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Chylothorax Associated with Dasatinib. Report of A Clinical Case Treated in Ambulatory Form

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1. Abstract

BCR-ABL tyrosine kinase inhibitors have changed radically the natural history of patients with chronic myeloid leukemia. Actually, this entity is considered a chronic disease. However, the presence of adverse events may limit the use of some drugs. Herein we report an interesting management of chylotorax associated with dasatinib. Dasatinib is a second-generation BCR ABL1 tyrosine kinase inhibitor. The importance of this case report is the ambulatory management of this complication.

2. Introduction

Dasatinib is a second-generation BCR ABL1 tyrosine kinase inhibitor approved for the treatment of patients with chronic myeloid leukemia (CML) and Philadelphia positive lymphoblastic acute leukemia [1,2]. Pulmonary complications have been described, including pleural effussion (10-28%), pulmonary hypertension (1-5%) and parenchymal opacities (<4%) [3]. The dasatinib-related chylothorax is a rare adverse effect and only a small number of case reports have been reported worldwide [2-10]. The interest of this case is the ambulatory mangement with long-lasting homemade drains with adequate response without complications during this treatment.

3. Case Report

A 29-year-old male diagnosed with CML undergoing treatment with dasatinib 100 mg/day for 7 years attended to emergency room, with a two-month history of dry, intermittent cough and dyspnea. At admission, he was afebril, with dyspnea at rest, ortopnea, blood arterial saturation was 85%. Bilateral pleural effusion syndrome (50 % in every site) was diagnosed clinically and confirmed by chest X-ray and thorax tomography. None lymphadenopathy, mediastinal tumors or lung infiltrates were documented. Bilateral diagnostic thoracentesis documented the presence of bilateral chylothorax (triglycerides of 853 mg/dl and 842 mg/dl from the right and left side, respectively). Thereafter, bilateral endopleural probes of 24 fr type Kardial Spirial, were set, obtaining a volume of right drainage of 500 ml and left of 400 ml. Later, during his hospitalization, a drainage of 3000 ml was obtained from the right side and 2600 ml from the side left. Total parenteral nutrition was given.

Aerobic, anaerobic and fungal cultures were negative. A few mesothelial reactive cells were documented. After discarding other causes of chylothorax, both were associated with the use of Dasatinib. A reduction in expenses was progressively documented according to the days. The patient was discharged, without complications and bilateral pleural effusions less than 100 cc. However, he had a recurrence of bilateral effusion greater than 50% of both hemithorax 5 days after discharge. On this occasion, bilateral PleurX-type were set and an ambulatory surveillance over time was done. Both pleural catheters had complete functionality, without documenting data of infection, dysfunction or entrapment within the pleural space. The extraction of the liquid pleural was performed using the PleurX at home. After 4 weeks, a significant reduction in pleural fluid volumes was documented. At at the sixth week there was no longer any pleural fluid expenditure by any of the catheters. After additional two weeks he restarted the oral diet and the treatment for CML was modified to nilotinib. After one year of follow-up the patient remains with complete molecular response for CML and without a relapse of chylothorax.

4. Discussion

This case with bilateral chylothorax was associated with Dasatinib after 7 years of treatment. Chylothorax is defined according to Light's criteria as a cloudy pleural effusion with triglycerides >110 mg/dL and cholesterol <200 mg/dL [8,10]. Although, the exact mechanism of this complication is unknown [4-10], an immune mechanism has been proposed, due to the presence of predominantly exudate lymphocytic. Also, an inhibition of platelet-derived growth factor beta receptor (PDGFR-β) expressed in pericytes, which is involved in the regulation of angiogenesis and lymphangiogenesis, resulting in disruption of the tumor vasculature, which can result in significant fluid retention has been implicated [1-3]. Another mechanism is the inhibition of Scr kinase, which is expressed in the majority of hematopoietic cells in the tissue pulmonary. Vascular permeability is mediated by endothelial growth factor vascular, which depends directly on Src-cellular. On the other hand, it regulates independently focal adhesions and adherens unions, which are key in the regulation of cell adhesion [6,7]. The proposed treatment for chylothorax secondary to dasatinib is discontinuation of the drug or a dose reduction, diuretics, glucocorticoids, and thoracentesis. In this case the treatment was changed to Nilotinib, total parenteral nutrition was started, glucocorticoids and thoracentesis with placement of bilateral pleural drainage [9,10]. In our case, the management was initially done with endopleural catheters for 4 days. After discarding infectious process and other ethiology, it was discharged with homemade bottles of PleurX for 7 weeks with outpatient monitoring. Finally, the resolution of chylothorax occurred at 4months.Here we present the management of an atypical chylothorax secondary to Dasatinib by means of long-lasting homemade drains with adequate response without presenting any type of complication during and at the end of treatment..

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