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CASE REPORT

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Dasatinib-Related Pulmonary Toxicity

Toxicidad pulmonar por dasatinib

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ABSTRACT

Paciente de sexo masculino, 70 años, con leucemia mieloide crónica en tratamiento con dasatinib, desarrolla insuficiencia respiratoria asociada a toxicidad pulmonar por dicho fármaco.

Key words: Dasatinib; Tyrosine Kinase Inhibitor; Pulmonary Toxicity

RESUMEN

Paciente de sexo masculino, 70 años, con leucemia mieloide crónica en tratamiento con dasatinib, desarrolla insuficiencia respiratoria asociada a toxicidad pulmonar por dicho fármaco.

Palabras clave: Dasatinib; Inhibidor de la tirosina quinasa; Toxicidad pulmonar

INTRODUCTION

Patients with lymphohematological neoplasia may develop pulmonary diseases as a consequence of the immunosuppression that is typical of the disease or the one produced by the chemotherapeutic or immunomodulating agents used for the treatment[1].

There is a wide variety of drugs available for the treatment of this condition. Various regimens that have shown potential pulmonary toxicity are of particular interest to the pulmonologist who has to deal with differential diagnoses[2].

CASE REPORT

70-year-old male patient with the following medical history: bilateral blindness, renal carcinoma with nephrectomy plus radiation therapy, and chronic myeloid leukemia. The patient received treatment with imatinib for one year, and then switched to dasatinib, 140 mg/d due to therapeutic failure.

The patient went to the emergency service (before the pandemic) after 15 days of dry cough, fever and progressive dyspnea. Chest X-ray was performed: right lung alveolar infiltrate. A blood culture was taken and the patient began treatment with levofloxacin, 750 mg/d with diagnosis of pneumonia. After 72 h, due to a lack of clinical response, it was decided that the patient had to be hospitalized. On admission, the patient had a fair general condition, with fever, saturating 93% on room air. Laboratory tests: Hb (hemoglobin): 8 g/dL; PCR (polymerase chain reaction) 9 mg/L; no leukocytosis; creatinine of 1.6 mg/dL. New blood cultures are taken and the patient begins antibiotic treatment with ampicillin/sulbactam + clarithromycin by endovenous route.-

Progressive deterioration, tachypnea and use of mask with reservoir bag due to respiratory failure. Treatment switch to meropenem and transfer to intensive care unit due to persistent fever. Chest tomography: air trapping, bilateral apical alveolar infiltrate, bilateral pseudonodular images, mild left pleural effusion (Figure 1).

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Normal echocardiogram. Fibrobronchoscopy with bronchoalveolar lavage performed. Culture for common germs, microbacteria and fungi: negative. PCR for *Pneumocystis jiroveci*: negative. Negative cytological test.

Dasatinib was suspended under suspicion of pulmonary toxicity, and replaced with corticosteroid treatment showing clinical, gasometric and imaging improvement. Patient is discharged after 7 days, with indication for one month of oral corticosteroids. New outpatient chest tomography without pulmonary infiltrates required (Figure 2).

DISCUSSION

Dasatinib is a second-line ABL tyrosine kinase inhibitor, with oral bioavailability, active against BCR-ABL mutants resistant to imatinib. It is also used as a first-line treatment.[3, 4] The adverse events include fever, myalgia, pulmonary arterial hypertension, pleural effusion (exudate), bronchospasm and pulmonary infiltrates ("ground glass", septal thickening, focal or pseudonodular consolidation). Pulmonary manifestations normally appear one month after first day of treatment and can appear up to two years post-treatment. They seem to have a dose-dependent effect, probably the result of an immune-mediated mechanism[5, 6].

The Bergeron study identified 9 out of 40 patients (22.5%) with chronic myeloid leukemia (CML) in chronic phase who received dasatinib and developed pulmonary anomalies. Six of those patients had pleural effusion (all exudated), and seven subjects showed changes in the lung parenchyma with "ground glass" or alveolar opacities and septal thickening (four patients had pleural effusion and changes in the pulmonary parenchyma)[7].

With regard to the pleural effusion, if it has the necessary volume, a diagnostic thoracocentesis must be performed to differentiate the exudate from the transudate and also a culture has to be done to discard pleural infection. In cases of minimum liquid, continuation of the tyrosine kinase inhibitor (TKI) may be considered, with close clinical and radiological monitoring, whereas in cases of moderate or large pleural effusion, it would be suitable to consider dose reduction, TKI

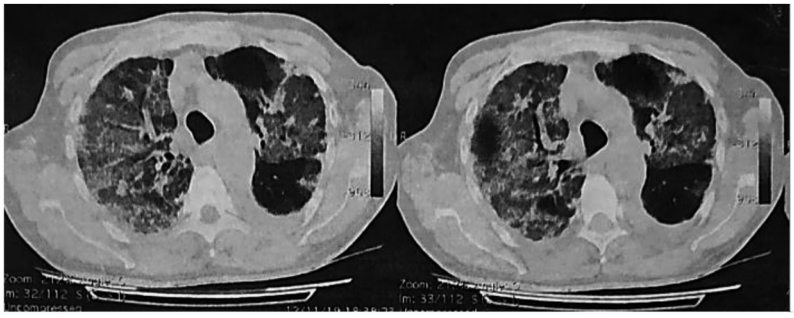

Figure 1. Chest tomography on admission to therapy.

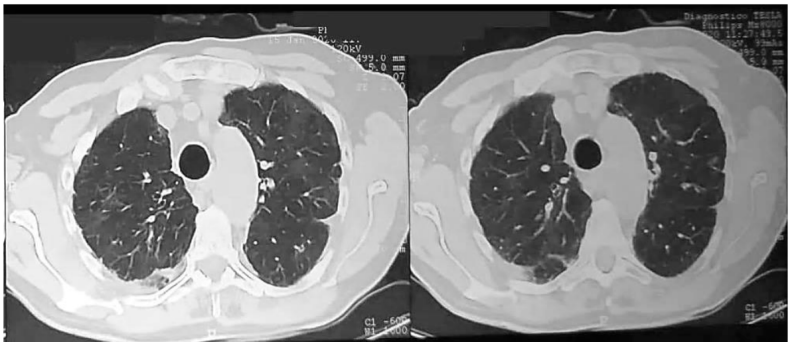

Figure 2. Control chest tomography after treatment with corticosteroids.

suspension or switch to an alternative treatment option for CML[8].

The thoracocentesis, bronchoalveolar lavage and biopsy show lymphocyte predominance (with lymphatic build-up shown in the biopsy)[9].

Drug suspension and subsequent use of systemic corticosteroids resolved the condition. The drug can be used again in the minimum effective dose without worsening the symptoms[10].

CONCLUSION

Dasatinib-related pulmonary toxicity shall be included as one of the differential diagnoses of patients with respiratory symptoms and pulmonary infiltrates. Lack of response to antibiotics, the negative result of bacteriological tests, and the clinical and imaging progression led to the suspicion of the entity. The improvement observed after drug suspension and the use of corticosteroids confirmed the diagnosis.

Conflict of interests

Authors declare there isn't any conflict of interest in relation to the contents of this article.

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