

Double Trouble: A Case of Concurrent Opportunistic Infections

To the Editor:

Patients with systemic lupus erythematosus (SLE) are at increased risk of infection. We present the case of a patient with SLE who developed concurrent opportunistic infections while receiving immunosuppressive therapy.

A 56-year-old man with a 30-year history of SLE was transferred to our institution from a referring hospital for the evaluation of headaches and change in mental status.

His disease had previously been characterized by polyarthritis, serositis, erythematous malar rash, and nephritis. He had received treatment with cyclophosphamide and azathioprine 10 years prior, and was maintained thereafter with hydroxychloroquine 400 mg PO daily with disease stability. In the 2 years preceding this presentation, he had developed recurrent pleurisy and worsening renal dysfunction, and was thus started on treatment with prednisone 15 mg to 25 mg PO daily along with mycophenolate mofetil 720 mg PO twice daily that he received continuously until his hospitalization.

Prior to a scheduled visit with his rheumatologist, he presented to his local hospital with 10 days of headache. Upon admission to our unit, he was found to have bilateral horizontal diplopia, fever, nonproductive cough, and a pulmonary nodule (Figure 1). On examination, he was hemodynamically stable, but hypoxic (SpO₂ 88%), and had fluctuating levels of alertness. He had findings of increased intracranial pressure (ICP) without meningismus, including bilateral cranial nerve VI palsies and blurred optic disc margins on fundoscopy.

Lumbar puncture demonstrated an elevated opening pressure of 44 cm H₂O, elevated leukocytes of 34 cells/mm³ (lymphocyte predominance), protein 0.46 g/l (normal range 0.2–0.4 g/l), and glucose 0.8 g/l (normal range 0.6–0.8 g/l). Cryptococcal antigen was positive in cerebrospinal fluid (CSF; 1:2048) and blood (1:1024), and cultures of both grew *Cryptococcus neoformans*. The patient's complement levels were within normal limits (C3 1.75 g/l, C4 0.51 g/l), and he demonstrated slightly worsened renal dysfunction with creatinine 184 μmol/l (baseline 150 μmol/l) without change in the severity of proteinuria, consistent with relative quiescence in his SLE disease activity.

Computed tomography (CT) of the head was normal. CT of the chest revealed a 4.6 cm cavitary lung lesion. Bronchoalveolar lavage culture was

negative for *C. neoformans*; however, *Nocardia farcinica* was isolated. Human immunodeficiency virus testing was negative. CSF and blood cultures were negative for *N. farcinica*, as well as for acid-fast bacilli, including *Mycobacterium tuberculosis*.

Treatment was initiated with liposomal amphotericin B 4 mg/kg intravenously (IV) daily and flucytosine 100 mg/kg PO daily as induction therapy for cryptococcal meningitis, followed after 6 weeks by consolidation therapy with fluconazole 600 mg PO daily for 8 weeks, and then maintenance fluconazole 400 mg PO daily. Serial lumbar punctures with CSF drainage were performed for management of elevated ICP. Pulmonary nocardiosis was treated with 20 mg IV trimethoprim-sulfamethoxazole every 6 h, but subsequently changed to meropenem 2 g IV twice daily because of worsening renal function. Mycophenolate was held and prednisone rapidly tapered. The patient's mental status and diplopia improved and the pulmonary lesion resolved. However, he required prolonged hospitalization and eventually died.

Patients with SLE are at increased risk of infection as a result of the disease itself and its treatment. They may develop alterations in complement, cytokine production, and changes to humoral and cell-mediated immunity^{1,2,3}, and opportunistic infections with organisms such as *Pneumocystis*, *Nocardia*, mycobacteria, and fungi are more likely to occur as a result, sometimes concurrently⁴. Central nervous system (CNS) infections pose an additional challenge as their clinical manifestations may be attenuated by immunosuppression, and can also mimic SLE cerebritis^{5,6}.

The incidence of fungal infections in patients with SLE ranges from 0.64% to 1.04% per patient per year in case series, with organisms including *C. neoformans*, *Candida* sp., and *Aspergillus* sp. most commonly identified^{7,8}. Of these, *C. neoformans* accounts for over 50% of invasive fungal infections and can present as isolated pulmonary, CNS, or as disseminated disease. Treatment of severe disease consists of induction therapy with amphotericin B with or without flucytosine, followed by consolidation and maintenance with fluconazole. Management of elevated ICP is an important adjunct to therapy⁹.

The management of *Nocardia* infections is complex and requires prolonged therapy with 1 or more agents, adjusted based on susceptibility testing¹⁰. As with *C. neoformans*, infections with *Nocardia* may present with concurrent pulmonary and CNS involvement.

There are no guidelines regarding the management of immunosuppression in patients with SLE who develop severe infections. In general,

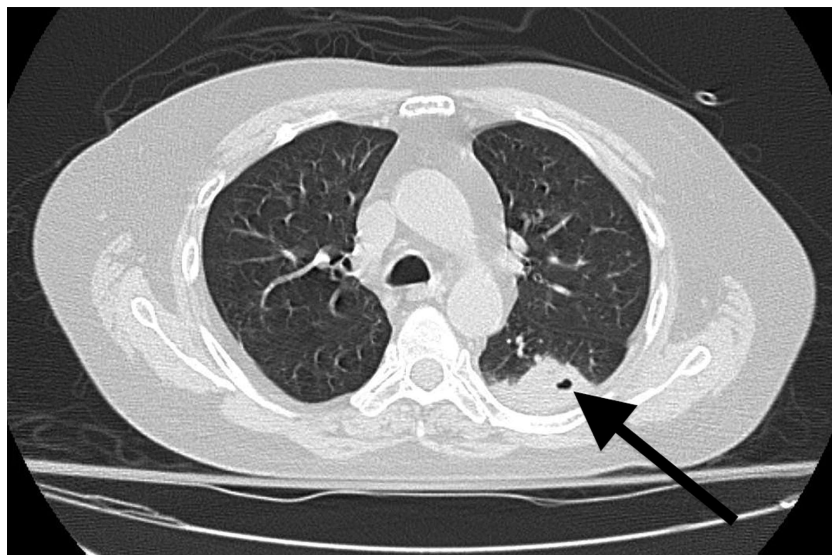


Figure 1. Chest computed tomography demonstrating 4.6 cm cavitary lung lesion (arrow), later identified as *Nocardia farcinica*.

glucocorticoids should be tapered to the minimal dose required for disease control. Decisions regarding additional immunosuppressants must be made on a case-by-case basis.

Opportunistic infections in patients with SLE may be challenging to recognize, but must be considered when patients present with changes in clinical status. In addition, multiple conditions may exist concurrently, even when a single disease may appear to explain the entire clinical picture.

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