Lenalidomide Induced Late-Onset Acute Respiratory Distress Syndrome

Lenalidomidin İndüklediği Geç Başlangıçlı Akut Solunum Distresi

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ABSTRACT

A 77-year-old man with multiple myeloma (MM) presented with shortness of breath to the emergency department. He also had history of chronic obstructive pulmonary disease, chronic pulmonary embolism and nephrectomy due to malignancy 10 years ago. He had been treated for 9 months with lenalidomide because of MM. He diagnosed with adult respiratory distress syndrome due to lenalidomide. We aimed to demonstrate late onset and destructive effects of lenalidomide on the lungs.

Keywords: Lenalidomide, pulmonary toxicity, side effect, dyspnea

ÖZ

Multiple miyelomlu (MM) 77 yaşındaki erkek hasta acil servise nefes darlığı nedeniyle başvurdu. Öyküsünden kronik obstruktif akciğer hastalığı, kronik pulmoner emboli ve 10 yıl önce kansere bağlı nefrektomi geçirdiği anlaşılmaktaydı. MM nedeniyle 9 aydır lenalidomide kullanmaktaydı. Lenalidomide bağlı yetişkin solunum yetmezliği sendromu tanısı aldı. Geç başlangıçlı lenalidomidin akciğerlerdeki yıkıcı etkilerini sunmayı amaçladık.

Anahtar Kelimeler: Lenalidomide, akciğer toksisitesi, yan etki, dispne

Introduction

Acute lung injury is a diffuse, inflammatory injury that causes increased pulmonary vascular permeability and lung weight that leads to loss of aerated tissue. Acute lung injury not only occurs as a result of inhaled substances, but also oral and parenteral drugs may be harmful [1]. There is a previously published case of organizing pneumonia leading to acute respiratory distress syndrome (ARDS) after long-term administration of lenalidomide [2]. Here, we presented an old man with various co-morbidities whose reason of lung injury was diagnosed as late effect of lenalidomide after detailed evaluation.

Case Report

A 77-year-old man with multiple myeloma (MM), chronic obstructive pulmonary disease (COPD) and a 50-pack-year smoking history presented with shortness of breath to our emergency department (ED). He was on oxygen use via concentrator at home. He had also history of pulmonary embolism (PE) two years ego and nephrectomy due to malignancy 10 years ago. He had been treated for 9 months with lenalidomide because of MM and warfarin medication due to PE. His body temperature was 38.6 °C with a pulse rate of 118 beats/minute and a blood pressure of 102/84 mmHg. His oxygen saturation was 72% on room air. The physical examination revealed generalized decrease in breath sounds, prolonged expiratory phase and basal crackling bilaterally. Arterial blood gas revealed hypoxemia with respiratory alkalosis with a pH: 7.51, PaO2: 50 mmHg, PCO2: 21 mmHg, HCO3: 16 mmol/L and a PaO2/FiO2 ratio of 121.9. We managed the patient with inhaled bronchodilator, i.v. prednisolone, i.v. cephtriaxone, ranitidine and low molecular weight heparin (enoxaparin). Laboratory tests included WBC: 7.200/µ, absolute neutrophil count: 6.000/µL, hemoglobin: 18 g/dL, hematocrit: 53.4%, platelet: 93.000/µ, C-reactive protein: 210 mg/dL, sedimentation: 23 mm, creatine kinase: 960U/L, creatinine: 1.6 mg/dL, blood urea nitrogen: 30 mg/dL. His bacteriological cultures (blood and sputum) were negative. There was sinus tachycardia on

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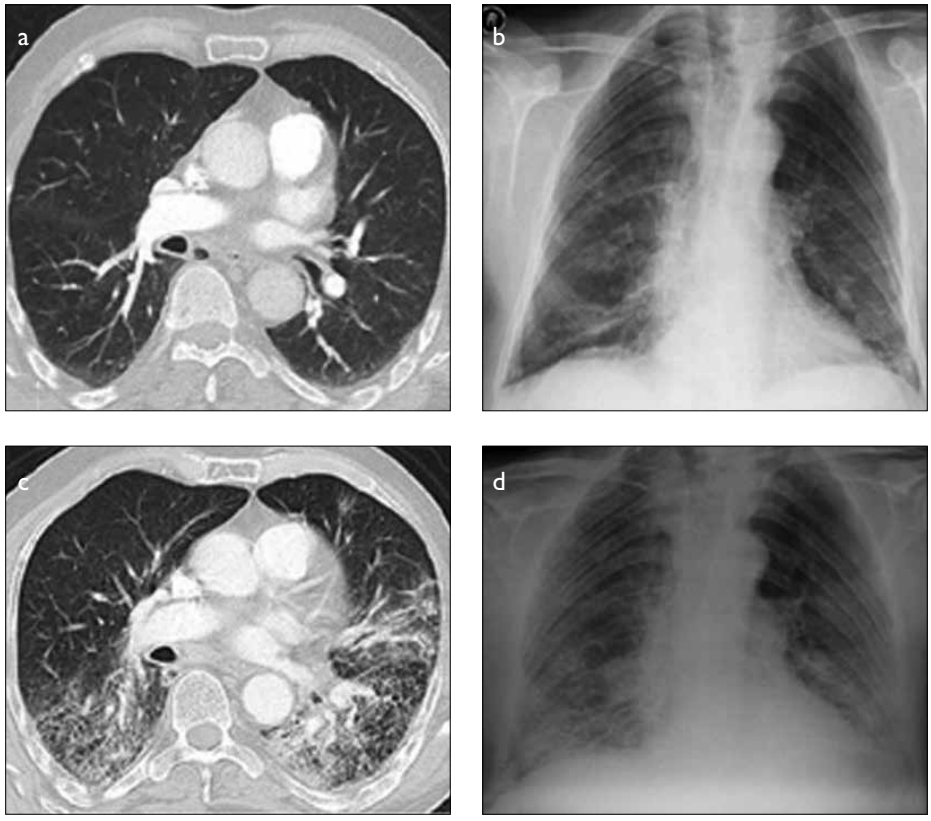

Figure 1. a-d. There was bilaterally diffuse panlobular emphysema and increased aeration in CT performed two years ago (a, b). New imaging showed interlobular septal thickening, increased fibrotic density, ground glass appearance and prominent bronchovascular markings (c). In addition, there was incomplete consolidation areas and increased opacity in the lingular lob and in bilateral lower lobes (d).

the 12-lead electrocardiography. Chest radiography revealed hyper- inflated lung fields bilaterally. We performed thoracic computerized tomography (CT) angiography to exclude acute pulmonary embolism and pneumonia. There was bilaterally diffuse panlobular emphysema and increased aeration in CT performed two years ago (Figure 1a, b), new imaging showed interlobular septal thickening, increased fibrotic density, ground glass appearance and prominent bronchovascular markings (Figure1c). In addition, there was incomplete consolidation areas and increased opacity in the lingular lob and in bilateral lower lobes (Figure 1d). Pulmonary arteries were evaluated as normal. We thought that this condition was induced by lenalidomide and the drug was withdrawn. Despite treatment with oxygen, bronchodilator, steroid and ceftriaxone during 3 days, his condition worsened with a PaO2/FiO2 ratio of 90.2 on 3rd day. We planned to perform bronchoscopy with broncho-alveolar lavage, but we could not due to the declining of his situation. We tried positive pressure ventilation; however, he died on the 3rd day due to severe adult respiratory distress syndrome possibly because of lenalidomide.

Discussion

With this case report, we wanted to attract attention to lenalidomide induced late-onset acute respiratory distress syndrome.

Our case had many common points with the case by Gorguner and Akgun. [1]. First, both of them had late-onset acute respiratory distress syndrome occurring after about 9 months. Second, they presented similar pneumonia symptoms and physical and laboratory examination findings. Third, our patient had mild thrombocytopenia while their case had bicytopenia. Forth, both of them did not respond to anti-biotherapy.

Our case was one of the few cases of ARDS possibly caused by lenalidomide. Despite prescribed high dose steroids and broad spectrum antibiotics, the patient got worse and died. We should pay attention to venous and/or arterial thrombosis caused by lenalidomide [3]. Besides, it was recently shown that warfarin did not change the plasma level or anticoagulant effect to warfarin or the plasma level of lenalidomide [4].

The reason of ARDS in this patient might be acute PE on the ground of chronic PE; or COPD exacerbation might cause similar clinical situation. However, we excluded these possibilities with imaging and laboratory findings.

In conclusion, physicians should be aware of late and destructive effects of lenalidomide on the lungs.

Informed Consent: Written informed consent was obtained from the patient.

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Conflict of Interest: No conflict of interest was declared by the authors.

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References

1. Gorguner M, Akgun M. Acute Inhalation Injury. Eurasian J Med 2010; 42: 28-35. [CrossRef]
2. Mankikian J, Lioger B, Diot E, et al. Pulmonary toxicity associated with the use of lenalidomide: case report of late-onset acute respiratory distress syndrome and literature review. Heart Lung 2014; 43: 120-3. [CrossRef]
3. Bagratuni T, Kastritis E, Politou M, et al. Clinical and genetic factors associated with venous thromboembolism in myeloma patients treated with lenalidomide-based regimens. Am J Hematol 2013; 88: 765-70. [CrossRef]
4. Weiss D, Knight R, Zhou S, Palmisano M, Chen N. Evaluation of Pharmacokinetic and Pharmacodynamic Interactions when Lenalidomide is Co-administered with Warfarin in a Randomized Clinical Trial Setting. Clin Drug Investig 2015; 35: 455-61. [CrossRef]