ISSN: 2754-4761

Journal of Pulmonology Research & Reports

SCIENTIFIC Research and Community

Case Report

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A Unique Case of Bilateral Chylothorax in a Patient Treated with Dasatinib for CML

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ABSTRACT

We describe an interesting case of an elderly woman with CML who presented with bilateral recurrent effusion. Pleural fluid analysis revealed lymphocyte-predominant exudative pleural fluid negative for malignant cells. She was started on antitubercular medications on an empirical basis with no improvement. On re-evaluation with repeat fluid analysis, the fluid from both sides turned out to be chylothorax. Infectious, malignant causes were ruled out. She was on Dasatinib for 2 years before she developed effusion. A diagnosis of drug-induced effusion was made and the offending drug was withheld. Her effusion cleared and pleurodesis was done bilaterally. She remains clinically and radiologically better on follow-up to date.

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Received: February 05, 2024; **Accepted:** February 09, 2024, **Published:** February 16, 2024

Keywords: Dasatinib, Pleural Effusion, Chylothorax, Drug-Induced Effusion, Lymphocytic Effusion

Introduction

Pleural effusion can be noted in many cases due to diverse causes. The fluid analysis can identify common causes based on whether the fluid is transudative or exudative depending on Light's criteria [1]. Transudative effusion can result from cardiac, renal, or hepatic failure. Exudative effusions can result from infections, malignancy, inflammatory conditions like connective tissue disease, pulmonary embolism, or drugs [2]. The management of pleural effusion depends on the etiology of effusion [3]. Usually depending on the cell count, biochemical parameters, and cytology the diagnosis of tubercular effusion (TB) is commonly made in India. Drug-induced lung toxicity can range from pulmonary infiltrates to pleural involvement. Pleural involvement can be effusions, pleural thickening or pleuritis. Usually drug induced effusions are eosinophilic in nature and exudative [4]. It is usually a diagnosis of exclusion.

We now present the case of an elderly lady who presented with exudative effusion wrongly diagnosed as TB effusion, received treatment with no response, and eventually turned out to be due to Dasatinib used for chronic myeloid leukemia (CML).

Case Report

A 72-year-old elderly woman diagnosed case of chronic myeloid leukemia for 2 years, presented with shortness of breath for 2 months. She was a well-controlled diabetic. She was well nourished with a BMI of 20 kg/ m^2. She never had any chronic respiratory illness or allergic symptoms in the past. She experienced chest discomfort, heaviness, and worsening breathlessness for 5 days. She had no radiation of pain or any relation with food intake. She had no wheezing or features suggestive of paroxysmal nocturnal dyspnea or any fever episodes. She had no history of any trauma or recent surgery. She had no history of contact with any patient infected with tuberculosis. Initially, she presented to another health care unit wherein a chest radiograph was taken which showed moderate left-sided effusion. Pleural aspiration and analysis revealed a high straw-colored fluid, exudative lymphocytic with borderline high ADA. Her pleural cultures and PCR analysis for TB were negative. The pleural fluid cytological analysis did not render any malignant cells. Pleural fluid for triglycerides or cholesterol is not usually done as part of routine pleural fluid analysis unless there is a gross milky appearance or in cases of high suspicion. In an endemic country like India with this acute on-chronic picture and suggestive fluid study, tubercular effusion was suspected. She was empirically initiated on 4 antitubercular medicines (ATT) Isoniazid, Pyrazinamide, Rifampicin, and Ethambutol) as per the government TB control program. Despite 4 weeks of ATT, she did not feel better and showed worsening clinically as well as radiologically with a new onset of right-sided effusion. With this background, she was referred to us. Her mantoux was non-reactive (4 mm). The plan was to proceed with a medical thoracoscopy and pleural biopsy, but the patient opted out due to social reasons.

Chest X-ray showed bilateral moderate to large effusion (Figure 1). CT chest did not show any parenchymal involvement or mediastinal node worsening. Thoracentesis was performed from both sides and sent for analysis separately. Her pleural fluid on the right side was muddy and her left side was pus-like in gross appearance (Figure 2). The fluid was not foul-smelling. Fluid cytology and flow analysis were performed to find out any evidence of malignant involvement. She had exudative lymphocytic effusion with chylomicron positivity. Her TB PCR studies also turned negative. Her pleural fluid analysis reports are given in the tabular column below. Lymphoscintigraphy did not demonstrate any lymphatic leaks.

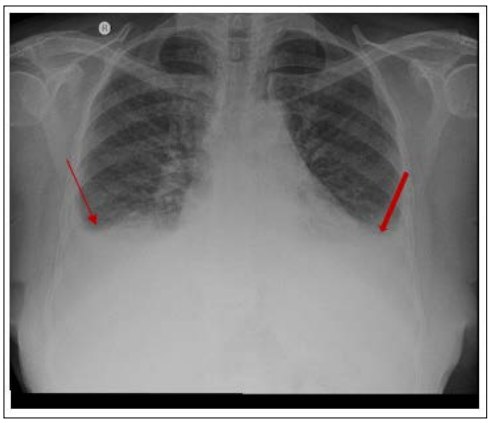

Figure 1

Figure 2: Showing Chylothorax

Table 1: Pleural Fluid Characteristics

Pleural analysis	Right	Left
Color	Muddy	Pus
Total counts per mm^3 (Lymphocytes %)	3200 (98%)	3900 (97%)
Protein mg/dl	4.9	4.3
Adenosine deaminase level(ADA) U/L	19.3	25
Sugar	102	98
LDH U/L (Serum LDH- 230)	280	340
Triglyceride mg/dl	450	917
Chylomicron	Positive	Positive
Cholestrol mg/dl	66	72

Detailed drug history revealed she was on Dasatinib 100 mg once daily, a Tyrosine Kinase inhibitor for her CML. The etiology of chylous effusion was deemed secondary to the drug Dasatinib after ruling out any malignant involvement with PET CT and fluid studies. Thus, a diagnosis of Dastinib-induced bilateral chylothorax was made. An intercostal pigtail drain (ICD) (Figure 3) was inserted bilaterally and her diet was restricted to medium-chain fats. The plan was to change to total parenteral nutrition if fat loss in pleural fluid worsened. Dasatinib and ATT were stopped. Around 2 litres of fluid were drained from each side and pleurodesis with povidone iodine was attempted on both sides. She became clinically better, her ICD was removed, and discharged. Hemato oncology team discussed with her further chemotherapy options to maintain remission. The drug was well tolerated by her for the last 2 years and she achieved molecular remission. Hence, the patient and her family wanted to continue with the same drug despite these complications. She was advised thoracic surgeon's opinion for consideration of decortication to prevent future events but they opted out. Considering this after a brief drug holiday of 4 weeks she was reinitiated on low dose Dasatinib at 50 mg once a day with advice to reconsider other options if a recurrence of effusion happens. She remains on close follow and is in deep molecular remission up to date. She remains on close follow-up. Her chest X-ray after 2 months of pleurodesis is shown in Figure 4.

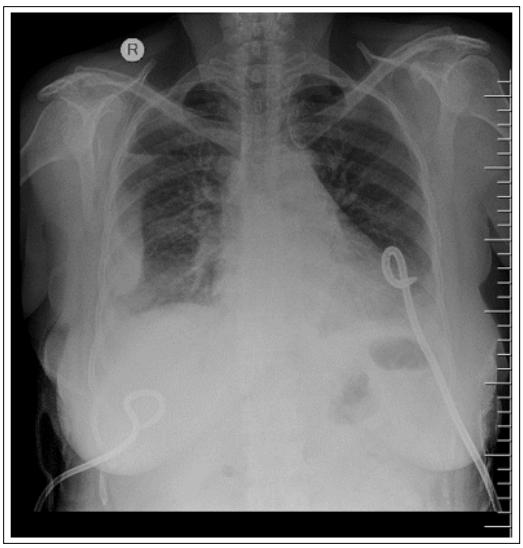

Figure 3

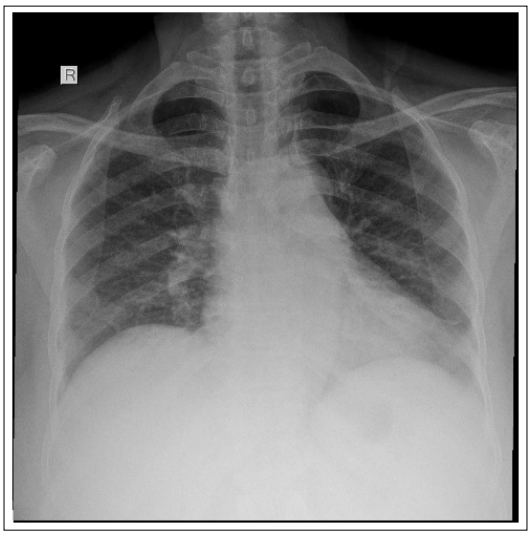

Figure 4

Discussion

Drug-induced effusion is usually a diagnosis of exclusion. Several drugs can cause pleural effusion. The exact reason for inducing pleural effusion is unknown. The presentation can vary from the incidental finding of effusion to acute pleuritis or pleural thickening. The possible mechanisms can be a direct toxic effect, hypersensitivity or allergic reaction, oxygen-free radical production, suppression of the antioxidant defenses, or drug-induced inflammation [1].

Chylothorax can occur secondary to obstruction or injury to the thoracic duct or its branches. It is characterized by its milky appearance and elevated triglycerides>1.24mmol/L(>110mg/dl) or the presence of chylomicrons in the fluid analysis. It is important to differentiate from pseudochylous effusion as in endemic countries, Tuberculosis can be a major cause of pseudochylous effusion.

Dasatinib is a potent tyrosine kinase inhibitor drug used for chronic myeloid leukemia (CML) treatment. Skin rash, pancytopenia, nausea, and fluid retention, including pleural effusion are the common adverse events with this drug. The incidence rate of pleural effusion with dasatinib has previously been reported to range from approximately 20%-35% [2].

In the DASISION study, around 28 % of patients on dasatinib developed mild, moderate, or severe levels of effusion [3]. Dasatinib effusion are usually exudative and lymphocyte-predominant. This could be due to an immune-mediated reaction [4]. For the elderly population, comorbidities like heart disease, hypertension, hypercholesterolemia, associated autoimmune disease, rash, drug dosage, and the presence of lymphocytosis, duration, and dosage of dasatinib have been described as risk factors for developing pleural effusion in patients treated with dasatinib [5].

Chylothorax has been rarely reported as a secondary effect of dasatinib. It has been found to occur especially in long-term treated patients, although its pathophysiology is not yet fully understood. Microscopic disruption of the lymphatic channels has been proposed as the key mechanism behind dasatinib-induced chylothorax [6]. The management of drug-induced effusion is usually avoidance of the drug. In the case of Dasatinib, dose reduction can have a positive impact on further occurrence of effusion without any limitation to its efficacy on CML [3]. In our case, the drug was stopped briefly. Even though effusions are common with prolonged usage of Dasatinib, only very few cases of dasatinib-induced bilateral chylothorax have been reported in the literature so far [7-8]. The need for broad diagnostic work in case of effusion in a patient with comorbidities coming from an endemic region remains crucial here. Initial misattribution to TB and then exposure to antitubercular medicines could have been avoided with a detailed history and systematic approach to analyzing the pleural fluid.

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Conclusion

This is a unique case of dasatinib-induced, bilateral chylothorax. After ruling out other causes of chylothorax like trauma, malignancy, and infections, the etiology was considered to be due to dasatinib. The exact mechanism of effusion or chylothorax in dasatinib-induced effusion is still unclear.

References

1. Light RW (2013) The Light Criteria. Clinics in Chest Medicine 34: 21-26.
2. Jany B, Welte T (2019) Pleural Effusion in Adults-Etiology, Diagnosis, and Treatment. Dtsch Arztebl Int 116: 377-386.
3. Shen Wagner J, Gamble C, MacGilvray P (2023) Pleural Effusion: Diagnostic Approach in Adults. afp 108: 464-475.
4. Iftikhar A, Renz J, Kanagarajan K (2020) DRUG-INDUCED BILATERAL EOSINOPHILIC PLEURAL EFFUSIONS. Chest 158: A1270.
5. Martínez RJG, Gea CS, Martin Riera V, Ruiz ARG, Barzanti RP, et al. (2023) Dasatinib-induced chylothorax: a clinical laboratory's perspective. EJIFCC 34: 76-80.
6. Quintás Cardama A, Kantarjian H, O'brien S, Borthakur G, Bruzzi J, et al. (2007) Pleural effusion in patients with chronic myelogenous leukemia treated with dasatinib after imatinib

failure. J Clin Oncol 25: 3908-3914.

7. Cortes JE, Saglio G, Kantarjian HM, Baccarani M, Mayer J, et al. (2016) Final 5-Year Study Results of DASISION: The Dasatinib Versus Imatinib Study in Treatment-Naïve Chronic Myeloid Leukemia Patients Trial. JCO 34: 2333-2340.
8. De Lavallade H (2008) Pleural effusions in patients with chronic myeloid leukaemia treated with dasatinib may have an immune-mediated pathogenesis. British Journal of Haematology 141: 745-747.
9. Hughes TP, Laneuville P, Rousselot P, Snyder DS, Rea D, et al. (2019) Incidence, outcomes, and risk factors of pleural effusion in patients receiving dasatinib therapy for Philadelphia chromosome-positive leukemia. Haematologica 104: 93-101.
10. Baloch ZQ, Abbas SA, Bhatti H, Braver Y, Ali SK (2017) Dasatinib-Induced Chylothorax in Chronic Myeloid Leukemia. Baylor University Medical Center Proceedings 30: 71-73.
11. Haddad C, Kewan T, Saleem T, Daw H (2021) BILATERAL CHYLOTHORAX AND ANASARCA CAUSED BY DASATINIB IN A PATIENT WITH CHRONIC MYELOGENOUS LEUKEMIA. Chest 160: A1365.
12. Chen B, Wu Z, Wang Q, Li W, Cheng D (2020) Dasatinib-induced chylothorax: report of a case and review of the literature. Invest New Drugs 38: 1627-1632.