Central Nervous System Infections Associated with Immunosuppressive Therapy for Rheumatic Disease

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KEYWORDS

• Central nervous system infection • Immunosuppression
• Immunomodulatory therapy • Rheumatic disease

KEY POINTS

- Rheumatologists should be familiar with central nervous system (CNS) infections associated with immunosuppressive therapy, and changes in neurologic function should be queried at every clinic visit.
- The risk of infection associated with glucocorticoids increases with dose and duration of therapy, and combination regimens likely compound the risk of infection.
- Although few data suggest increased risk of CNS infection from methotrexate, rheumatologists should be familiar with the neurotoxic side effects that can develop.
- Tumor necrosis factor inhibitors increase the risk of granulomatous and bacterial infections and can also cause idiopathic granulomatous or demyelinating reactions.
- Rituximab is associated with rare cases of progressive multifocal leukoencephalopathy; patients should be carefully monitored clinically and clinicians should maintain a high index of suspicion.

INTRODUCTION

The risk of opportunistic infections and pathogens that can cause disease in healthy hosts is heightened in patients with rheumatologic conditions treated with immunosuppressive and immunomodulatory agents.[1] In addition, immune dysregulation

Disclosures: The authors have no disclosures to report.
Funding: This work was supported by NIH/NCATS KL2TR000143 (F.C. Chow).
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Rheum Dis Clin N Am 43 (2017) 607–619
http://dx.doi.org/10.1016/j.rdc.2017.06.009
rheumatic.theclinics.com

associated with underlying rheumatic disease may predispose to infectious complications. Infections of the central nervous system (CNS) are particularly important to recognize given high associated morbidity and mortality and the complexity of distinguishing between CNS infections and neurologic manifestations of rheumatic disease. This article first presents 2 illustrative cases followed by a discussion of a selection of commonly used agents in the treatment of rheumatic disease and the risk of CNS infections associated with their use.

Case 1

A 25-year-old woman with systemic lupus erythematosus (SLE) presented with 3 weeks of headache, photosensitivity, and vomiting. Her SLE had been treated with varying doses of prednisone, up to 50 mg daily, and azathioprine 200 mg daily. Lumbar puncture showed normal opening pressure. She had a moderate lymphocyte-predominant pleocytosis, mildly increased protein, and normal glucose. Cryptococcal antigen was positive in the serum and cerebrospinal fluid (CSF). She was treated with intravenous amphotericin B liposomal and flucytosine followed by oral fluconazole with complete resolution of her symptoms. She has continued on maintenance fluconazole while on immunosuppression for active SLE.

Case 2

A 61-year-old woman with rheumatoid arthritis (RA) presented with headaches, vertigo, and painful paresthesias on the trunk. A brain and spine MRI scan with contrast showed diffuse ring-enhancing lesions (Fig. 1). She had most recently been treated

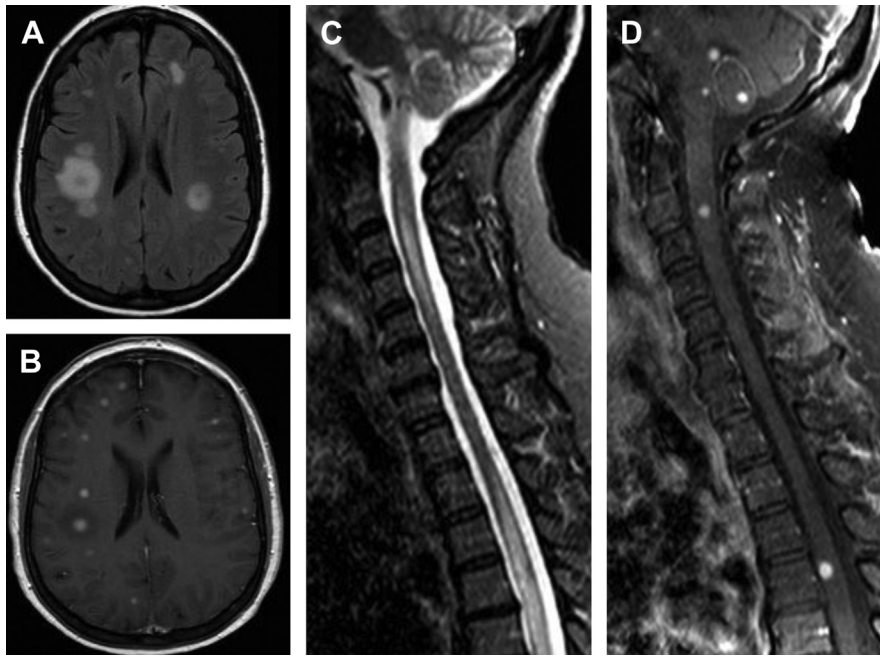

Fig. 1. Histoplasma encephalomyelitis in the setting of prior rituximab and methotrexate use. (*A*) Axial T2-FLAIR (fluid-attenuated inversion recovery) brain MRI, (*B*) axial T1 postcontrast brain MRI, (*C*) midsagittal T2 MRI of the spine, (*D*) axial T1 postcontrast MRI of the spine.