Case Report

Hypertension as a rare adverse effect caused by infliximab in the treatment of Crohn's disease: a case report

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Background: Infliximab is an effective drug for the treatment of Crohn's disease. As a rare and unique adverse effect of infliximab, hypertension should be paid enough attention in clinical work. At present, there is no relevant case report. We report a case of a 38-year-old man with Crohn's disease who had no history of hypertension and developed hypertension symptoms during infliximab treatment.

Case Description: The patient was treated with 5 mg/kg infliximab on August 27, 2020. From August 27, 2020 to October 20, 2020, the patient underwent 3 treatment sessions. After each injection of infliximab, the patient's blood pressure became elevated, accompanied by dizziness and symmetrical numbness of both lower limbs. Amlodipine benazepril tablets were given orally to control blood pressure. Under close monitoring, 5 mg/kg infliximab was used again. After 10 min of infusion, blood pressure rose to 160/118 mmHg. Infusion was discontinued immediately, after which blood pressure decreased to normal. Adrenal computed tomography did not indicate adrenal hyperplasia or space occupying lesions, and the detection of hypertension related indicators in standing and supine position was abnormal. Since follow up, the patient has stopped using infliximab and has had no hypertension-related symptoms, even without antihypertensives. Measured blood pressure was within the normal range.

Conclusions: Hypertension, as one of the rare adverse reactions of infliximab in the treatment of Crohn's disease, should be paid enough attention.

Keywords: Infliximab; Crohn's disease (CD); hypertension; case report

Submitted Jun 16, 2022. Accepted for publication Jul 26, 2022.
doi: 10.21037/apm-22-807
View this article at: https://dx.doi.org/10.21037/apm-22-807

Introduction

Antitumor necrosis factor drugs were the first biologic agents approved for the treatment of Crohn's disease (CD). Infliximab is a monoclonal antibody against tumor necrosis factor (TNF), which has completely changed the treatment of CD. It is effective in improving clinical symptoms and promoting endoscopic healing (1). In terms of pharmacological action, infliximab can inhibit the combination of TNF and its receptor, so that TNF loses its biological activity, thereby reducing the infiltration of inflammatory cells into the intestinal lesions. The common adverse reactions of infliximab in clinical application include infection, heart failure and so on. However, hypertension can be a rare but potential side-effect of the infliximab. We report a case of a 38-year-old man with CD who had no history of hypertension and developed hypertension symptoms during infliximab treatment. This case can remind us that we need to pay attention to the changes of blood pressure and be prepared for sudden hypertension during the treatment of Crohn's disease with infliximab. We

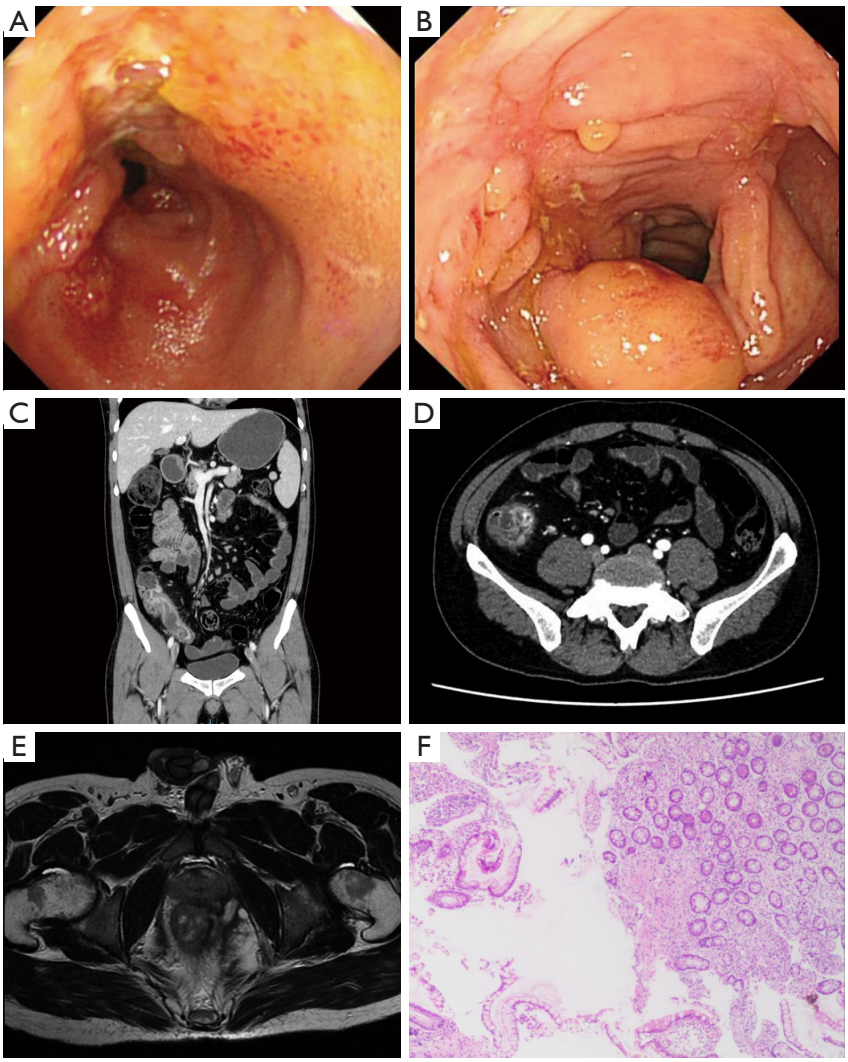

Figure 1 Imaging information for auxiliary diagnosis. (A) Longitudinal ulcer of terminal ileum. (B) Longitudinal ulcer of proximal ileocecal valve of ascending colon. (C,D) Segmental thickening of small intestine, terminal ileum, and ileocecal part in groups 4–6. (E) High complex sphincter external anal fistula with local abscess formation, right posterior anal canal low sphincter internal fistula with abscess formation, fistula local communication with each other; left anal canal low sphincter anal fistula; inflammatory changes of anal canal. (F) Multisegment mucosal biopsy showing local erosion of mucosa with infiltration of a large number of lymphocytes, plasma cells, and neutrophils; disordered and expanded crypts; regeneration and repair of glands; proliferation of lymphoid tissue in submucosa; accumulation of tissue cells and individual multinucleated giant cells; and uneven distribution of inflammation (HE, ×40). HE, hematoxylin and eosin.

present the following article in accordance with the CARE reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-22-807/rc).

Case presentation

The patient had repeated perianal pain for 4 years, and in April 2008, he was admitted to the Sixth Affiliated Hospital of Sun Yat-sen University due to perianal pain with rupture of a lesion, ulceration, and pus. He was diagnosed with anal fistula and was treated with thread-hanging therapy. The perianal pain reoccurred following operation. In August 2020, the symptoms of perianal distension and pain worsened, and he was rehospitalized. Following examination, CD was definitively diagnosed, as shown in *Figure 1*. The patient had no history of hypertension.

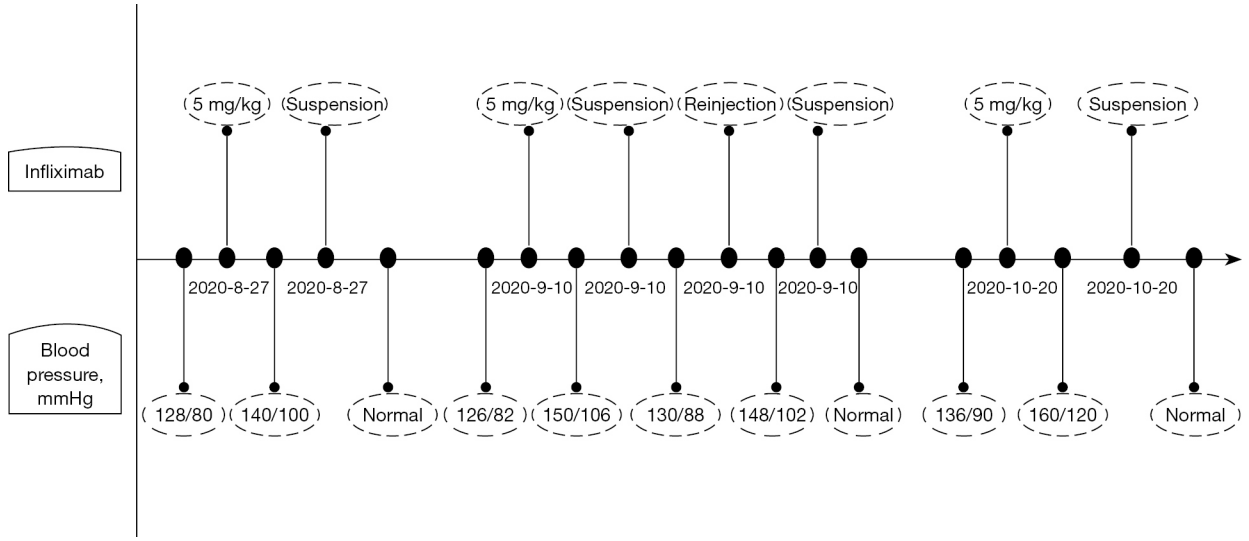

Figure 2 Infliximab therapy. Blood pressure changes.

Infliximab (5 mg/kg) was selected for treatment on August 27, 2020. From August 27, 2020 to October 20, 2020, the patient underwent 3 treatment sessions. After each injection of infliximab, the patient's blood pressure became elevated, as shown in *Figure 2*. Symptomatically, the patient developed hypertension with dizziness and symmetrical numbness of both lower limbs. The relevant inspection results are shown below: the (standing) aldosterone/renin ratio (ARR) value was 119.61 (reference value: 0–30), the (recumbent) ARR value was 148.13 (reference value: 0–30); 17-hydroxycorticosteroid: 3.1 mg/24 h (reference value: 2.0–10.0); 17-ketosterol: 6.5 mg/24 h (reference value: 6.0–25.0); Urine vanillic mandelic acid: 2.6 mg/24 h (reference value: ≤12.0); Adrenocorticotropic hormone (ACTH) + cortisol: 0 am, 8 am, 4 pm were normal; The level of potassium ion in blood is always normal; Color Doppler ultrasound of bilateral renal arteries showed that the blood flow parameters of bilateral renal arteries were normal. Adrenal computed tomography showed no adrenal hyperplasia or space-occupying lesions.

Amlodipine benazepril tablets were given orally to control blood pressure. Blood pressure was stable between 110–120 and 65–78 mmHg. Under close monitoring, 5 mg/kg infliximab was used again. After 10 min of infusion, blood pressure increased to 160/118 mmHg. Infusion was discontinued immediately, after which blood pressure decreased to normal. Since follow-up, the patient has stopped using infliximab and has had no hypertension-related symptoms, even without antihypertensives. The measured blood pressure was within the normal range. All procedures performed in this study were in accordance with the ethical standards of the institutional and national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

Antitumor necrosis factor drugs were the first biologic agents approved for the treatment of CD. Infliximab is a monoclonal antibody against TNF, which has completely changed the treatment of CD (2). It is effective in improving clinical symptoms and promoting endoscopic healing, but it also has some side-effects, including allergic reaction, increased risk of infection, tumors (e.g., lymphoma), and autoimmune diseases (e.g., psoriasis and systemic lupus erythematosus). Hypertension is a rare but potential side-effect of the infliximab (3).

Here, we present a rare case requiring withdrawal of infliximab due to severe hypertension in a patient with CD. Infliximab's hypertension-inducing mechanism is unclear. Blood pressure is regulated by the renin–angiotensin system, in which angiotensin-converting enzyme (ACE) plays a central role. It has been reported that ACE is negatively regulated by TNF in human endothelial cells (4). As a monoclonal antibody against TNF, infliximab can

positively regulate ACE by inhibiting its expression and changing renin and aldosterone secretion, therefore inducing an increase in blood pressure. Our patient was managed using infliximab, which activates the renin-angiotensin system and changes the secretion of aldosterone and renin, therefore inducing hypertension. To the best of our knowledge, there are no similar reports on infliximab withdrawal due to severe hypertension.

If infliximab is used in the treatment of CD, medical staff should pay attention to changes in blood pressure.

Conclusions

Infliximab can regulate ACE by changing renin and aldosterone secretion, therefore inducing an increase in blood pressure. However, the mechanism warrants further exploration.

Acknowledgments

Funding: This work was supported by the 13th Zhaoyang Talent Project of Guangdong Provincial Hospital of Traditional Chinese Medicine (No. 2Y2022YL29) and the Special Project of Science and Technology Innovation Strategy of Guangdong Province (No. pdjh2021b0123).

Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://apm.amegroups.com/article/view/10.21037/apm-22-807/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://apm.amegroups.com/article/view/10.21037/apm-22-807/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

References

1. Vande Casteele N, Feagan BG, Wolf DC, et al. Therapeutic Drug Monitoring of Tumor Necrosis Factor Antagonists in Crohn Disease: A Theoretical Construct to Apply Pharmacokinetics and Guidelines to Clinical Practice. Inflamm Bowel Dis 2021;27:1346-55.
2. Peyrin-Biroulet L, Sandborn WJ, Panaccione R, et al. Tumour necrosis factor inhibitors in inflammatory bowel disease: the story continues. Therap Adv Gastroenterol 2021;14:17562848211059954.
3. Uyanikoglu A, Ermis F, Akyuz F, et al. Infliximab in inflammatory bowel disease: attention to adverse events. Eur Rev Med Pharmacol Sci 2014;18:2337-42.
4. Mudersbach T, Siuda D, Kohlstedt K, et al. Epigenetic control of the angiotensin-converting enzyme in endothelial cells during inflammation. PLoS One 2019;14:e0216218.

Cite this article as: Zhao X, Mo J, Zhang B, Tang J. Hypertension as a rare adverse effect caused by infliximab in the treatment of Crohn's disease: a case report. Ann Palliat Med 2022;11(9):3001-3004. doi: 10.21037/apm-22-807