Elevated Serum IgE Prior to Acute Severe Infusion Reaction During Infliximab Maintenance Therapy in a Crohn’s Disease Patient

To the Editor:

Intercepting tumor necrosis factor alpha (TNF-α) by antibodies to this cytokine, such as infliximab (IFX) and adalimumab, is currently the best hope for improving the treatment of patients with Crohn’s disease (CD). However, formation of antibodies to IFX (ATI), episodes of infusion reaction (IR), as well as the loss of response to the currently available anti-TNF-α biologics by a significant fraction of patients are serious issues that limit the efficacy and safety of anti-TNF-α therapy. Accordingly, identification of a marker that can predict an IR episode is desirable. A 42-year-old male patient was referred to our hospital with symptoms including diarrhea, abdominal pain, and weight loss together with polyarticular arthropathy. He was diagnosed with colonic CD based on endoscopic findings, showing large longitudinal ulcers and classic cobblestone patterns in the colon without small bowel involvement. His arthritis was judged to be a type 2 polyarticular extraintestinal manifestation without joint destruction, seronegative for rheumatoid factor.

The first therapeutic regimen for this patient in our hospital was oral prednisolone (PSL, 10 mg/day), oral mesalamine (5-ASA, 1500 mg/day), and methotrexate (16 mg/week). Two months later, methotrexate was withdrawn due to nausea and was switched to azathioprine (AZA, 50 mg/day). However, his CD Activity Index (CDAI) and disease activity score (DAS28-4) for arthritis were 160 and 4.75, respectively. With these medications, neither the patient’s colonic lesions nor joint symptoms reached the remission stage.

Subsequently, medication with IFX (5 mg/kg/day) was initiated together with 100 mg intravenous hydrocortisone and 50 mg intramuscular promethazine, administered 30 minutes before every scheduled IFX infusion (as a prophylactic measure). His CDAI and joint symptoms improved markedly (Fig. 1A). IFX infusion at 8-week intervals was continued as maintenance therapy in this patient. Twenty-one months after initiating IFX therapy the patient developed an acute severe IR and his blood pressure fell to below 90/60 mmHg, together with pallor, breathing difficulties, and hypoxemia (indicated by a dotted line in Fig. 1A). We decided to cease IFX therapy due to this severe IR. Additionally, AZA was discontinued due to nausea after 22 months. The patient worsened with an increase in stool frequency and swollen/tender joint counts. We tried induction therapy with adalimumab at 24 months but the patient developed injection site reactions consisting of edema, erythema, and pruritus at the second adalimumab infusion and adalimumab was discontinued. Although the patient did not have any recorded history of allergic reactions such as pollinosis, he showed hypersensitivity reactions to both anti-TNF-α biologics.

We decided to look for serum factors potentially related to the infusion reaction. Stored sera at time 0 (patient naïve for IFX), 19 months (8 weeks before IR), 21 months (the day of severe IR), and 29 months (8 months after the cessation of IFX due to IR) were prepared for the measurement of IFX according to a new fluid-phase enzyme immunoassay. In the same test samples, ATI was assayed by a double-antigen enzyme-linked immunosorbent assay. The ATI titer increased to 1:128 by 19 months and became negative 29 months after the last IFX infusion. The CDAI and DAS28-4 were 100 and 4.4, respectively.

FIGURE 1. (A) Time course of disease activity scores, ATI, and serum IgE obtained before and after severe infusion reaction to IFX. CDAI <150, remission; DAS 28-4 <2.3, remission; ATI >1.69 μg/mL, positive; IgE <408 ng/mL, normal. (B) Changes in CDAI and DAS 28-4 following GMA therapy.

Copyright © 2011 Crohn's & Colitis Foundation of America, Inc.
DOI: 10.1002/ibd.21157
Published online 2 September 2011 in Wiley Online Library (wileyonlinelibrary.com).

E156
Inflamm Bowel Dis • Volume 17, Number 12, December 2011