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CASE REPORT: CHYLOTHORAX IN A PATIENT WITH CHRONIC MYELOID LEUKEMIA SECONDARY TO DASATINIB USE

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INTRODUCTION

Dasatinib is a second-generation tyrosine kinase inhibitor widely used in the treatment of chronic myeloid leukemia (CML). CML is characterized by a translocation between chromosomes 9 and 22, forming the Philadelphia chromosome (Ph). This chromosome is detected in 95% of all CML patients and in 20-30% of patients with acute lymphoblastic leukemia (ALL). The formation of the Ph chromosome leads to the production of a chimeric protein called BCR-ABL, which is associated with uncontrolled ABL tyrosine kinase activity. Dasatinib works by controlling kinase activity.

This drug is generally well-tolerated but can be associated with reversible or manageable adverse effects. These include cytopenias, fluid retention in 35% of patients, pleural effusion in 14-32%, diarrhea in 3-31%, and skin allergies in 10-20%. Of the pleural effusions described, most are predominantly exudative with lymphocytic predominance, and chylothorax has been reported in a very small percentage of patients.

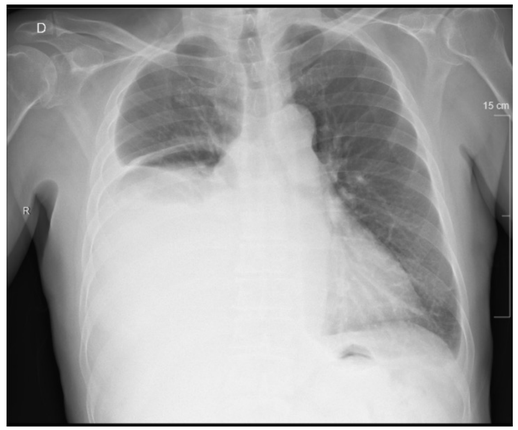
The diagnosis of chylothorax is based on the biochemical analysis of pleural fluid, which contains chylomicrons and elevated triglyceride and lymphocyte levels. There is high suspicion if the pleural fluid chemistry shows triglycerides greater than 110 mg/dL. The following case involves a 74-year-old male with a diagnosis of CML in 2011 and chronic dasatinib use after failure of imatinib, who developed chylothorax.

CASE REPORT

A 74-year-old male with a diagnosis of CML in 2011 was initially treated with imatinib from 2011 to 2016. After 5 years, the patient experienced loss of molecular response with a BCR-ABL IS of 29%, prompting a switch to dasatinib at a daily oral dose of 100 mg. In August 2017, the patient developed dyspnea and pleuritic pain, and a chest X-ray revealed bilateral pleural effusion with right-side predominance. The medication was temporarily discontinued, and the patient was treated conservatively with diuretics and oral steroids, resolving the pleural effusion. After the effusion resolved, dasatinib was restarted at the same dose in April 2019. Mutation analysis revealed the D276G mutation (resistant to imatinib, partially resistant to nilotinib, unknown for dasatinib).

CASE REPORT

Five months after resuming dasatinib, the patient again experienced dyspnea and pleuritic pain. Imaging studies documented a recurrence of bilateral pleural effusions, with right-side predominance. Due to the recurrent effusions, a diagnostic and therapeutic thoracentesis was performed, extracting 750 cc of milky fluid from the right side and 550 cc from the left side. The analysis of the right pleural effusion showed exudative fluid with 76% lymphocytic predominance, triglycerides at 588 mg/dL, proteins at 5.35 g/dL, and LDH at 129 IU/L. The left pleural effusion was exudative lymphocytic with 85% lymphocytes, triglycerides at 1071 mg/dL, proteins at 5.21 g/dL, and LDH at 116 IU/L. Initial management of the effusion was mainly conservative with low-fat dietary recommendations, short courses of steroids, and low doses of diuretics, along with suspension of the medication. However, the patient required multiple thoracenteses over the past year. Currently, the patient has been off the medication for 13 months with a negative BCR-ABL molecular study (IS not detectable), and his CML is being managed expectantly.



A. Xray of initial pleural effusion in August 2017



B. Xray after first thorecenteses in September 2017

CONCLUSIONS

Dasatinib-induced chylothorax is an infrequent but possible complication. In any patient on dasatinib presenting with chylothorax, a drug-related complication should be ruled out. If the pleural effusion does not improve, dose reduction or discontinuation of the medication and/or eventual switch to another tyrosine kinase inhibitor should be considered if warranted. Further research is needed to determine the pathophysiological mechanism of chylothorax development in patients with chronic dasatinib use to define better therapeutic approaches.

REFERENCES

1. Al-abcha, A. *et al.* (2019) 'Chylothorax: Complication attributed to dasatinib use', *BMJ Case Reports*, 12(12). doi:10.1136/bcr-2019-231653.
2. Baloch, Z.Q. *et al.* (2017) 'Dasatinib-induced chylothorax in chronic myeloid leukemia', *Baylor University Medical Center Proceedings*, 30(1), pp. 71–73. doi:10.1080/08998280.2017.11929535.
3. Bhatnagar, M., Fisher, A., Ramsaroop, S., Carter, A., & Pippard, B. (2024). Chylothorax: Pathophysiology, diagnosis, and management—A Comprehensive Review. *Journal of Thoracic Disease*, *16*(2), 1645–1661. https://doi.org/10.21037/jtd-23-1636
4. Cortes, J.E. *et al.* (2017) 'Pleural effusion in dasatinib-treated patients with chronic myeloid leukemia in chronic phase: Identification and Management', *Clinical Lymphoma Myeloma and Leukemia*, 17(2), pp. 78–82. doi:10.1016/j.clml.2016.09.012.
5. Conchon, M. *et al.* (2010) 'Dasatinib', *Revista Brasileira de Hematologia e Hemoterapia*, 33(2), pp. 131–139. doi:10.5581/1516-8484.20110034.
6. Garcia-Zamalloa, A. *et al.* (2023) 'Dasatinib-induced chylothorax beyond 5 years of treatment: Is there actually any limit?', *European Journal of Case Reports in Internal Medicine* [Preprint]. doi:10.12890/2023_003921.
7. Huang, Y.M. *et al.* (2015) 'Dasatinib-related chylothorax', *Turkish Journal of Hematology*, 32(1), pp. 68–72. doi:10.4274/tjh.2012.0196.
8. JASTI, V., WILLETT, A. and ANDERSON, J. (2022) 'Dasatinib-induced chylothorax', *Chest*, 161(6). doi:10.1016/j.chest.2022.04.113.
9. Kelly, R.L. *et al.* (2022) 'Diagnostic pitfalls of chylothorax after dasatinib treatment of chronic myeloid leukemia', *American Journal of Case Reports*, 23. doi:10.12659/ajcr.938319.
10. Quintás-Cardama, A., Kantarjian, H., O'Brien, S., Borthakur, G., Bruzzi, J., Munden, R., & Cortes, J. (2007). Pleural effusion in patients with chronic myelogenous leukemia treated with dasatinib after imatinib failure. *Journal of Clinical Oncology*, *25*(25), 3908–3914. https://doi.org/10.1200/jco.2007.12.0329
11. Tsimberidou, A.-M. (2009) 'Dasatinib in chronic myeloid leukemia: A Review', *Therapeutics and Clinical Risk Management*, p. 281. doi:10.2147/tcrm.s3425.