritis. Dermatological examination found four nontender, fluctuant nodules on the patient's back – two on the left flank, and one each at the right and left parascapular regions. There was no drainage or overlying erythema.

Routine blood tests showed a hemoglobin concentration of 128 g/L, a platelet count of $211\times10^9$/L, and an elevated leukocyte count of $12.5\times10^9$ g/L. Urinalysis was normal. An electrocardiogram showed normal sinus rhythm at 94 beats/min. A set of blood cultures and a urine culture were obtained. Sputum cultures were requested, but no sample was obtained. Her initial chest x-ray showed a 4 cm right upper lobe mass extending to the lateral chest wall. She was initially treated with parenteral cefuroxime 750 mg and clindamycin 600 mg, both every 8 h. Subsequent investigations included a chest computed tomography (CT) scan, which demonstrated a $4\times3\times3$ cm lobulated soft tissue mass in the posterior aspect of the right upper lobe abutting the right chest wall (Figure 1). No bony destruction or adenopathy was seen. A head CT scan with contrast was obtained, which revealed a large ($1.5\times3.5$ cm) ring-enhancing, multiloculated cystic lesion in the right cerebellar hemisphere (Figure 2). In addition, four smaller lesions of similar appearance were seen in the cerebrum, the largest measuring $1\times1$ cm.

What is your diagnosis?

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## DIAGNOSIS

At presentation, the provisional diagnosis was malignancy, likely metastatic from the lung. The skin lesions were also thought to be metastatic lesions. On the fourth day of her admission, the blood cultures were reported to be growing *Nocardia asteroides* in two of the aerobic bottles. The patient was immediately started on cotrimoxazole (trimethoprim/sulphamethoxazole 160 mg/800 mg) intravenously every 6 h.

On the sixth hospital day, three of the subcutaneous nodules were aspirated, all of which grew *N asteroides*. A transthoracic echocardiogram failed to reveal any valvular vegetations. She remained hemodynamically stable throughout her admission, and the fever defervesced within the first few days of therapy. Her slurred speech also resolved within days. Although her gait disturbance persisted, she was able to walk with a walker.

A cranial CT scan one month later showed no resolution of the lesions; however, surgical drainage of the lesions was not indicated, because there was no evidence of increased intracranial pressure and there had been no progression of her symptoms. A repeat chest x-ray at the present time showed the right upper lobe lesion had decreased in size. Intravenous amikacin 500 mg every 12 h was added to the antibiotic therapy, with regular monitoring of levels and audiometry testing. In addition, prednisone was tapered to 12.5 mg daily, and cyclosporin was stopped without any exacerbation of her rheumatoid arthritis or necrotizing scleritis. Another head CT scan, completed another month later, showed a small reduction in the size of the lesions. Approximately three months after admission, the patient was discharged on oral cotrimoxazole, one double strength tablet twice/day, to complete a 12-month course. She had received eight weeks of parenteral treatment with cotrimoxazole and four weeks of amikacin. She was also discharged on prednisone 12.5 mg daily, which was further tapered and discontinued over six months.

She experienced a slow but complete resolution of her neurological symptoms after discharge from the hospital. A CT head scan after nine months of treatment showed marked improvement, with only small residual enhancement at the sites of two lesions – one in the posterosuperior right temporal lobe and one in the left parietal lobe. All other lesions had completely resolved, including the one in her posterior fossa. Cotrimoxazole was discontinued after one year of initiating therapy.

Nocardiosis is an uncommon invasive disease caused by aerobic actinomycetes of the *Nocardia* genus. The organism is ubiquitous in nature, and is found in soil and decaying organic matter. It is a thin, branching, filamentous Gram-positive rod, which is also partially acid-fast. It can be grown on most routine culture media, but growth is slow. Infections are environmentally acquired; there is no known person-to-person transmission. Humans are usually infected with *Nocardia* species through the respiratory tract when the organism becomes airborne. Cell-mediated immunity is important in clearing *Nocardia* species from the initial site of infection and preventing dissemination. Consequently, patients with a deficiency of cell-mediated immunity, such as those on chronic steroid therapy, or those with lymphoma or AIDS, are at higher risk for infection (1,2).

The most common site of infection is the lung. Nocardial pneumonia is typically subacute – dyspnea, pleuritic pain and hemoptysis are uncommon. The organism has a propensity for hematogenous spread, most commonly to the central nervous system and soft tissues (1,2). Skin involvement usually occurs following local trauma. The prognosis of disseminated nocardia infection is poor, with fatality rates up to 40% (3).

Given its rarity and diversity of presentations, antimicrobial treatment has been directed by experience, animal models and in vitro studies (4). Most experience in treating nocardiosis has been with sulphonamide-containing therapies. Cotrimoxazole, in doses of 15 mg/kg/day of trimethoprim and 75 mg/kg/day of sulphamethoxazole, is a widely used combination (2). Sulphonamide blood levels may be measured early to ensure desired peak levels of 100 to 150 μg/mL (5), although this assay is not widely available. Many case reports document intolerance to or treatment failures with sulphonamides (6-9). Successful alternative regimens have included imipenem with erythromycin (6), imipenem with amikacin (10), ceftriaxone with amikacin (11) and ofloxacin (12). There have been reports of successful treatment despite the continuation of immunosuppressive therapy (13-15).

Nocardial brain abscess carries a high mortality rate, especially if there are multiple lesions and patients are immunocompromised. In a review of 131 patients with nocardial brain abscesses, the lowest mortality was found to be for those patients who underwent craniotomy and excision (24%) versus aspiration and/or drainage (50%), or antibiotic therapy alone (30%) (16). Cerebellar abscesses are usually treated with surgical drainage (17-21). Prolonged courses of medical therapy are needed in all cases, because nocardial infections tend to relapse. Immunosuppressed patients with pulmonary or systemic nocardiosis are generally treated for one year (1). In human immunodeficiency virus-infected patients, it may be necessary to continue therapy indefinitely. If the disease is unusually extensive or if the response to therapy is slow, treatment duration may also be extended.

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