Dear Editor,

A 60-year-old female was admitted to our clinic with fever, headache, weakness, and confusion. Her past medical history was unremarkable other than ulcerative colitis (UC), and she received 4 g/day mesalamine, 100 mg/day azathioprine, and 25 mg/day prednisolone on admission. Because of UC activation 1 month previously, azathioprine and prednisolone were initiated at initial doses of 50 and 40 mg/day, respectively. The prednisolone dose was decreased by 5 mg weekly, whereas the azathioprine dose was increased to 100 mg in the second week. Physical examination revealed that her body temperature was 38.4°C. She had right hemiparesis, neck stiffness, and confusion. Laboratory test results were as follows: hemoglobin level, 10.9 g/dL (11.7–15.5 g/dL); white blood cell (WBC) count, 2×10³/μL (4.1–11.2×10³/μL); platelet count, 125×10³/μL (159–388×10³/μL); neutrophil count, 1.7×10³/μL (1.8–6.4×10³/μL), and C-reactive protein level, 15.8 mg/dL (0–0.3 mg/dL). Liver enzyme and creatinine levels were normal. Magnetic resonance imaging (MRI) findings of the patient were consistent with meningitis. Lumbar puncture was performed, and cell count of the cerebrospinal fluid (CSF) was 600/mm³ WBCs, with 40% neutrophil and abundant erythrocytes. Gram-positive rods were detected in the Gram stain of CSF. Meropenem plus ampicillin was administered to the patient for a central nervous system (CNS) infection. Azathioprine was discontinued, and the prednisolone dose was gradually reduced (5 mg/1–4 day) because of the infection. The control cranial MRI in the second week revealed a left thalamo-mesencephalic abscess (Figure 1).

Listeria monocytogenes (LM) was identified in the CSF culture. Meropenem was switched to gentamicin, and gentamicin plus ampicillin was continued for 1 month. The patient clinically improved, and the control cranial MRI in the sixth week showed a marked improvement of the abscess (Figure 2). She was discharged from the hospital with continuing treatment of 4 g/day mesalamine for UC.

Figure 1. Cranial magnetic resonance image revealing left thalamo-mesencephalic abscess. The lesion is T2 hypointense and T1 hyperintense and has an irregularly contrast-enhanced rim. Diffusion-weighted imaging shows restricted diffusion in the central region of the lesion

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Ulcerative colitis is a prototype of inflammatory bowel disease (IBD) that primarily affects the mucosa of the colon and rectum. Immunosuppressive therapies such as steroids, azathioprine, and anti-tumor necrosis factor (anti-TNF) agents (infliximab and adalimumab) are usually required during the course of the disease, which predispose the host to life-threatening opportunistic infections. It was previously demonstrated that these agents increase the infection risk in IBD with the odds ratios (ORs) of 3.4 (95% CI, 1.8–6.2), 3.1 (95% CI, 1.7–5.5), and 4.4 (95% CI, 1.2–17.1) for corticosteroids, azathioprine/6-mercaptopurine, and infliximab, respectively. The infection risk is higher with a combination of immunosuppressive agents and is the highest in the first 3 months of treatment. An age of >50 years has been reported to be an independent risk factor for opportunistic infections (OR, 3; 95% CI, 1.2–7.2) (1).

Listeria monocytogenes is an opportunistic gram-positive bacterial pathogen that predominantly causes CNS infections in immunocompromised patients (2). CNS infections due to LM have been reported to be extremely rare in UC patients, and almost all cases are related to anti-TNF agents (3-5). Besides anti-TNF agent-related cases, one UC case complicated with LM has been reported in the literature; the case was related to azathioprine therapy (6). The current case is the second reported occurrence that is related to azathioprine therapy. The contributory factor for infection in this case appeared to be the older age of the patient and the combination therapy of azathioprine and prednisolone.

In the literature, various CNS infections due to LM have been reported in UC patients, including meningitis, encephalitis, cerebritis, and brain abscess. Patients generally present with fever, altered mental status, headache, and focal neurological findings (3-6). Culture, Gram stain, cell count, and glucose/protein measurement of CSF; blood cultures; and cranial MRI are used for a definitive diagnosis (2). A combination of antibiotics is used for treating LM. Ampicillin plus gentamicin is the generally preferred combination of antibiotics and others include trimethoprim/sulfamethoxazole, erythromycin, vancomycin, and meropenem (2-4). The differential diagnosis of LM-related CNS infections in UC patients includes aseptic meningitis/meningoencephalitis, lymphocytic encephalomyloneuritis, and other opportunistic agent-associated infections such as Toxoplasma gondii, Cryptococcus neoformans, and Mycobacterium spp. (7-12). The mortality rate of LM-related CNS infections has been reported to be 17%–62%, and LM cerebritis and cerebral abscess have a higher mortality rate than meningitis and meningoencephalitis. However, there are no data regarding the mortality rates in UC patients (2).

In conclusion, LM should be considered in UC patients, particularly elderly ones, with CNS symptoms/findings who are using not only anti-TNF agents but also other immunosuppressive drugs, including azathioprine and corticosteroids, and a combination of immunosuppressive agents.

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