Acute Psychosis in an Adolescent Treated With Infliximab for Crohn's Disease

To the Editor: Infliximab is a monoclonal antibody against tumor necrosis factor-α (TNF-α) and has been shown to be 81% more efficacious than placebo in Crohn's disease patients who have had an inadequate response to conventional therapy.[1] While there are case reports of suicide attempts after treatment with infliximab for inflammatory bowel diseases,[2,3] and reports of anti–TNF-α treatment leading to psychosis in elderly patients with rheumatologic disorders,[4] to our knowledge, this is the first case of a pediatric patient with Crohn's disease who developed acute psychosis after treatment with infliximab.

Case report. A 15-year-old white male high school honors student, with a history of Crohn's disease since age 12 years and a history of obsessive-compulsive disorder and attention-deficit disorder, received his first 3 infliximab infusions over a 2-month period for treatment of poorly controlled Crohn's disease. One month after the third infusion, his teacher and parents noticed odd changes in his personality, which included inappropriate verbal outbursts, increased agitation, and defiant behavior over the course of 2 days. He then became verbally threatening and combative with his mother and was brought to the emergency department. In the emergency department, he was seen by psychiatry staff and found to have disorganized thought process with loose associations, echolalia, delusions of thought broadcasting and grandeur, distractibility, and severe psychomotor agitation. He had no history of recreational drug or alcohol use. Extensive workup results were all within normal limits including a head computed tomography scan, brain 3 magnetic resonance imaging, routine electroencephalograph, Lyme Western blot, urinalysis, lumbar puncture, cerebrospinal fluid culture, serum herpes simplex virus polymerase chain reaction, rapid plasma reagin, vitamin B_{12}, folate, thyroid-stimulating hormone, stool culture, stool ova and parasite, and urine toxicology screen.

The patient was started on haloperidol, which was titrated to 1 mg twice a day. Although this tempered his agitation and aggression, his psychosis did not completely resolve, and he experienced an acute dystonic reaction that led to the discontinuation of the medication. He was discharged home but came back in a few days for worsening behavior along with agitation and abusive speech. Treatment with olanzapine titrated to 7.5 mg twice a day resulted in resolution of his psychotic symptoms. However, on the fourth day of olanzapine treatment, a fourth infliximab infusion was administered, and shortly after, he suddenly became agitated and combative and appeared to experience visual hallucinations. The infliximab treatment was terminated, and he was discharged home with outpatient follow-up. At present, olanzapine has also been discontinued. He attends weekly group therapy at an outpatient facility and has returned to his normal mental status.

Given the timing of his initial presenting symptoms within the 3 months of his initial infliximab infusions and the immediate relapse of psychotic symptoms after his fourth infliximab infusion, we believe that the patient's psychosis is best explained by a psychotic reaction to infliximab. He was consistently psychotic with no fluctuations of consciousness to suggest coincidental delirium, and no substance-induced cause was identified.

It is interesting to note that his psychosis responded better to an atypical neuroleptic compared to a typical one. There is evidence that atypical neuroleptics inhibit activated microglia release of proinflammatory cytokines, especially nitric oxide and TNF-α.[5] Anti–TNF-α therapy has numerous well-recognized adverse events, such as infection and malignancy. However, there is very little information in the literature pertaining to psychiatric side effects.

We suggest that patients treated with infliximab for Crohn's disease could experience an acute psychosis. Treatment with an atypical antipsychotic may be considered over the typical antipsychotics. However, more controlled prospective studies are required to confirm our suspicion of causality between infliximab and psychosis to guide treatment.

References

1. Targan SR, Hanauer SB, van Deventer SJ, et al A short-term study of chimeric monoclonal antibody cA2 to tumor necrosis factor alpha for Crohn's disease: Crohn's Disease cA2 Study Group. *N Engl J Med*. 1997;337(15):1029–1035.
2. Eshuis EJ, Magnin KMMY, Stokkers PCF, et al. Suicide attempt in ulcerative colitis patient after 4 months of infliximab therapy: a case report. *J Crohn's Colitis*. 2010;4(5):591–593.
3. Fidder H, Schnitzler F, Ferrante M, et al. Long-term safety of infliximab for the treatment of inflammatory bowel disease: a single-center cohort study. *Gut*. 2009;58(4):501–508.
4. McGregor L, Saunders SA, Hunter JA, et al. Acute psychosis in three patients receiving anti-tumor necrosis factor-α therapy. *Rheumatology (Oxford)*. 2008;47(8):1254–1255.
5. Bian Q, Kato T, Monji A, et al. The effect of atypical antipsychotics, perospirone, ziprasidone and quetiapine on microglial activation induced by interferon-gamma. *Prog Neuropsychopharmacol Biol Psychiatry*. 2008;32(1):42–48.

Michael R. Locher, BS
Abdulkader Alam, MD
al.alam@stonybrookmedicine.edu

Author affiliations: Departments of Psychiatry and Internal Medicine (Dr Alam), Stony Brook School of Medicine (Mr Locher), Stony Brook, New York.

Potential conflicts of interest: None reported.

Funding/support: None reported.

Published online: July 30, 2015.

Prim Care Companion CNS Disord 2015;17(4):doi:10.4088/PCC.15l01781