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CASE REPORT

Diarrhoea in a patient with metastatic melanoma: Ipilimumab ileocolitis treated with infliximab

Rob ME Slangen, Alfonsus JM van den Eertwegh, Adriaan A van Bodegraven, Nanne KH de Boer

Rob ME Slangen, Department of Gastroenterology and Hepatology, HagaZiekenhuis, 2545 CH Den Haag, The Netherlands
Alfonsus JM van den Eertwegh, Department of Medical Oncology, VU University Medical Centre, 1007 MB Amsterdam, The Netherlands
Adriaan A van Bodegraven, Nanne KH de Boer, Department of Gastroenterology and Hepatology, VU University Medical Centre, 1007 MB Amsterdam, The Netherlands
Author contributions: Slangen RME wrote the manuscript and was involved in the medical treatment of the ipilimumab ileocolitis as a consulting doctor of the Gastroenterology and Hepatology department; van den Eertwegh AJM was the treating Medical Oncologist and critically reviewed the manuscript; van Bodegraven AA and de Boer NKH performed the colonoscopy and critically reviewed the manuscript; all authors approved the final version of the manuscript.
Correspondence to: Nanne KH de Boer, MD, PhD, Department of Gastroenterology and Hepatology, VU University Medical Center, PO Box 7057, 1007 MB Amsterdam, The Netherlands. khn.deboer@vumc.nl
Telephone: +31-20-4440613 Fax: +31-20-4440554
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Abstract

Administration of ipilimumab, a cytotoxic T-lymphocyte associated antigen-4-blocking monoclonal antibody, leads to enhancement of the anti-tumor T-cell respons and as a result shows a significant survival benefit in metastatic melanoma patients. Therefore patients are currently receiving this promising therapy as a second-line strategy. Unfortunately, by activation of the T-cell immune reponse, ipilimumab therapy may lead to an unwanted induction of different autoimmune phenomena. Diarrhoea and colitis occur in up to one third of patients. Here we present a case of ipilimumab induced ileocolitis which was successfully treated with infliximab, an anti-tumor necrosis factor monoclonal antibody, after corticosteroid therapy failure. Although formal trials are lacking, recently publicated series suggest that infusional therapy of infliximab is effective in ipilimumab induced ileocolitis.

Key words: Melanoma; Ipilimumab; Colitis; Infliximab; Cytotoxic T-lymphocyte associated antigen-4

Core tip: This paper presents a case of ipilimumab induced ileocolitis which was successfully treated with infliximab, an anti-tumor necrosis factor monoclonal antibody, after corticosteroid therapy failure. Although formal trials are lacking, recently publicated series suggest that infusional therapy of infliximab is effective in ipilimumab induced ileocolitis.

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INTRODUCTION

Ipilimumab administration has shown a survival benefit in metastatic melanoma patients, therefore more patients are likely to receive this therapy as a second-line treatment. Unfortunately, ipilimumab therapy may lead to an unwanted induction of autoimmune phenomena. Here we present a case of ipilimumab induced ileocolitis successfully treated with infliximab after corticosteroid therapy failure.

CASE REPORT

A 53-year-old man with a medical history of metastatic melanoma (metastasized to lungs, lymph nodes and peri-

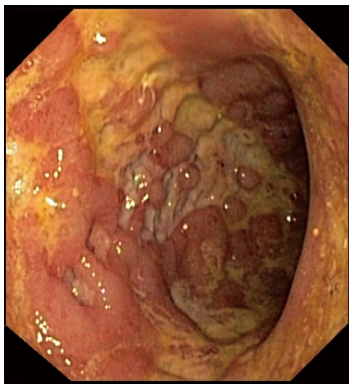

Figure 1 Deep ulcerations in the colon (endoscopic image).

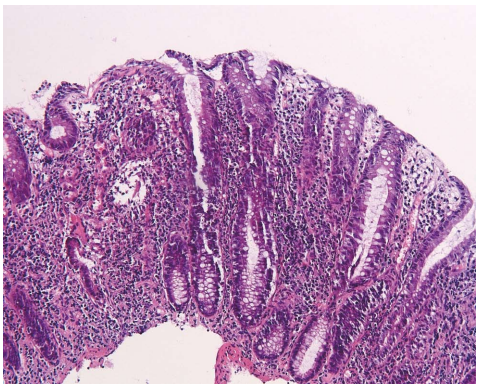

Figure 2 Histopathology of colon biopsies (hematoxylin and eosin staining, × 10).

cardium), was presented at our endoscopy ward because of highly frequent, non-bloody diarrhoea without fever. His medication consisted of morphinomimetics and haloperidol. Four weeks earlier, he started with ipilimumab (3 mg/kg body weight), a fully humanized IgG antibody against the Cytotoxic T-lymphocyte associated Antigen-4 (CTLA-4), of which he had received two administrations. His diarrhoeal complaints had started one week after the second infusion. Routine stool cultures, including *Clostridium difficile*, were negative. A colonoscopy was performed, which showed a patchy colitis with deep, confluent Crohn-like ulcerations (Figure 1). Histopathological examination demonstrated a severe cryptitis with a few abscesses. No granulomas or architectural changes were seen (Figure 2). Furthermore, cytomegalovirus infection was excluded. A computed tomography-scan was performed, showing diffuse thickening of the wall of the entire colon and terminal ileum. A diagnosis of ileocolitis associated with anti-CTLA-4 treatment was made. Our patient was treated with prednisolon (1 mg/kg) for 10 d without beneficial clinical effect. For that reason, intravenous infliximab therapy was initiated (a chimeric IgG antibody against tumour necrosis factor-α) in a dosage of 5 mg/kg body weight (at week 0 and 2)[1,2], after two administrations his diarrhoeal complaints resolved completely.

DISCUSSION

Two recent studies demonstrated that ipilimumab therapy improves survival of patients with metastatic melanoma[1,2]. Unfortunately, blocking of CTLA-4 by ipilimumab[3], may lead to an induction of a variety of autoimmune phenomena. This may comprise inflammation of the gastrointestinal tract, leading to diarrhoea and colitis being reported in up to 31% of patients[1].

As ipilimumab administration has shown a survival benefit in metastatic melanoma patients[1,2], more patients are likely to receive this therapy as a second-line treatment. Moreover, trials of ipilimumab are ongoing in metastatic non-small cell lung cancer[4] and in castration-resistant metastatic prostate cancer patients[5]. Therefore, it is to be expected that ipilimumab induced colitis will be encountered more often.

So far, by clinical judgement, corticosteroids are most often prescribed as a first-line treatment for ipilimumab induced colitis. In prednison-refractory cases, infliximab has shown to be an effective second line treatment[6-9]. The beneficial administration of infliximab in these patients is underlined by our case.

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