




Chylous pericardial effusion with cardiac tamponade in a child treated with imatinib

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Brief Report

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Abstract

Chylous pericardial effusions are extremely rare outside of thoracic and cardiac surgery patients. We report the case of an 8-year-old girl with history of recurrent benign giant cell granulomas who developed a large chylous pericardial effusion with cardiac tamponade soon after beginning therapy with imatinib. In this article, we discuss the presentation, diagnosis, and management and review the published literature of this rarely reported side effect of this medication.

Case

The patient is an 8-year-old girl with KBG syndrome (a rare genetic syndrome characterised by characteristic facial features, short stature, developmental delay, and behavioural issues). Her medical history is also notable for benign giant cell granulomas in the bilateral maxillae, initially diagnosed in 2018, who underwent surgical debulking and was subsequently treated with denosumab for 2 years. After initial response to treatment, she developed recurrence in January 2022. She was started on imatinib at a dose of 340 mg/m² once daily, 9 days prior to hospital presentation.

A few days after starting imatinib, she began complaining of palpitations. She presented to outpatient care, where her electrocardiogram revealed sinus tachycardia. A Holter monitor was placed, and workup for sinus tachycardia was initiated including complete blood count and thyroid panel, which were normal. Her tachycardia persisted, and she subsequently developed tachypnoea and increased work of breathing and inability to lay flat, for which she presented to the Emergency Department.

Upon presentation, she was tachycardic to 155 beats per minute, tachypnoeic to 36 breaths per minute, oxygen saturation 98%, and blood pressure 110/71, without pulsus paradoxus identified. She was sitting in a stretcher with the head of the bed raised, in moderate respiratory distress. Cardiac exam revealed distant heart sounds without murmur, rub, or gallop. There was tachycardia with regular rhythm. She exhibited increased work of breathing with belly breathing and accessory muscle usage. Her extremities were mildly cool but well perfused with 1+ distal pulses. She was alert and interactive, answering questions appropriately, though speaking with shortness of breath.

A chest radiograph was performed which revealed cardiomegaly and small bilateral pleural effusions. Echocardiogram was then performed which revealed a very large circumferential pericardial effusion with echocardiographic findings suggestive of cardiac tamponade, with prominent collapse of the right atrial free wall and collapse of the right ventricular free wall (Fig 1).

She was brought emergently to the cardiac catheterisation lab for pericardiocentesis, with drainage of 460 millilitres of milky-appearing fluid and placement of a pericardial drain (Fig 2). Analysis of the pericardial fluid was consistent with chyle (250 nucleated cells/μL with 79% lymphocytes, total protein 4.7 g/dL, cholesterol 66 mg/dL, triglycerides 946 mg/dL, lactate dehydrogenase 289 U/L).

Her imatinib was discontinued. Over the following days, she continued to have chylous output from the pericardial drain and recurrence of a small-to-moderate pericardial effusion on echocardiogram. She returned to the catheterisation lab 1 week later for drain manipulation and replacement, with another 250 ml of chyle removed. The chylous drainage persisted, and she was transferred to another institution for possible lymphatic intervention. Prior to further lymphatic imaging being obtained, the drainage stopped and echocardiogram showed resolution of the effusion. She was ultimately discharged 18 days after her initial presentation. She has since been followed as an outpatient without significant reaccumulation of pericardial fluid.

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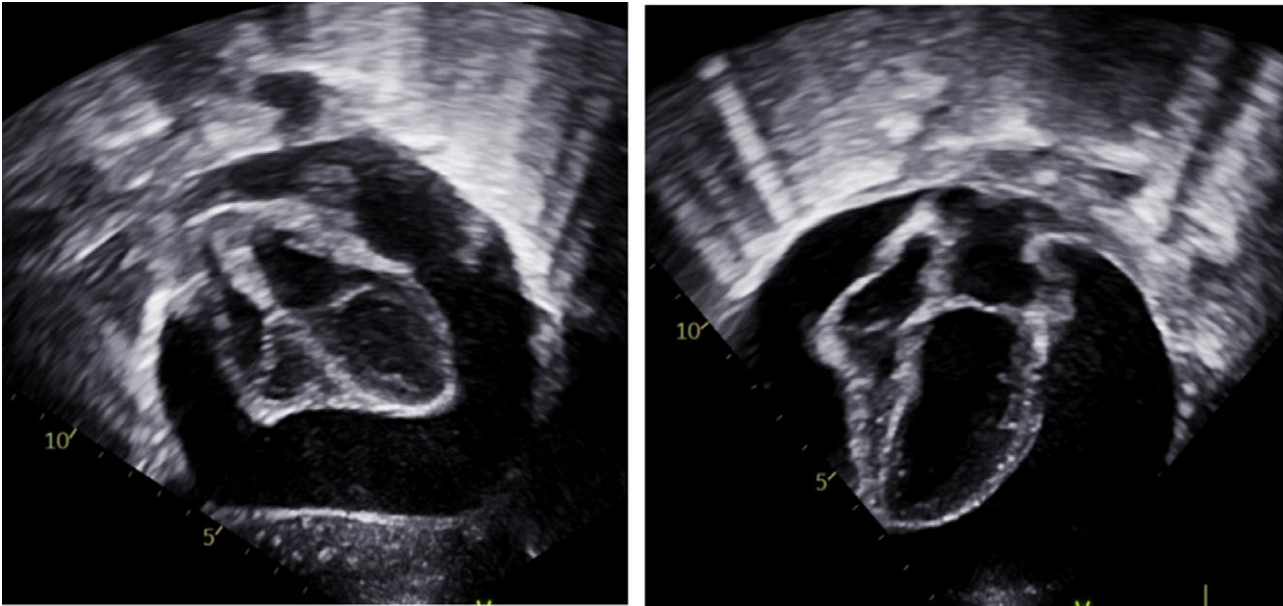


Figure 1. Echocardiogram: Subcostal long (left) and apical (right) views revealing very large circumferential pericardial effusion with collapse of the right atrial and right ventricular free wall.



Figure 2. Image of pericardial fluid draining from pericardial drain in the days following pericardiocentesis.

Discussion

This case details the development of a large chylous pericardial effusion causing cardiac tamponade that is temporally associated with the initiation of imatinib, which resolved in the weeks following discontinuation of imatinib therapy without recurrence.

Imatinib is an oral ABL-class tyrosine kinase inhibitor which is used for a number of oncologic indications, most notably chronic myelogenous leukaemia. Imatinib is known to cause fluid retention and oedema, and can occur acutely soon after initiation of therapy, with rapid improvement following discontinuation of therapy.¹ Pleural effusions have been described as rare side effects of treatment with imatinib, though are much more commonly seen with other more potent medications in the same class, such as the second-generation ABL-class tyrosine kinase inhibitor dasatinib.² Pericardial effusions have also been reported, most commonly in the adult population, but with rare reports in children.³⁻⁶

Pericardial effusions secondary to tyrosine kinase inhibitor treatment can lead to cardiac tamponade, either from acute onset, large size, or a combination of both.⁷⁻⁸ The mechanism of pleural and pericardial effusions secondary to tyrosine kinase therapy is not entirely clear, but appears to be the result of serosal inflammation.³

Chylous effusions have been described much more rarely, with case reports seemingly limited to therapy with dasatinib, which has 325-fold greater activity against BCR-ABL as compared to imatinib.⁸ Chylous pericardial effusions are particularly important to manage, as they carry a high risk of the development of scarring and fibrosis, potentially resulting in constrictive pericarditis.⁹ Treatment consists primarily of drainage of chyle from the pericardial space, often followed by continuous drainage via a pericardial drain until resolution, as well as a low-fat diet to minimise chyle production.¹⁰ In our case, cessation of imatinib therapy led to fairly prompt and complete resolution of chylous effusion in a period of 2 weeks, without recurrence noted at multiple follow up visits.

Conclusion

Pleural and pericardial effusions are known side effects of therapy with tyrosine kinase inhibitors. Chylous effusions are much less described and are mostly limited to more potent second-generation medications. This case describes a massive chylous pericardial effusion leading to cardiac tamponade requiring emergent pericardiocentesis in a child recently started on imatinib, which resolved promptly following cessation of imatinib therapy. This case adds to the limited body of literature regarding chylous effusions secondary to tyrosine kinase inhibitors and is the first known case of chylous pericardial effusion causing tamponade secondary to imatinib in a child. Providers, including paediatric providers, should be aware of this association and monitor closely with a high vigilance for effusions if symptoms develop.

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Conflicts of interest. None.

References

1. Kim KW, Shinagare AB, Krajewski KM, et al. Fluid retention associated with imatinib treatment in patients with gastrointestinal stromal tumor: quantitative radiologic assessment and implications for management. *Korean J Radiol* 2015; 16: 304–313. DOI [10.3348/kjr.2015.16.2.304](https://doi.org/10.3348/kjr.2015.16.2.304).
2. Banka R, Udawadia Z. Imatinib-induced pleural effusion: a case report. *J Postgrad Med* 2017; 63: 55–57. DOI [10.4103/0022-3859.194227](https://doi.org/10.4103/0022-3859.194227).
3. Kelly K, Swords R, Mahalingam D, et al. Serosal inflammation (pleural and pericardial effusions) related to tyrosine kinase inhibitors. *Target Oncol* 2009; 4: 99–105.
4. Breccia M, Alimena G. Pleural/pericardic effusions during dasatinib treatment: incidence, management and risk factors associated to their development. *Expert Opin Drug Saf* 2010; 9: 713–721.
5. Cortes J, Mauro M, Steegmann JL, et al. Cardiovascular and pulmonary adverse events in patients treated with *BCR-ABL* inhibitors: data from the FDA Adverse Event Reporting System. *Am J Hematol* 2015; 90: E66–72. DOI [10.1002/ajh.2393](https://doi.org/10.1002/ajh.2393).
6. Terry C, Avery P, Morton S, et al. Imatinib-induced pericardial effusion in a child. *BMJ Case Rep* 2019; 12: e229975. DOI [10.1136/bcr-2019-229975](https://doi.org/10.1136/bcr-2019-229975).
7. Barton JC, Jones SC, Lamberth WC, et al. Cardiac tamponade associated with imatinib mesylate therapy of chronic myelogenous leukemia. *Am J Hematol* 2002; 71: 139–140. DOI [10.1002/ajh.10186](https://doi.org/10.1002/ajh.10186).
8. Wattal S, Rao MS, Chandra GN, et al. Dasatinib induced cardiac tamponade—a rare association. *J Clin Diagn Res* 2017; 11: FD03–FD04. DOI [10.7860/JCDR/2017/24633.9418](https://doi.org/10.7860/JCDR/2017/24633.9418).
9. Yacoub M, Quintanilla Rodriguez BS, Mahajan K. Constrictive-effusive pericarditis. In *StatPearls* [Internet]. StatPearls Publishing, Treasure Island, FL, 2022.
10. Rochefort MM. Review of chylopericardium. *Mediastinum* 2022; 6: 3. DOI [10.21037/med-20-64](https://doi.org/10.21037/med-20-64).