

Editorial

Dasatinib and Chronic Constrictive Pericarditis: First Two Observations

Conan PL^{1,3*}, Malfuson JV^{2,3} and Rivière F^{1,3}

¹Department of Pneumology, Percy Military Hospital, France

²Department of Hematology, Percy Military Hospital, France

³French Military Health Service Academy, Val de Grâce Hospital, France

*Corresponding author: Pierre-Louis Conan, Department of Pneumology, Percy Military Hospital – 101 Avenue Henri Barbusse – 92140, Clamart, France

Received: April 01, 2016; Accepted: April 20, 2016;

Published: April 22, 2016

Keywords

Chronic myeloid leukemia; Chronic constrictive pericarditis; Tyrosine kinase inhibitor; Dasatinib

Editorial

The most frequent non-hematologic adverse reaction involved by the Dasatinib is pleural effusions. These ones are associated up to 30% of cases to pericardial effusion [1]. We report two cases of chronic pericardial effusion under Dasatinib.

Two patients, respectively 55 and 64 years old, were hospitalized for the exploration of a gradual onset dyspnoea.

They were treated by Dasatinib, 100 mg per day since respectively 5 and 24 months for a chronic myeloid leukemia (CML) on chronic phase. Dasatinib had been instaurated after 18 and 24 months of imatinib because of a poor tolerance (edema of the lower limbs).

The first one has a heart disease with stent, hypertensive and type 2 diabetic. The physical examination and blood tests were without abnormality. The second one was obese and suffer from chronic obstructive pulmonary disease. The physical examination went normal. The laboratory tests recognized a moderate inflammatory biologic syndrome (CRP 33 mg/L), and a moderate bicytopenia with a microcytic anemia (9.2 g/dL) and 120 000 platelets/mm³.

The chest radiographs showed minimal pleural effusions and a cardiomegaly. Transthoracic cardiac ultrasounds objectified pericardial effusion having, respectively a 5 mm and a 21.5 mm circumferences with tricuspid valve regurgitation flux of 2.95 meter/second for the second patient. Cardiac Magnetic Resonance Imagery found a pericardial thickening from 4 to 6 mm for the first patient and 95 mm for the second one with hypertension of the right cavities for both of them.

In both cases, the search for tuberculosis was negative, while serum protein electrophoresis, renal function, autoimmune balance, troponin and BNP were regular. No other cause of chronic constructive Pericarditis had been found. The pleural effusions were net-lymphocytic (20000/mm³ with 94% part of lymphocytes, pleural

proteins ratio/blood 38/73, pleural LDH ratio/blood 278/444 and 3200/mm³ with 98% part of lymphocytes, pleural LDH/blood 0.7, pleural proteins/blood 0.6).

To both patients, the cardiac catheterization found a post capillary pulmonary arterial hypertension and an equalization of the diastolic ventricular pressures with a typical appearance, dip-plateau without any argument for a restrictive heart disease.

It was two constrictive chronic Pericarditis complicated by a post capillary pulmonary arterial hypertension (group 2) without improvement despite a relay from another tyrosine kinase inhibitor (Bosutinib), diuretics and pericardial drainage for the second patient. We hadn't prescribed glucocorticoides.

Main pulmonary adverse effects of Dasatinib are pleural effusion and precapillary pulmonary arterial hypertension. Both of them continued to be theorized more closely and eventually reversible after discontinuation of the medication Dasatinib.

Pericardial effusions are less studied in the literature. Patients presented risk factor of pleural effusion [2]: a prior cardiopulmonary disease, hypertension and were treated for several months.

Pleural liquids were exudative and lymphocyte-dominated. Rather than fluid retention, it let supposed that the probable immune mechanism which cause pleural effusion takes part in the Pericarditis appearance via the clonal expansion of the T and NK cells [3], the non-specific inhibition of PDGF beta or increase of vasculature permeability due to the SRC family kinase inhibition [4]. This explains the lack of improvement despite diuretics cures.

Furthermore, we didn't observed any large granular lymphocytes clonal expansion, significantly associated to the occurrence of effusions and of a better survival [4].

We report here, Dasatinib-induced chronic constrictive Pericarditis proven by a right-side cardiac catheterization and non-reversible despite the discontinuation of the treatment. Care must be taken to prevent the appearance of the pericardic effusion in order to previously detect it, therefore avoiding the probable constrictive evolution, in case of chronicization of the effusion.

References

1. Eskazan AE, Soysal T, Ongoren S, Gulturk E, Ferhanoglu B, Aydin Y. Pleural and pericardial effusions in chronic myeloid leukemia patients receiving low-dose dasatinib therapy. *Haematologica*. 2011; 96: e15.
2. Valent P. Severe adverse events associated with the use of second-line BCR/ABL tyrosine kinase inhibitors: preferential occurrence in patients with comorbidities. *Haematologica*. 2011; 96: 1395-1397.
3. Bergeron A, Réa D, Levy V, Picard C, Meignin V, Tamburini J, et al. Lung abnormalities after dasatinib treatment for chronic myeloid leukemia: a case series. *Am J Respir Crit Care Med*. 2007; 176: 814-818.
4. Paydas S. Dasatinib, large granular lymphocytosis, and pleural effusion: Useful or adverse effect? *Crit Rev Oncol Hematol*. 2014; 89: 242-247.