

# Acute Heart Failure Induced by Ponatinib: A case of Ponatinib-Induced Cardiomyopathy with Acute Coronary Syndrome

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## Introduction

- Ponatinib is an oral third-generation tyrosine kinase inhibitor and is approved for patients with chronic myeloid leukemia (CML) or Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ALL).
- Ponatinib has a potent effect against CML or Ph+ALL, but the phase 2 trial revealed that it often induces cardiac disorders such as heart failure and acute coronary syndrome.<sup>1)</sup>
- Herein, we describe a case of Ph+ALL which accompanied two major adverse cardiac events induced by ponatinib, and report its clinical course and cardiac imaging.

## Case Presentation

- An 81-year-old woman with Ph+ALL developed acute heart failure with global left and right ventricular systolic dysfunction 2 months after starting treatment with ponatinib.
- An echocardiogram revealed her left ventricular ejection fraction (LVEF) decreased to 36% (down from 82%), and coronary angiography showed 90% stenosis in the proximal left anterior descending coronary artery.
- A percutaneous coronary intervention was performed and an everolimus eluting stent was implanted in the stenotic lesion. (Figure 1)
- A cardiac magnetic resonance imaging (MRI) study was performed 2 months after revascularization, which showed her LVEF decreased to 23% even though revascularization had been performed.
- High-intensity areas on T2-weighted images and late gadolinium enhancement (LGE) were found at the free wall of the right ventricle, right ventricular insertion points, and mid septum in the mid-wall to the epicardium. (Figure 2)

## Case Presentation (continued)

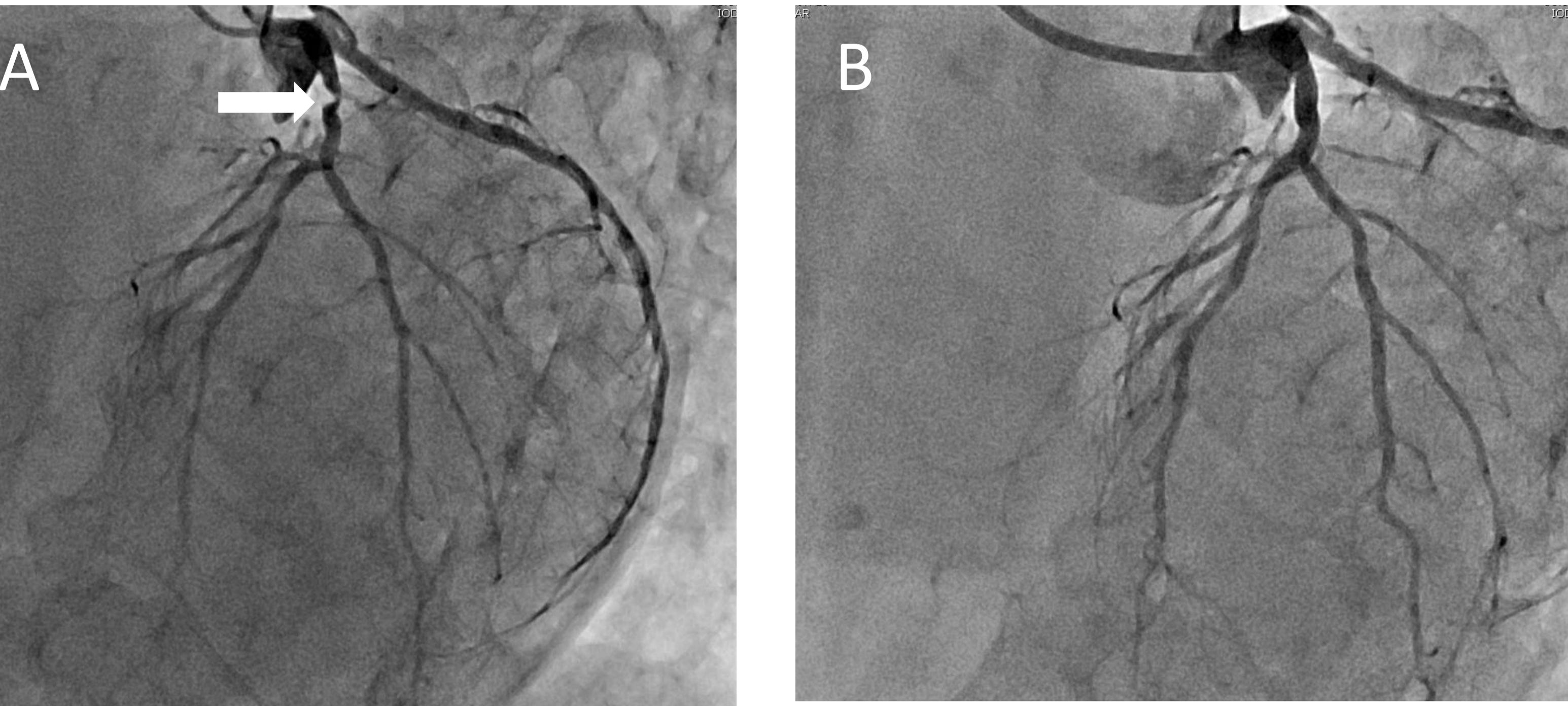


Figure 1: (A) Coronary angiography showed 90% stenosis in the proximal left anterior descending coronary artery. (B) After implanting everolimus eluting stent in the lesion.

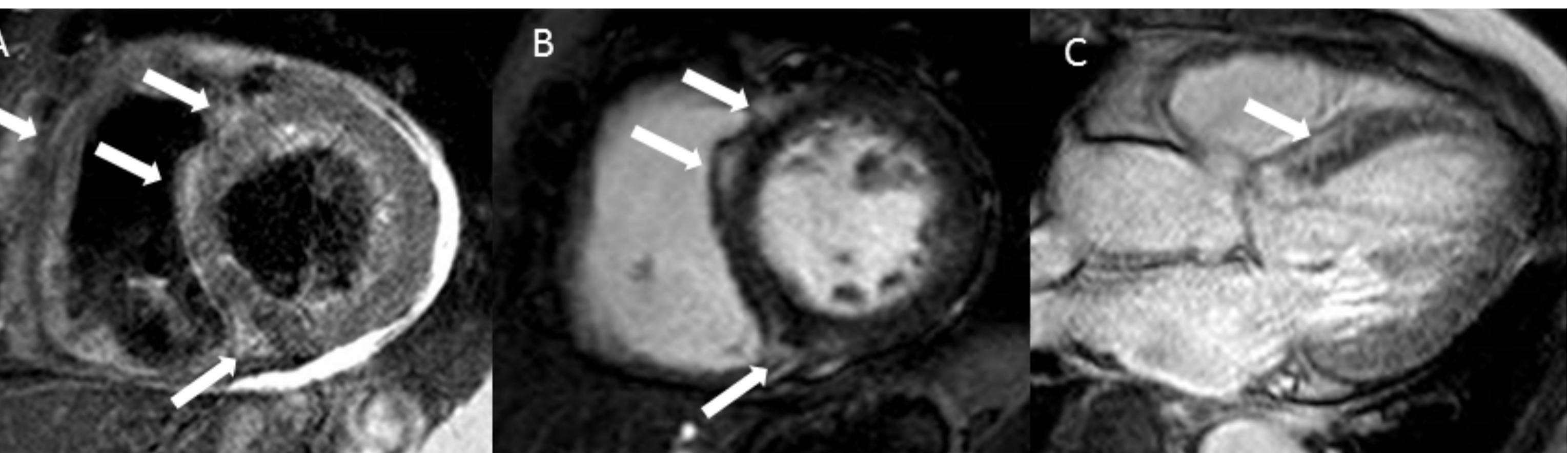


Figure 2: Cardiac magnetic resonance imaging showing high intensity area on T2-weighted image at free wall of right ventricle, right ventricular insertion points, and mid septum (white arrows in A), and late gadolinium enhancement at the same area. (white arrows in B, C)

• Although ponatinib might have been the cause of her cardiac dysfunction, she continued her treatment with ponatinib because it was the only effective drug for her leukemia. Unfortunately, she became resistant to ponatinib 1 month later and died of progression of leukemia.

## Discussion

- Coronary arterial stenosis was initially suspected as the main cause of cardiac dysfunction, but the systolic dysfunction persisted even after the revascularization.
- Cardiac MRI suggested that myocardial edema and fibrosis existed in the mid-wall to the epicardium of both right and left ventricle, which is unusual to be seen in ischemic heart disease.
- Thus, coronary arterial disease was very unlikely to be the main cause and cardiomyopathy was suspected as the main mechanism.
- As for another TKIs, sunitinib is known to induce LV dysfunction. Endomyocardial biopsies from patients who developed heart failure on sunitinib revealed no edema, inflammation, or fibrosis in the cardiomyocytes<sup>2)</sup>. Another previous report demonstrated no LGE in sunitinib-induced cardiac dysfunction<sup>3)</sup>. Comparing the current case with these previous reports, ponatinib might induce cardiac dysfunction by another mechanism than sunitinib.
- Still, the mechanisms of ponatinib-induced cardiac dysfunction are not clear, and further studies are needed.

## Reference

- 1) Cortes JE, et al. A phase 2 trial of ponatinib in Philadelphia chromosome-positive leukemias. *N Eng J Med* 2013;369:1783-96.
- 2) Chu TF, et al. Cardiotoxicity associated with tyrosine kinase inhibitor sunitinib. *Lancet* 2007;370:2011-9.
- 3) Ching-Fen, et al. Cardiac magnetic resonance imaging in sunitinib malate-related cardiomyopathy: no late gadolinium enhancement. *J Chin Med Assoc* 2009; 72(6): 323-327.

## Disclosure

- The authors have no financial conflicts of interest disclose concerning the study.