LETTER TO THE EDITOR

Immune-mediated colitis: Important to recognize and treat

Dear Sir,

Adverse effects related to biologic monoclonal antibodies are common; potentially life threatening and can involve almost every organ. Ipilimumab, a cytotoxic T-lymphocyte-associated-antigen-4-antagonist (CTLA-4), has been approved for treatment of advanced melanoma. We report a case of ipilimumab immune-mediated side effects involving multiple organ systems (pancolitis, hypophysitis), simultaneously.

A 73-year-old man with metastatic melanoma involving the spine was treated with ipilimumab (Yervoy®) every three weeks. After the third cycle he developed fatigue, anorexia, and watery, non-bloody diarrhea (5–8 stools/24 h). He was diagnosed with ipilimumab immune-mediated hypophysitis leading to panhypopituitarism with hypothyroidism and adrenal insufficiency. Therapy with oral prednisone (60 mg twice daily) and replacement of thyroid hormones and testosterone was initiated. Fatigue and anorexia were resolved quickly; he continued to have mild diarrhea. Prednisone was tapered at 50% increments weekly. Two weeks later he presented with severe bloody diarrhea (10–15 stools/24 h). Comprehensive infectious work up and computed tomography of the abdomen and pelvis were unrevealing. Colonoscopy showed severe edema, erythema, friability, and deep ulcerations throughout the colon (Fig. 1). Microscopic pathology demonstrated patchy areas with increased neutrophils and lymphocytes within the lamina propria and scattered ulcers (Fig. 1). Treatment with methylprednisolone (150 mg twice daily) intravenously and hydrocortisone enemas were started. As diarrhea continued after 3 days infliximab (5 mg/kg) intravenously was administered with dramatic improvement of diarrhea after one dose. The patient was discharged on a slow steroid taper and infliximab infusions every two weeks (total of six infusions) with no recurrence of diarrhea. The patient died of progressive melanoma six months later.

Immune-mediated colitis occurs at a median onset of 6–7 weeks and can be rapid. The reported incidence is about 3–21% for grades 1–2 colitis and 5–17% for grades 3–4 colitis, respectively. Infections need to be ruled out. Colonoscopy should be considered for persistent or severe symptoms. The histological appearance in drug-induced, immune-mediated colitis is non-specific, not concordant

with inflammatory bowel diseases and features of chronicity are lacking.

In summary, immune-mediated colitis can occur rapidly. Mild to moderate diarrhea should be treated early with steroids over a prolonged period of time with a slow taper (30–45 days). Severe diarrhea should be treated immediately with high dose of intravenous steroids, adding infliximab if no improvement after 5–7 days. In cases of severe toxicity or multiple organ systems' involvement intravenous steroids and/or infliximab should be considered as the initial treatment. Many questions regarding immune-mediated colitis remain unanswered. No predictive marker for the occurrence of gastrointestinal toxicity related to ipilimumab or similar monoclonal antibodies has been validated, yet. Management specifically modes of administration and dosage of steroids is not clearly defined. Infliximab should be considered but we don't know how it may possibly impact the evolution of the cancer being treated.

Conflict of interest

No conflict of interest for all authors.

FURTHER READING


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13 September 2013

1873-9946/$ - see front matter. Published by Elsevier B.V. on behalf of European Crohn's and Colitis Organisation.

http://dx.doi.org/10.1016/j.crohns.2013.09.019
Figure 1  Deep ulceration as well as severe edema and friable mucosa throughout the entire colon. H&E stain with increased numbers of neutrophils and lymphocytes within the lamina propria and scattered inflammatory cells within the colonic epithelium with foci of ulceration.