Salmonella Bloodstream Infection Secondary to Treatment with Baricitinib in COVID-19

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TO THE EDITOR,

Coronavirus disease 2019 (COVID-19), first identified in 2019, constitutes a global major public health burden. Most of morbidity and mortality is derived by the severe inflammatory reaction (cytokine release syndrome) that ensues in later stages. Baricitinib, a selective JAK inhibitor primarily used for the treatment of rheumatoid arthritis (RA) [1], was shown to reduce mortality in COVID-19 hospitalized patients in combination with remdesivir [2]. Baricitinib has been associated with a higher risk of infection (especially herpes zoster) and venous thrombosis, both in RA [1] and COVID-19 patients [3]. Arterial thrombosis was also more prevalent in COVID-19 patients receiving baricitinib [3]. Bacterial co-infections in COVID-19 patients treated with baricitinib are mainly mediated by pulmonary and catheter-associated blood stream pathogens [4]. To the best of our knowledge, this is the first case of *Salmonella enterica* bacteremia in an otherwise healthy, baricitinib-treated COVID-19 patient.

A 40-year-old man presented with severe COVID-19 pneumonia several days after exposure to a confirmed COVID-19 case. His past medical history was unremarkable. The patient was unvaccinated for COVID-19. He denied any chronic medications, smoking history, or illicit drug use.

On arrival, oxygen saturation was 87% while breathing ambient air and improved with nasal supplementation of 2 L/min of oxygen. Other vital signs were normal. Chest X-ray indicated diffuse patchy infiltrates consistent with COVID-19 infection. Polymerase chain reaction (PCR) test for COVID-19 was positive. Dexamethasone (6 mg/day) and enoxaparin (40 mg/day) were initiated according to guidelines. Within hours of admission, however, the patient's clinical condition quickly deteriorated, necessitating high flow nasal cannula support (HFNC). He was transferred to the intensive care unit, and baricitinib (4 mg per day) was initiated after human immunodeficiency virus infection was ruled out. Blood culture obtained at this point was negative for bacterial growth. The patient's respiratory condition gradually improved.

Two days after starting baricitinib, the patient developed leukocytosis (up to 26 × 10^9/L), followed by a high-grade fever and rigors. Repeated blood cultures indicated *Salmonella enterica* serovar typhimurium (O:4) bacteremia. He had no gastrointestinal symptoms and no exposure to animals or infected food. Stool culture was negative for Salmonella. He was treated with ceftriaxone for 14 days.

In addition, 7 days into baricitinib treatment, D-Dimer levels increased from 0.37 mg/L at admission to 13.67 mg/L (normal range 0–0.5 mg/L). Computed tomography pulmonary angiogram indicated right lobar pulmonary embolism (PE) and left sub segmental PEs. Enoxaparin dose was increased to 80 mg twice a day. Despite therapeutic anticoagulation, the patient developed acute critical ischemia of his left upper extremity, likely secondary to a prior insertion of an arterial line. Left brachial, radial, and ulnar pulses were absent and doppler confirmed absence of flow at the radial artery. An urgent thrombectomy was recommended but was declined by the patient. Therefore, he was managed conservatively with enoxaparin and iloprost, resulting in gradual clinical improvement.

Although both vascular complications were probably multifactorial, their presence in a healthy, young male suggests association with baricitinib and COVID-19. The combined thrombotic risk merits balancing risk versus benefit when considering baricitinib. We suggest that surveillance of systemic infection and enhanced thrombo-prophylaxis (e.g., with therapeutic dose enoxaparin) be considered in such cases.

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