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Posterior Reversible Encephalopathy Syndrome in a Patient With Crohn's Disease on Infliximab

To the Editor:

Posterior reversible encephalopathy syndrome (PRES) is a rare and somewhat poorly understood clinical syndrome, with endothelial dysfunction resulting in subcortical vasogenic edema as a result of (i) inflammatory cytokines that increase vascular permeability, or (ii) acute changes in blood pressure (BP) that surpasses the upper limit in cerebral autoregulation, resulting in hyperperfusion.¹ PRES usually manifests as seizures, encephalopathy, and in severe cases, acute hemorrhage or obstructive hydrocephalus that can lead to brainstem compression and death. Potential causes of PRES include elevated BP, eclampsia, and preeclampsia, biologics, autoimmune disorders, and infection.² Typical magnetic resonance imaging (MRI) findings include bilateral vasogenic edema in the parietal and occipital subcortical white matter, though it can frequently affect the frontal lobes as well.³

A 24-year-old African American woman presented to our emergency department with severe abdominal and perianal pain, nausea, and vomiting, which were worsening over the last few months.

On examination, she was in moderate distress. She was afebrile, with a BP of 100/68 mm Hg, heart rate of 90 beats/min, and respiratory rate of 20 breaths/min. On abdominal examination, she was diffusely tender to palpation with tenderness in the lower abdominal quadrants and a tender and fluctuant left labia.

Laboratory values at admission showed leukocytosis [white blood cell (WBC) count 18,000/cmm with 82% neutrophils], microcytic anemia (hemoglobin 9.9 g/dL), and hypoalbuminemia (serum albumin 1.9 g/dL). Computed tomography of the abdomen and pelvis showed diffuse circumferential wall thickening of the anorectum, and inflammatory changes in the perineal region with a 4 cm fluid collection.

This presentation was concerning for fistulizing colonic Crohn's disease (CD) with a perirectal abscess; she was admitted and started on intravenous antibiotics. On day 3, a flexible sigmoidoscopy revealed multiple perianal fistulas and showed diffusely erythematous mucosa with increased friability up to the sigmoid colon. Endoscopic biopsies confirmed active CD. On day 6 of admission, the left labial fluid collection was drained. Subsequently, the patient developed bloody bowel movements, causing worsening anemia and tachycardia that required blood transfusions. The vital signs were stable with: BP of 116/72 mm Hg, heart rate of 100 beats/min, and respiratory rate of 18 breaths/min. Her WBC count had decreased to 9500/cmm.

She was started on infliximab with a loading dose of 5 mg/kg. Steroids were held to promote abscess healing. Preinfusion labs revealed an erythrocyte sedimentation rate (ESR) of 30 mm/h and high-sensitivity C-reactive protein (hsCRP) of 29 mg/dL. Her clinical condition and inflammatory markers improved after the initial infusion. However after 5 days, she started reporting worsening perineal pain and rectal bleeding with a rise in ESR to 30 mm/h and hsCRP to 67 mg/dL. Given her symptoms, rising inflammatory markers, and low serum albumin, she was given a second dose of IV infliximab 7 days after the first dose and started on IV methylprednisolone. Her symptoms improved in addition to her labs: ESR 10 mm/h, hsCRP 12.3 mg/dL, hemoglobin 11 g/dL, and WBC 8000/cmm.

After the first infliximab infusion, the patient's BP was 143/98 mm Hg, but after receiving the second infusion, the BP peaked at 185/120 mm Hg. Three days after the second infusion, she developed 2 episodes of generalized tonic clonic seizures. Appropriate treatment was given. Electroencephalogram showed diffuse nonspecific cerebral dysfunction with no epileptiform activity.

Computed tomography angiography of the head and neck showed no infarction or hemorrhage. MRI of the brain revealed scattered T2/FLAIR signal abnormalities in the subcortical white matter of bilaterally predominantly in the frontal and posterior parietal lobes, consistent with PRES.

Her BP improved to a normal range over the following week and she did not have any further seizures. Repeat MRI brain showed improvement in PRES-associated white matter changes.

The patient was discharged 1 week later on an immunomodulator. Biological therapy was discontinued due to its potential association with PRES as either a direct effect or a result of antitumor necrosis factor-induced hypertensive crisis.

Although the presence of CD in these patients may have contributed to the development of PRES, we believe the most significant factors were the presence of infliximab and second dosing within 7 days of the first infusion. Our patient only developed neurological symptoms after her second infusion, which may indicate a dose-dependent adverse effect, with the incidence of PRES increasing as plasma levels of infliximab rise. However, we do not have serum infliximab levels available. As earlier dosing of biologics is becoming a more common practice, it will be interesting if we start to see a rise in similar neurological events.

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The authors declare that they have nothing to disclose.

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DOI: 10.1097/MCG.0000000000000557