

Dasatinib: A rare cause of recurrent cardiac tamponade

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Abstract

Dasatinib is one of the second-generation tyrosine kinase inhibitors (TKI) that used as the first line for the treatment of Philadelphia chromosome (Ph) positive chronic myeloid leukemia (CML). Several cardiovascular side effects such as pleural-pericardial effusion, pulmonary hypertension, prolonged QTc interval, and platelet dysfunction have been reported. A 59-year-old female with worsening dyspnoea was diagnosed with cardiac tamponade twice in six months period after initiation of Dasatinib 100 mg per day for CML. She was successfully treated with drainage of effusion percutaneously and discontinuation of Dasatinib. Recurrent cardiac tamponade is a rare complication related to the use of Dasatinib. It should be kept in mind that Dasatinib is a potential agent for pericardial effusion, especially when other possibilities are excluded.

Keywords: dasatinib, recurrent cardiac tamponade, cardiac effects

1. Introduction

Dasatinib is one of the second-generation tyrosine kinase inhibitors (TKI) used for the treatment of Philadelphia chromosome (Ph) positive chronic myeloid leukemia (CML) by hematologists as a first-line treatment option. It also can be used when developing intolerance or resistance to other treatments in CML and Ph (+) acute lymphoblastic leukemia (ALL) (1). Its effectiveness is significantly higher compared to imatinib, the first generation of this group of drugs. It shows 325-fold more activity against the native BCR-ABL gene that is the target of the drug (1). However, in opposition to positive features, several cardiovascular side effects such as pleural-pericardial effusion, pulmonary hypertension, prolonged QTc interval, and platelet dysfunction are increasingly reported (2, 3).

Several clinical conditions can cause pericardial effusions, such as viral infections or other infections, metabolic diseases, reduced lymphatic drainage (congestive heart failure, cirrhosis, nephrotic syndrome), autoimmune diseases, cardiac injury, uremia, drug hypersensitivity, traumatic or idiopathic (5). In addition, pericardial effusion is common in malignant diseases. This could be as a result of the spreading of the primary disease or as a side effect of antineoplastic drugs or radiation therapy (4). Also, pericardial effusion may be the first manifestation of the disease. The patient could be presented with cardiac tamponade as a result of rapidly increasing pericardial effusion.

Here, we discussed a case that presented with a drug-associated recurrent cardiac tamponade who have treated with Dasatinib 100 mg per day for chronic myeloid leukemia.

2. Case Report

A 59-year-old female patient has been admitted cardiology outpatient clinic with several complaints such as shortness of breath, palpitations, and fatigue. It was learned from her medical history that she was treated with the diagnosis of cardiac tamponade in another cardiology clinic three months ago after the onset of similar symptoms and had been using colchicine dispert. She was treated with Nilotinib up to six months ago with the diagnosis of CML three years ago. Upon admission on physical examination, she was hemodynamically unstable and had the signs of cardiac tamponade, which are cold and sweaty extremities, pronounced jugular venous distention, reduced heart sounds, hypotension (blood pressure was 100/60mmHg), tachycardia (heart rate was 110/min) and abdominal tenderness. Electrical alternans with heart rate 100/min were revealed in electrocardiography (Fig. 1a). Laboratory data were as follows: white blood cell count 5.06 bin/uL (26.2% neutrophils and 62.9% lymphocytes); platelet count 166 bin/uL; haemoglobin 8.2 g/dl; creatinine 0.57 mg/dl; AST 19 U/lt; ALT 12 U/lt; total protein 5.5 gr/dl; albumin 3.41 g/dl; LDH:234 U/lt; CRP <3.14 mg/L and sedimentation 26 mm/h. The urinalysis was unremarkable. Echocardiography revealed large pericardial effusion which surrounds all around the heart, with the collapse of the right atrium and right ventricle occurring early diastole (Fig. 1b). Initial echocardiography-guided pericardiocentesis was performed, and approximately 1000 ml of fluid was percutaneously drained. The exudative nature of the fluid (fluid total protein 4.2 g/dl; fluid albumin 2.83 g/dl, serum-fluid albumin gradient 0.58; fluid LDH level 305 U/lt and serum-fluid LDH ratio 1.5)

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was revealed after pericardial fluid analysis.

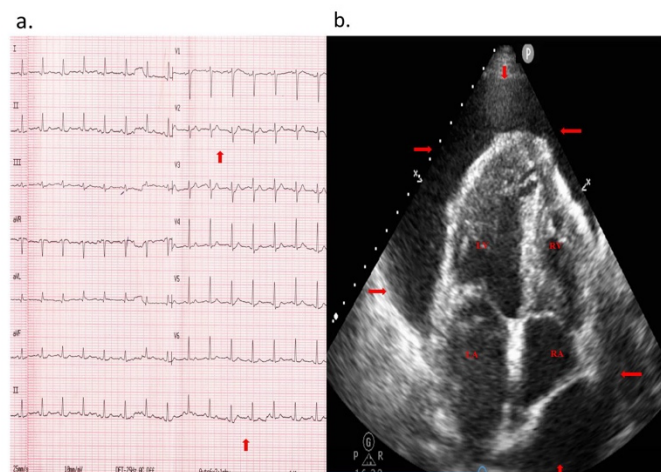


Fig 1: (a) The electrocardiography showing electrical alternans with sinus tachycardia (arrows indicate the alterne QRS waves). (b) Transthoracic echocardiography (apical four chamber view) showing the pericardial effusion (arrows indicate the fluid). LV: Left ventricle; RV: Right ventricle; LA: Left atrium; RA: Right atrium

It was learned from the first center that the effusion drained three months ago was also exudative. Etiological evaluations were made. There was no infection history or sign and no pathological findings were detected in thorax, abdomen and breast imaging in terms of malignancy. Cytological analysis of pericardial fluid was non-specific. The patient's symptoms began six months ago after changing Nilotinib therapy to 100 mg Dasatinib per day. As the etiology of pericardial effusion is unknown, we considered that there might have been a Dasatinib-associated pericardial effusion after literature research. (6-7). We directed the patient to hematology, and dasatinib therapy was replaced with Nilotinib again after BCR/ABL gene evaluation. The patient was discharged uneventfully with colchicine dispart therapy. Pericardial effusion was not repeated in the patient's three- and six-month follow-up after discontinuation of Dasatinib therapy.

3. Discussion

To the best of our knowledge, this is the first case report of recurrent cardiac tamponade as a complication associated with Dasatinib.

KML has transformed from a deadly disease into a controllable form with the treatment of BCR-ABL tyrosine kinase inhibitors. The first approved imatinib from this group was followed by many new generations such as Dasatinib, Nilotinib, Bosutinib, Ponatinib. Dasatinib, which is one of the new generation TKIs generally used cases in which imatinib treatment cannot be continued, is among the first-line treatment options due to its effectiveness (8). Cardiovascular effects have been investigated in detail in CML patients due to the significant effect on the success of treatment and overall survival. In this context, several cardiovascular effects, including pulmonary artery hypertension, congestive heart failure, pleural and pericardial effusion, QTc prolongation, and sudden cardiac death, have been reported related to Dasatinib (9).

The most common non-hematological adverse event in patients treated with Dasatinib is the occurrence of pleural effusions (7). Dasatinib-related pleural effusions are usually lymphocyte-dominant exudates. Concomitant pericardial effusion can be detected in 29% of cases (9, 10). The pathogenesis of effusions is still uncertain. However, the hypotheses focused on immune-mediated increased permeability and serositis due to Dasatinib which is not only tyrosine kinase but also a strong inhibitor of Src kinases and platelet-derived growth factor receptor β (PDGFR- β) (11). In previous studies, the presence of concomitant heart or lung diseases, hypertension, hypercholesterolemia, autoimmune diseases, skin rash related to treatment, and advanced age were identified as high-risk conditions for the development of effusions (12). Wattal et al. reported a case of a CML patient who received 100 mg Dasatinib daily, presented with pleural and pericardial effusion and regressed after Dasatinib treatment interruption (6). In a review of the 13 CML patients treated with 50 or 100 mg Dasatinib, Krauth et al. reported that four of the patients developed clinically significant pleural or pericardial effusion, and one of these patients had life-threatening massive pericardial effusion. (7). The treatment approach typically includes dose interruption or reduction, diuretics, short-term corticosteroid therapy, fluid drainage, and modification in CML maintenance therapy (13,14). In our case, we detected isolated cardiac tamponade, which we think is related to Dasatinib. As a result of continuing the drug, it was repeated twice within six months. However, no pericardial effusion occurred after the switching of the treatment.

As a complication of Dasatinib, cardiac tamponade, especially recurrent ones, is rarely seen. When other possibilities are excluded, it should be kept in mind that Dasatinib is a potential etiologic agent for pericardial effusion.

Conflict of interest

None to declare.

Acknowledgments

None to declare.

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