Case Report

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Ceftriaxone-induced Acute Hypersensitivity Pneumonitis: A Rare Case Report

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ABSTRACT

Hypersensitivity Pneumonitis (HP), also known as extrinsic allergic alveolitis, is a pulmonary disorder characterised by an inflammatory response of the alveoli and small airways due to exposure to a variety of antigens. HP can manifest as acute, subacute, or chronic, depending on the mode of onset and its duration. A broad spectrum of antigens, derived from fungi, bacteria, mycobacteria, birds, chemical sources, and certain drugs such as cyclophosphamide and sulfonamides, has been associated with the development of HP. However, HP developed by Ceftriaxone is an extremely rare occurrence. Here, the authors presented a case of a 26-year-old male who experienced the onset of HP immediately following the administration of injectable Ceftriaxone. He developed a sudden onset of breathlessness and cough, necessitating Mechanical Ventilation (MV) and steroid support. Radiological imaging indicated pneumonitis, and the symptoms gradually resolved after discontinuing Ceftriaxone. Ceftriaxone-induced acute HP represents an unusual clinical presentation. In the present case report, the authors highlighted the possibility of Ceftriaxone as a potential cause of HP, given its capacity for rapid reversal upon its timely removal.

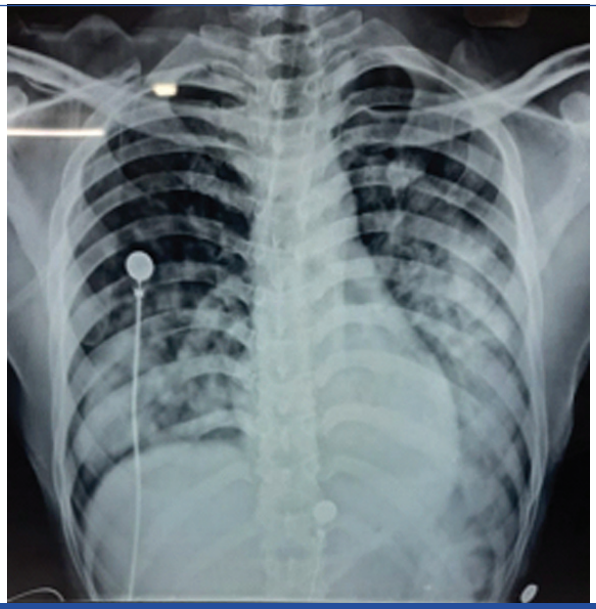
Keywords: Alveolitis, Corticosteroid, Pneumonia

CASE REPORT

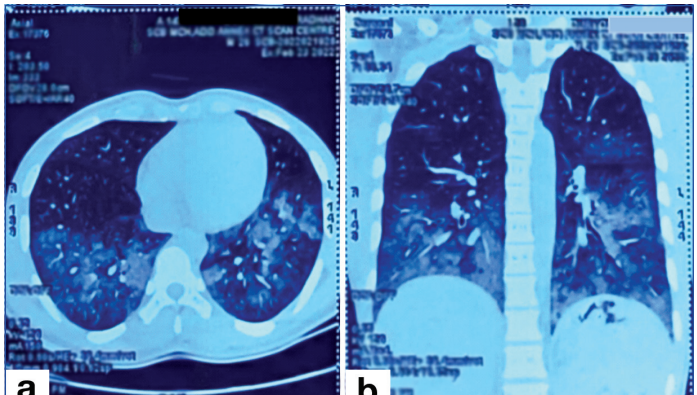
A 26-year-old male presented to the casualty with a sudden onset of breathlessness. There was no medical history of diabetes mellitus, hypertension, tuberculosis, or any other chronic illness. Upon examination, his pulse rate was 110 beats/min, blood pressure was 100/60 mmHg, respiratory rate was 26 breaths/minute, and oxygen saturation was 94% with ambient air. Auscultation of the chest revealed bilateral (B/L) crepitations. Consequently, he was admitted with a provisional diagnosis of pneumonia and was prescribed Intravenous (IV) Injection Ceftriaxone (1 gm IV twice daily) along with Injection Azithromycin (500 mg IV once daily). However, during his hospitalisation, the patient experienced a recurrence of cough and shortness of breath following the administration of Injection Ceftriaxone. He started producing a profuse amount of mucoid sputum, occasionally tinged with blood. Upon re-examination, his pulse rate had increased to 124 beats/min, blood pressure was 110/60 mmHg, body temperature was 36.8°C, respiratory rate was 36 breaths/minute, and widespread crepitations were detected bilaterally all over his chest. Oxygen saturation decreased to 76% with ambient air, and he developed acute hypoxemic respiratory failure. The patient was shifted to the Intensive Care Unit (ICU) and put on non invasive ventilation.

The chest X-ray, on the day of symptom development, showed patchy non-homogeneous opacities in the middle and lower zones of the right lung and the upper, middle, and lower zones of the left lung [Table/Fig-1]. The following day, a High-resolution Computed Tomography (HRCT) scan of the thorax displayed a large area of ground glass opacity in the bilateral lower lobes and a small area of ground glass opacity in the bilateral upper lobes of the lungs, suggestive of pneumonitis [Table/Fig-2a,b]. Both the Electrocardiogram (ECG) and echocardiography reports were normal.

Laboratory tests revealed a white blood cell count of 10,840/µL (78% neutrophils, 14% lymphocytes, 3% eosinophils), C-Reactive Protein (CRP) level of 12.3 mg/L, and serum procalcitonin level of 0.7 ng/mL. Nevertheless, there was no peripheral blood eosinophilia, and the Absolute Eosinophil Count (AEC) was 130/cumm. Sputum microscopy, differential count, and culture reports were all normal. Unfortunately, auto-antibody screening and Bronchoalveolar Lavage (BAL) analysis were not performed due to the unavailability of the respective facilities



[Table/Fig-1]: Digital chest X-ray Posteroanterior (PA) view showing patchy non-homogenous opacities in the middle and lower zones of the right lung and the upper, middle and lower zones of left lung.



[Table/Fig-2]: HRCT thorax: a) Axial view showing large area of ground glass opacity in bilateral lower lobes of the lungs; b) Coronal view showing large areas of ground glass opacity in bilateral lower lobes and small area of ground glass opacity in the bilateral upper lobes of the lungs, suggestive of Pneumonitis.

at that time. Furthermore, the Coronavirus Disease 2019 (COVID-19) Reverse Transcription-Polymerase Chain Reaction (RT-PCR) test was negative.

Further inquiry discovered that the patient had received treatment for acute gastroenteritis at a local hospital two days prior to presenting at the hospital. Shortly after receiving intravenous antibiotics, specifically Ceftriaxone at the local hospital, the patient developed a sudden onset of breathlessness, leading to the referral to our hospital. Ceftriaxone was promptly discontinued, and the patient was treated with injection hydrocortisone. Subsequently, the symptoms gradually improved the following day, and the patient was weaned off the ventilator accordingly. After three days of hospitalisation, the patient's condition improved, and he was discharged. A follow-up X-ray was planned; however, it could not be done as the patient did not give consent for the same. On the follow-up visit after seven days, the patient was doing well.

DISCUSSION

A rare case of ceftriaxone-induced HP was reported. Chest X-ray and HRCT of the thorax revealed diffuse ground glass opacities in both lungs. Other possible causes considered were healthcare-associated pneumonia, infectious bronchiolitis, and pulmonary embolism. Infectious etiologies were ruled out by a normal leukocyte count, serum procalcitonin level, sputum microscopy, and culture. COVID-19 pneumonia was ruled out by a negative RT-PCR test. Cardiovascular causes were dismissed based on normal ECG and echocardiographic findings. Furthermore, the symptoms subsided after discontinuing ceftriaxone and administering steroid treatment.

Drug-induced interstitial lung disease has a wide range of presentations, ranging from benign infiltrates to acute respiratory distress syndrome [1]. One such pattern is HP, a pulmonary disease characterised by an inflammatory response of the alveoli and small airways due to exposure to various antigens. HP is also known as extrinsic allergic alveolitis. It is a lymphocytic allergic response in the lungs that occurs from exposure to airborne organic antigens like occupational dust, microorganisms, etc. Additionally, it also includes drug-induced lung inflammation and fibrosis [2]. The presentation of HP can be categorised as acute, subacute, or chronic based on the duration of symptoms [3]. In the acute form, there is an immune complex-mediated activation of the complement cascade and alveolar macrophages, leading to cytokine production and maturation of Cluster of Differentiation 8 (CD8) cells into cytotoxic cells [2]. Drug-induced HP occurs due to the immune response of our body against a pharmacological agent [4]. Diagnosing drug-induced HP is challenging, as other potential causes must be ruled out [1]. Drugs that have been reported to induce HP include cyclophosphamides, sulfonamides, non steroidal anti-inflammatory drugs, carbamazepine, ciprofloxacin, sirolimus, ticlopidine, interferon-alpha, ampicillin, bupropion, cephalosporins, trimethoprim-sulfamethoxazole, etc., [5-9] [Table/Fig-3].

Drugs	
Ampicillin	Interferon-alpha
Bupropion	Sulfonamides
Carbamazepine	Ticlopidine
Ciprofloxacin	Trimethoprim-sulfamethoxazole
Cephalosporins	Sirolimus
Cyclophosphamides	Non-steroidal anti-inflammatory drugs

[Table/Fig-3]: List of drugs having proven potential to cause HP [5-9].

Cephalosporins are one of the most widely used antibiotics in recent years, and their adverse reactions are well studied. However, there are very few reports of cephalosporin-induced HP [10,11]. In the present case study (case-1), HP is caused by Ceftriaxone, a third-generation cephalosporin. A similar case has been reported in South Korea, where a patient developed HP following the administration of cephalosporins with identical R1 side chains (ceftriaxone, cefotaxime, cefepime). The patient's condition improved after discontinuation of the drugs (case-2) [4]. Another case study from the USA (case-3) reported Ceftriaxone-induced HP, presenting as acute respiratory failure, which also improved upon drug discontinuation [12]. These cases highlight the importance of recognising cephalosporins as potential triggers of HP [Table/Fig-4], even though such occurrences are rare.

	Case-1 Present study	Case-2 Lee SH et al., 2015 [4]	Case-3 Komal B et al., 2018 [12]
Drugs causing HP	Ceftriaxone	Ceftriaxone, cefotaxime, cefepime	Ceftriaxone
Presentation	Shortness of breath, cough	Shortness of breath, fever, cough	Acute respiratory failure
Chest radiography	Bilateral ground glass opacities	Bilateral ground glass opacities, consolidation, crazy paving pattern	Bilateral lung infiltration
Treatment	Mechanical Ventilation (MV), drug discontinuation, steroid	Drug discontinuation	Mechanical Ventilation (MV), drug discontinuation
Outcome	Improved	Improved	Improved

[Table/Fig-4]: Comparison between the presentation and outcome of three cases of ceftriaxone induced HP [4,12].

Diagnosis of HP is difficult due to nonspecific symptoms, variable radiological and BAL findings [2]. Therefore, it is essential to rule out other potential causes. One key indicator for diagnosis is the improvement of symptoms upon removal of the causative agent. Other common presentations of drug-induced HP include fever, cough, dyspnoea, and rash [12].

Similar to other hypersensitivity reactions, the management of drug-induced HP includes life-supporting measures, identifying and ceasing the causative pharmacological agent, and in severe cases, corticosteroid treatment [12]. Early diagnosis and intervention are essential for improving outcomes in these cases.

CONCLUSION(S)

Hypersensitivity reactions following the administration of cephalosporins are indeed common. However, Ceftriaxone-induced HP is a rare presentation. Therefore, clinicians should be aware of such a likely presentation, even in the absence of hallmark symptoms like rash and eosinophilia. Thus, HP should be considered as a differential diagnosis for patients with a similar presentation, as early diagnosis and prompt management can cure the condition and significantly reduce morbidity and mortality.

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