

Single Case

Recurrent Pneumothorax in a Pediatric Patient with Crohn's Disease Receiving Ustekinumab Treatment: Case Report

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Keywords

Crohn disease · Inflammatory bowel disease · Pneumothorax · Treatment · Ustekinumab

Abstract

Introduction: We present the case of a patient with Crohn's disease who experienced recurrent pneumothorax after starting treatment with ustekinumab. **Case Presentation:** A patient with Crohn's disease started an induction regimen with intravenous ustekinumab, and 2 months later he presented a left-sided pneumothorax. It had an atypical evolution that required surgical management. The medication was withdrawn and the pneumothorax resolved completely. One year later, he had a new flare-up of Crohn's disease and ustekinumab therapy was restarted, presenting a new episode of pneumothorax. **Conclusion:** To our knowledge, this is the first report of recurrent pneumothorax following two separate attempts to initiate ustekinumab.

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Introduction

Pneumothorax occurs when air enters the pleural space, leading to partial or complete lung collapse. It can develop spontaneously or result from trauma, underlying lung disease, or medical procedures. Crohn's disease is a chronic inflammatory bowel disease that can affect the entire gastrointestinal tract from the mouth to the anus. It is a progressive condition and can lead to bowel damage with the onset of abscesses, fistulas, and strictures, negatively impacting on patients' quality of life. The introduction of biologic drugs has definitely

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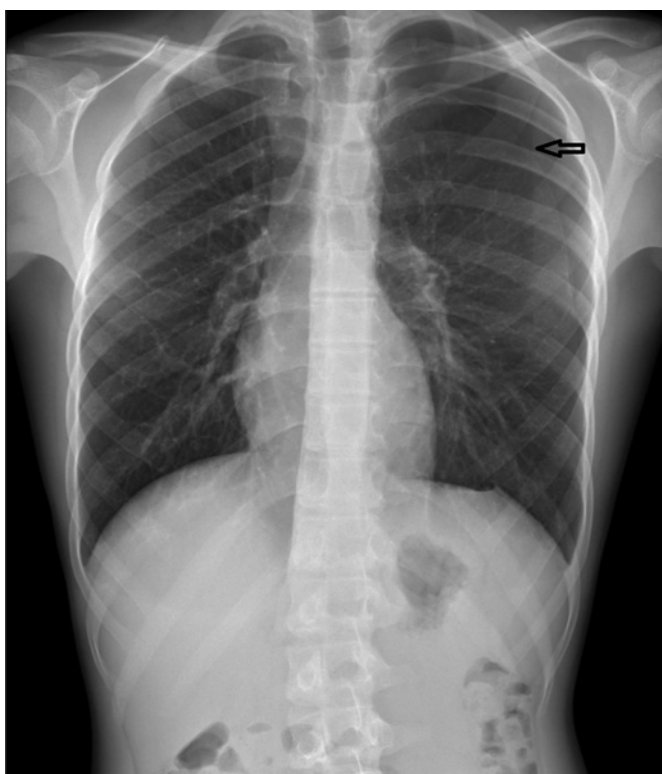


Fig. 1. Left pneumothorax.

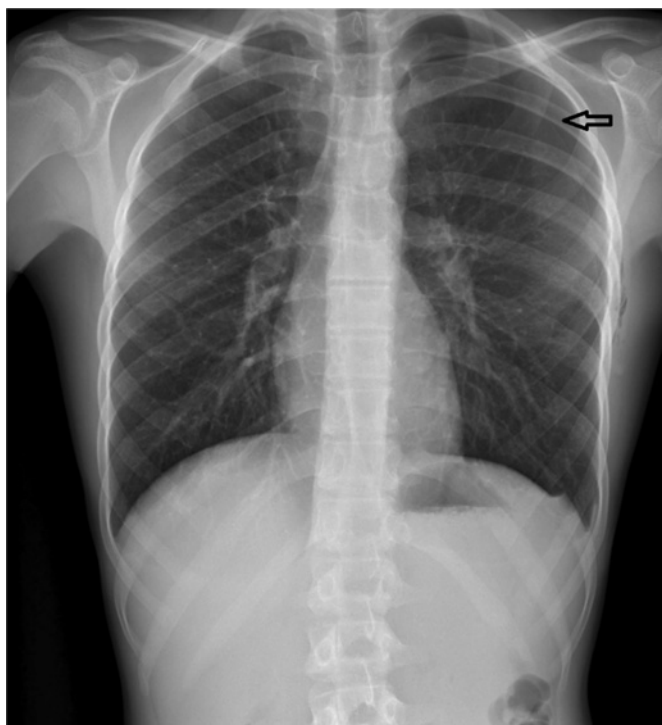


Fig. 2. Pneumothorax with atypical evolution: full lung expansion was not achieved despite properly placed drain, no air leak.

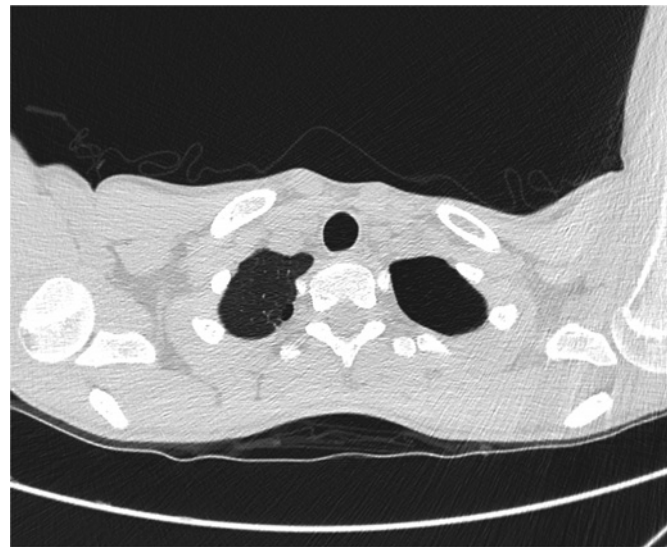


Fig. 3. Right apical bulla and left pneumothorax without bullae.

revolutionized the management of these patients by significantly improving the course of the disease. Ustekinumab is a monoclonal antibody directed against the p40 subunit of interleukins IL-12 and IL-23 [1] and represents a safe and effective treatment option for moderate and severe Crohn's disease [2, 3]. Mild side effects such as nasopharyngitis, headache, diarrhea, fatigue, or injection site erythema have been reported among ustekinumab users. Major side effects such as serious infections and hypersensitivity reactions are rare [2, 3]. We present the case of a patient with Crohn's disease who experienced recurrent pneumothorax after starting treatment with ustekinumab. Literature review identified only a single poster presentation potentially linking pneumothorax to ustekinumab in a patient with psoriatic arthritis [4].

Case Presentation

A 17-year-old boy, diagnosed with ileocolic Crohn's disease (A1a L3 B1 G1) at the age of 6 years, was initially treated with infliximab, which successfully managed the condition. However, he later developed treatment-related paradoxical psoriasis that was difficult to control and recurrent skin abscesses refractory to various antibiotic regimens. Consequently, a decision was made to transition to ustekinumab therapy. In June, 2022, the patient started an induction regimen with intravenous ustekinumab (260 mg), resulting in resolution of skin abscesses and a marked improvement in psoriasis. Two months later, in August 2022, he presented to the emergency department with dyspnea and chest pain. Chest radiographs confirmed a left-sided pneumothorax (Fig. 1). A chest drain was placed, resulting in an initial release of air, but full lung expansion was not achieved, and there was no further air leakage (Fig. 2). Given the atypical progression with absence of lung expansion, a chest CT scan was performed, revealing a left-sided pneumothorax without associated bullae and a right apical bulla (Fig. 3). The patient then underwent right bullectomy and resection of the left pulmonary apex, with bilateral thoracoscopic abrasive pleurodesis. Again, complete expansion of the left lung was not achieved following the intervention. In light of the temporal relationship between the start of ustekinumab and development of a pneumothorax with unusual evolution and no other apparent causes, the medication was withdrawn, and treatment was started

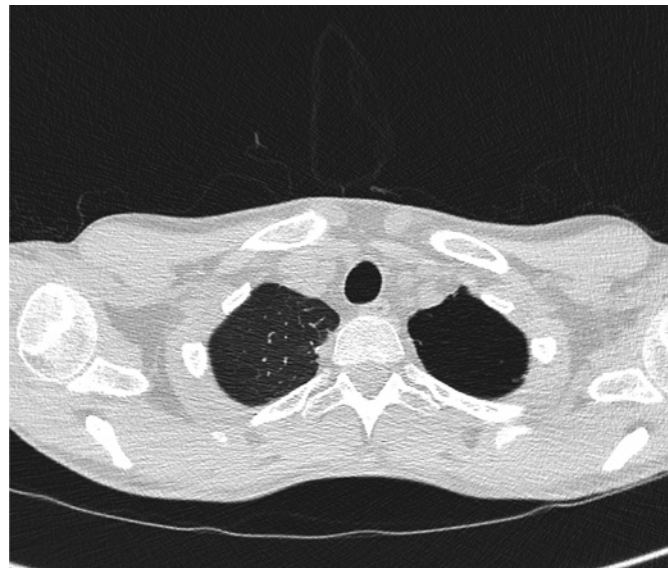


Fig. 4. Recurrence of pneumothorax after restarting medication.

exclusively with enteral nutrition and thiopurines. The pneumothorax resolved completely. In April, 2023, the patient experienced a new flare-up of Crohn's disease. Literature review identified only a single poster presentation potentially linking pneumothorax to ustekinumab [4] and this adverse effect was not cited in the drug insert [5]. Given this scant evidence, there seemed to be a low probability that the pneumothorax was caused by this drug. A decision was made to reinduce intravenous ustekinumab (260 mg), which resulted in significant improvements in clinical and laboratory outcomes. However, 1 month later, the patient returned to the emergency department with chest pain due to recurrence of the left apical pneumothorax (Fig. 4), which resolved with conservative management. Based on the association between initiation of ustekinumab and development of pneumothorax on two separate occasions, both resolving after discontinuation of the drug, the patient's treatment was changed to vedolizumab. This resulted in good clinical progress and no further pulmonary complications after 1 year of follow-up. The patient has good adherence to treatment with good control of the disease and no new adverse effects.

Discussion

Ustekinumab is a monoclonal antibody directed against the p40 subunit of interleukins IL-12 and IL-23, which are proteins that regulate the immune system and immune-mediated inflammatory disorders [1]. After an intravenous infusion for induction, it is administered subcutaneously for maintenance therapy. Subcutaneous ustekinumab maintained clinical response and remission in a substantial proportion of patients, in particularly those who are naïve to TNF antagonists. Immunogenicity rates remained low and the safety profile of the drug has been good [2, 3]. It has been suggested that inhibition of cytokines could affect immune regulation, leading to unusual inflammation in the lungs, such as noninfectious pneumonitis. In rare cases, this inflammation could contribute to the rupture of lung structures, resulting in pneumothorax [6]. Indeed, inflammatory bowel disease patients may develop pneumonitis or pulmonary fibrosis, which could predispose them to pneumothorax due to the fragility of

lung tissue affected by the disease [7]. However, pulmonary complications are more common in patients with a history of underlying lung disease or infections; our patient had no prior respiratory conditions or signs of active infection at the time the pneumothorax developed. To our knowledge, this is the first report of recurrent pneumothorax following two separate attempts to initiate ustekinumab, spaced apart in time. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see <https://doi.org/10.1159/000543991>).

Conclusion

More high-quality evidence is needed to link ustekinumab to pneumothorax, but based on the association between initiation of ustekinumab and development of pneumothorax on two separate occasions, both resolving after discontinuation of the drug, we consider that the use of ustekinumab can be related with that pulmonary complication. This case report does provide valuable experience and may be useful for the clinical practice of other professionals who encounter this rarely described adverse effect.

Statement of Ethics

This study protocol was reviewed and the need for approval was waived by “Comité Ética de Investigación con Medicamentos de Vall d’Hebrón Institut de Recerca.” Written informed consent was obtained from the participant and his parents for publication of the details of the medical case and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

M.F.B. and O.S.C. conceived the presented idea. M.F.B. wrote the paper with inputs of all authors. L.R.S. revised the radiological images. L.G.M. revised the surgical details.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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