Annals of Clinical and Medical Case Reports[R] ISSN 2639-8109 | Volume 16

Case Report Open Access

Upadacitinib-Induced Drug Fever – A Report of Two Cases

Zelinkova Zuzana[1-3*], Vanova Andrea[1], Mikus Peter[3] and Kadleckova Barbora[1]

[1]Department of Gastroenterology, Nemocnica Bory-Penta Hospitals a.s., Bratislava, Slovakia

[2]2nd Department of Internal Medicine at University Hospital and Faculty of Medicine, Palacký University in Olomouc, Czech Republic

[3]Department of Pharmaceutical Analysis and Nuclear Pharmacy and Toxicological and Antidoping Center, Comenius University, Bratislava, Slovakia

***Corresponding author:**

Zelinkova Zuzana,
Department of Gastroenterology, Nemocnica Bory-Penta Hospitals a.s., Bratislava, Slovakia and Department of Pharmaceutical Analysis and Nuclear Pharmacy and Toxicological and Antidoping Centre, Comenius University, Bratislava, Slovakia

Received: 20 July 2026
Accepted: 29 July 2026
Published: 02 Aug 2026
J Short Name: ACMCR

Citation:

Zelinkova Zuzana, Upadacitinib-Induced Drug Fever – A Report of Two Cases. Ann Clin Med Case Rep® 2026; V16(3): 1-3

1. Abstract

We report here two cases of drug-induced fever in Crohn` s disease (CD) patients treated with Upadacitinib (UPA). The first case is a 34-years old woman treated with UPA for her colonic CD. Fever appeared at the second day of treatment, had no other accompanying symptoms and persisted for two weeks of treatment. Infectious cause was not found and fever resolved only after stopping the treatment together with the treatment with systemic corticosteroids. Upon rechallenge with UPA, fever reappeared. The second case concerns a 19-years old man treated with UPA for his colonic CD. He developed fever after one week of treatment with no alternative explanation and resolution of fever upon stopping the treatment. Drug-induced fever is an underrecognized condition, can occur to any drug and may be difficult to be discriminated from underlying disease activity. With the expanding use of UPA in the field of various autoimmune disorders, the physicians should be alert to rule out this condition in a patient with otherwise unexplained fever occurring during this treatment.

2. Introduction

Drug-induced fever is relatively common condition often goes undiagnosed [1]. It refers to isolated otherwise unexplained fever that occurs in temporal relationship with the use of drug and resolves after stopping the drug [2]. Drug-induced fever can occur to any drug and may be difficult to be discriminated from underlying disease activity. From drugs used in IBD treatment, cases of drug-induced fever have been described for thiopurines [2-5] sulphasalazine [6] and mesalamine [7], biologics have not been reported to be associated with isolated drug-induced fever. In this short report, based on two cases of patients developing fever after having started Upadacitinib, we would like to draw the attention to the possibility of drug-induced fever in this situation.

3. Case Description

3.1. Case 1

A 34-years old woman with a history of upper gastrointestinal, ileocolic and perianal Crohn´s disease (CD) with stenosing and penetrating behaviour started treatment with Upadacitinib (UPA), 45mg a day for her severely active luminal colonic disease. She had been suffering from CD for 17 years, had experienced secondary loss of response to antiTNF biologics as well as Ustekinumab and a primary non response to vedolizumab.

The second day of treatment with UPA she started to have increased temperature to 37,5°C, and within 3 to 4 days, she developed fever up to 39°C, without any other complains except for stable abdominal symptoms of her luminal CD, i.e. diarrhoea and abdominal cramps. The fever was persistent during the whole first week of treatment, with decline after paracetamol. Her physical exam was unremarkable, abdominal ultrasound was normal except for colonic bowel wall thickening which was her stable finding. Laboratory results showed mild leucocytosis (13,3x109/L) with increased neutrophils (8,7x109/L), mild anaemia (haemoglobin 113g/L), thrombocytosis (741x109/L), and increased C-reactive protein (CRP - 45,3mg/L). After a week of UPA with fever, the treatment was interrupted but the fever was ongoing for subsequent four days when a revaluation took place. At that point again, clinical examination revealed no abnormalities, she had neutrophilic leucocytosis and further increase in CRP (118,9mg/L). No infectious source could have been detected – she had negative stool cultures including C. difficile toxin, PCR was negative for EBV/CMV systemic viremia, chest X-ray was normal as well as urinary analysis, abdominal

CT scan showed pancolitis without other abnormal findings, especially no free fluid or fluid collection. With suspected ongoing CD activity as the reason for fever, antibiotics (ciprofloxacin and metronidazole) together with systemic corticosteroids were started, UPA remained paused. Within two days, the fever resolved and inflammatory parameters decreased. Corticosteroids and antibiotics were stopped after five days and she restarted the treatment with UPA with the reappearance of fever up to 38°C at the second day of the use of UPA. The fever resolved after stopping UPA and restart of systemic corticosteroids (Figure 1). With no other treatment options available at that time, she was scheduled for subtotal colectomy with ileo-recto anastomosis that was performed four months later. During these four months, she had stable mild increase CRP between 30-50 mg/L, with no leucocytosis and no fever.

Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
Upadacitinib																						
Prednison																						
Antibiotics																						
Fever																						
C-reactive protein (mg/L)	67,7							45,3		118,9						40,5						27
Total leucocytes count (x10^9/L)	10,3							13,3								10,4						19
Absolute neutrophils count (x10^9/L)	7,5							8,7								6,65						17

Figure 1: Evolution of fever in temporal relationship with treatment and laboratory inflammatory parameters – patient 1. Fever (body temperature above 38,5°C) appeared at second day of treatment with Upadacitinib and resolved only after stopping Upadacitinib and with treatment of systemic corticosteroids; same pattern was repeated at rechallenge with Upadacitinib.

Day	-1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
Upadacitinib																							
Prednison																							
Fever																							
C-reactive protein (mg/L)	45,6								48,1											61,1			43,1
Total leucocytes count (x10^9/L)	7,45								9,91											12,4			10,5
Absolute neutrophils count (x10^9/L)	4,9								6,47											9,3			7,79

Figure 2: Evolution of fever in temporal relationship with treatment and laboratory inflammatory parameters – patient 2. The patient developed fever (body temperature above 38°C) after one week of treatment with Upadacitinib, together with neutrophilic leucocytosis and increase of C-reactive protein; fever resolved within one day after stopping Upadacitinib.

3.2. Case 2

A 19-years old man with colonic CD, non-penetrating, non-stenosing behaviour started UPA as a second line treatment after infliximab to which he had been primary non-responder. After two weeks of treatment with UPA, he presented at the emergency department with fever, loss of appetite and general malaise, no localizing symptoms. The fever was rising up to 38,5°C and started after one week of treatment with UPA, his abdominal complains slightly improved with decreased stool frequency from 10 to 5 bowel movements a day, without blood and cramps. The clinical exam was normal, laboratory exam showed mild neutrophilic leucocytosis (12,35x109/L) and increased CRP (61 mg/L compared to levels around 10 prior to the treatment with UPA) (Figure 2), no other abnormalities were found (normal liver enzymes, normal kidney function and urinary exam; stool cultures including C. difficile toxin were negative). On abdominal ultrasound, no abnormalities were found except for stable image of colonic bowel wall thickening with increased vascularization. Flexible recto-sigmoidoscopy showed severe CD activity with large ulcerations and mucosal fragility. He was admitted to the hospital, UPA was stopped with the resolution of fever the next. Systemic corticosteroids were started which led to rapid disappearance of fever and gradual improvement of his colitis symptoms. Hereafter, he started the treatment with mavrilimumab with good clinical response allowing steroids detraction.

4. Conclusion

Drug-induced fever is an underrecognized condition 1, especially when occurring during the treatment of diseases where, as it is the case of inflammatory bowel disease (IBD), fever can be a symptom of activity of the underlying disease. Thus, after exclusion of infectious ethology of fever in these patients, the clinical dilemma between drug-induced fever and disease activity remains.

We present here two cases of young patients with IBD who both developed fever in a temporary relationship to the start of treatment with UPA. In both patients, the ongoing disease activity represented alternative explanation for fever and prompted the start of systemic corticosteroids which both interfered with definitive diagnostic of drug-induced fever. In detailed analysis of the previous and subsequent clinical evolution of the disease, however, neither of the two patients had fever as accompanying symptom of disease activity, nor the neutrophilic leucocytosis and the observed magnitude of CRP during their use of UPA exceeded their CRP levels during past flares. In addition, the first patient had a clear reappearance of fever after re-exposure to the drug. Thus, Upadacitinib-induced fever is the most plausible diagnostic explanation in these patients.

To our knowledge, these are the first reports of drug-induced fever attributable to Upadacitinib or other Janus kinase inhibitors (JAKi) used for the treatment of IBD. A recent pharmacovigilance analysis of FDA reports showed that the immunomodulating agents are the most frequently associated with drug-induced fever8 but no JAKi are mentioned in this report.

In conclusion, given the abovementioned confusion between

disease activity and drug-induced side effect in an IBD patient experiencing isolated fever, the drug-induced fever in this particular condition is certainly underrecognized. By the present two cases, we would like to alert the physicians to the possibility of this condition being induced by Upadacitinib.

5. Acknowledgement

This work was funded by the EU Next Generation EU through the Recovery and Resilience Plan for Slovakia under the project No. 09I03-03-V04-00157".

References

1. Johnson DH, Cunha BA. Drug fever. Infect Dis Clin North Am. 1996; 10: 85-91.
2. Patel RA, Gallagher JC. Drug fever. Pharmacotherapy. 2010; 30: 57-69.
3. De Jong, DJ Derijks, L J Naber. Safety of thiopurines in the treatment of inflammatory bowel disease. Scand J Gastroenterol Suppl. 2003; 69-72.
4. Rehr EL, Swanson KA, Kern JA. Mercaptopurine-induced fever in a patient with Crohn's disease. Ann Pharmacother. 1992; 26: 907-909.
5. McBane S, Rojas C. Azathioprine-induced fever in sarcoidosis. Ann Pharmacother. 2011; 45: e19.
6. Hearing SD, Playfor S, Bentley SJ. High fever induced by sulphasalazine. Bmj. 1995; 311: 1204.
7. Suzuki K. Genetic Background of Mesalamine-induced Fever and Diarrhea in Japanese Patients with Inflammatory Bowel Disease. Inflamm Bowel Dis. 2022; 28: 21-31.
8. Li X, Zhang W, Wen X, Lin D. Drug-induced fever: a pharmacovigilance analysis based on the FDA adverse event reporting system. Int J Clin Pharm. 2026.