

## Case Report



# Imatinib (Gleevec) Induced Worsening of Pericardial Effusion in CML

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### ABSTRACT

Gleevec (imatinib mesylate) is indicated for the treatment of newly diagnosed adult patients with Philadelphia chromosome positive chronic myeloid leukemia (CML) in chronic phase. Gleevec is often associated with edema and occasionally serious fluid retention. Severe fluid retention (e.g., pleural effusion, pericardial effusion, pulmonary edema, and ascites) reactions were reported in 1.3% of newly diagnosed CML patients taking Gleevec, and in 2%-6% of other adult CML patients taking Gleevec. We report a case of a patient with CML and a pericardial effusion worsening after initiating Gleevec.

**Key Words:** Pericardial effusion, Imatinib, CML.

### ÖZET

#### Kronik Miyeloid Lösemide Imatinib (Gleevec) ile Atış Gösteren Perikardial Effüzyon

Gleevec (imatinib mesylate), Philadelphia kromozomu pozitif kronik fazdaki kronik miyeloid lösemili (KML) erişkin hastanın tedavisinde kullanılmaktadır. Gleevec, sıklıkla ödem ve şiddetli sıvı retansiyonuna neden olur. Gleevec alan ve yeni tanı konulmuş KML'li hastaların %1.3'ünde, erişkin hastaların ise %2-%6'sında sıvı retansiyon reaksiyonu (plevral effüzyon, perikardial effüzyon, pulmoner ödem ve asit gibi) olduğunu bildiren birkaç rapor yayınlanmıştır. Bu çalışmada, Gleevec başlandıktan sonra perikardial effüzyonu artan KML'li hasta rapor edildi.

**Anahtar Kelimeler:** Perikardial effüzyon, Imatinib, KML

Pericardial effusions are rarely seen in patients with CML (chronic myeloid leukemia) (1). Pericardial effusion implements a poor outcome and shortened survival time in patients with malignancy (2,3). We are reporting a case of CML with symptomatic pericardial effusion getting worse upon treatment with imatinib (Gleevec).

### CASE REPORT

A forty-nine year old African-American male presented to the emergency department with one week history of shortness of breath and early satiety. His temperature was 98.3F, blood pressure 145/80 mmHg, pulse 78 per minute, and respiratory rate 14/minute. Physical examination revealed hepatosplenomegaly and decreased breath sounds bilaterally. There were no distended neck veins neither distant heart sounds. Chest x-ray showed cardiomegaly, increased cardiac silhouette and bilateral pleural effusions. CBC showed leukocytosis (white cell count of 329,000/microliter) with a

low LAP (leukocyte alkaline phosphatase) score. Echocardiography showed mild pericardial effusion with otherwise normal echocardiogram. The patient was started on allopurinol 300 mg daily and hydroxyurea 2000-3000 mg daily. Peripheral blood FISH (fluorescent in-situ hybridization) test was positive for t (9;22) i.e. the Philadelphia chromosome bcr-abl. His bone marrow biopsy was consistent with accelerated phase of CML. The patient was subsequently started on imatinib (Gleevec) 600 mg daily. Three days after starting imatinib (Gleevec), he reported increased shortness of breath, and repeated echocardiogram showed increased pericardial effusion. The patient underwent pericardiocentesis with drainage of about 850 ml of fluid which was negative for bacterial, viral, fungal and acid-fast bacilli (AFB) cultures. Patient was continued on imatinib (Gleevec) which produced a significant drop in his white cell count. He did not have recurrence of the pericardial effusion.

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## DISCUSSION

Pericardial effusion is an extremely rare but potentially life threatening complication in CML patients. Heart and pericardium are much more likely to be involved in metastases than with primary cardiac tumors (4). Tumors that most commonly involve the heart and pericardium are lung, breast, lymphoma and melanoma (4). Malignancies, non-cardiac in origin, involve the heart and pericardium through four routes: lymphatic dissemination, hematogenous dissemination, local extension and transvenous route (4). There have been reports of new onset pericardial effusion in known CML patients who were treated with imatinib suggesting that the pericardial effusions were associated with imatinib treatment (1). Interestingly our reported case is peculiar in that the pericardial effusion was symptomatic and was present before starting imatinib, and got larger as shown by follow-up echocardiography upon treatment with imatinib.

Pericardial effusion in patients with malignancy could be malignant pericardial effusion, radiation-induced pericarditis, drug-induced pericarditis and idiopathic pericarditis (4). Echocardiography is the most frequently used method to detect pericardial effusion, though CT and MRI provide advantages when metastasis is in question (4). Pericardial effusion implements a poor outcome and shortened survival time in patients with malignancy (2,3).

The life threatening complication associated with pericardial effusion is cardiac tamponade where pericardial pressure is elevated and thus compliance of the ventricular muscle is decreased causing diastolic dysfunction and subsequently hypotension, distended neck veins and distant heart sounds.

CML may present with symptomatic pericardial effusion. Therapy with imatinib (Gleevec) can lead to worsening of the pericardial effusion in these patients specially those with very high white count. Our patient's shortness of breath get worse after starting imatinib, and his echocardiogram showed increase in the size of pericardial effusion for which he underwent pericardiocentesis. Patient was continued on imatinib therapy and the plan for him is to undergo allogeneic stem cell transplant.

Our case raise the question about the need of a baseline transthoracic echocardiogram (TTE) among CML patients with very high white cell counts who will be treated with imatinib, At any rate, these patients should be monitored very closely for any symptom or sign of pericardial effusion.

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