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Bleomycin-Induced Fatal Lung Toxicity Misdiagnosed as Covid-19 Pneumonia: A Case Report

Covid 19 Pnömonisi ile Karışan Bleomisine Bağlı Fatal Akciğer Toksisitesi: Olgu Sunumu

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Abstract

Bleomycin is a chemotherapeutic agent that is preferred for the treatment of testicular cancer, lymphoma and some squamous cell carcinomas. Bleomycin-induced lung toxicity is a common, but rarely fatal side-effect, and the radiological image of which can be confused with other reasons which makes organizing pneumonia pattern. We report here on the case of a 40-year-old male patient with testicular cancer with bleomycin-induced fatal lung toxicity that was misdiagnosed as Covid-19 pneumonia. The patient suffered subsequent fatal spontaneous pneumomediastinum, pneumothorax, and pulmonary interstitial and subcutaneous emphysema, and died from respiratory failure.

Key words: *Bleomycin, lung toxicity, covid-19, organizing pneumonia.*

Özet

Bleomisin testis kanseri, lenfoma ve bazı skuamöz hücreli kanserlerin tedavisinde tercih edilen kemoterapotik bir ajandır. Bleomisine bağlı akciğer toksisitesi sık karşılaşılmakla birlikte nadiren fatal yan etkiye neden olmaktadır. Ayrıca bleomisine bağlı akciğer hasarının radyolojik görüntüleri diğer organize pnömoni paterni yapan nedenler karışabilmektedir. Bu olgu sunumunda bilinen testis kanseri tanısı olan 40 yaşında erkek hastanın, Covid 19 pnömonisi ile karışan bleomisin bağlı fatal akciğer hasarı sunulmaktadır. Hasta bu zeminde spontan fatal pnömotoraks, pnömomediasten ve pulmoner intersisyal ve subkütan amfizem gelişimi nedeniyle respiratuar arrest kaynaklı kaybedilmiştir.

Anahtar Sözcükler: *Bleomisin, akciğer toksisitesi, covid-19, organize pnömoni.*

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Bleomycin is a chemotherapeutic agent that has been isolated from Streptomyces verticillus, and that has been used successfully for the treatment of testicular cancer, lymphoma and squamous cell carcinomas. The main limitations of bleomycin therapy are dose-dependent lung toxicity and fibrosis. It can rarely cause fatal lung toxicity. Accordingly, early diagnosis and treatment, and the prevention of limiting toxicities such as bleomycin-induced lung injury, are important.

CASE

A 40-year-old male patient with a history of diabetes and testicular cancer was admitted to the emergency department of our hospital with dyspnea. A physical examination revealed blood pressure of 120/63 mmHg, oxygen saturation of 83%, body temperature of 36.8°C and a C-reactive protein level of 0.022 g/L (N: 0.005 g/L). Other blood test results were normal. Following a physical examination, the patient was referred to the Radiology Department for an anteroposterior chest radiograph. A chest X-ray showed increased reticular opacities in the upper and lower zones, left lung multifocal scattered opacities in the perihilar region. A subsequent chest computed tomography (CT) revealed an organized stage of Coronavirus Disease 2019 (COVID-19) pneumonia with diffuse fibrotic changes (Figure 1 and 2). Based on the results, the patient was hospitalized in the infectious disease inpatient clinic. Hydroxychloroquine, azithromycin ceftriaxone were started. In the first week of hospitalization, the polymerase chain reaction (PCR) test result for COVID-19 was twice negative, and the respiratory pathogen test result and sputum culture were also negative. The patient was not evaluated by bronchoscopy. When serologic test results came up negative, the patient was re-evaluated based on medical history, which revealed that he had undergone three cycles of an etoposide-bleomycin-cisplatin chemotherapy protocol, and had actually experienced shortness of breath for two months, since the last dose. Following this re-evaluation, the patient was diagnosed with bleomycin-induced pneumonitis. Other medications were stopped, and steroid treatment was started. On the eighth day of hospitalization, the patient's partial pressure of oxygen (PaO_2) levels decreased suddenly and he was referred to the Radiology department for a further anteroposterior chest radiograph and chest CT, which revealed bleomycin-induced diffuse fibrosis, pulmonary interstitial pneumonia and spontaneous pneumomediastinum, pneumothorax and pulmonary interstitial emphysema (Figure 3 and 4). The patient was transferred to the intensive care unit and a chest tube was inserted. Despite the treatment protocol, the patient died from respiratory failure after a few hours.

DISCUSSION

Bleomycin, the most significant side effect of which is lung toxicity, is a chemotherapeutic agent that is preferred for the treatment of testicular cancer, lymphoma and some squamous cell carcinomas. Due to Bleomycin-induced lung toxicity (BILT), an endothelial and interstitial capillary edema, and an increase in surfactant overproduction and fibroblasts production were observed as a result of the mediators released by macrophages. These findings were consistent with the histological findings of diffuse alveolar damage, interstitial pneumonia and interstitial pulmonary fibrosis (1-3).

BILT presents with such clinical manifestations as fever, dyspnea, pleurisy and substernal pain. Patient older than 70, cumulative doses higher than 450 mg, renal insufficiency, administration path, oxygen treatment, smoking, granulocyte colony-stimulating factor (G-CSF) administration and bleomycin hydrolase activity are some of the predisposing factors (4-8).

A BILT diagnosis is based on exclusion, and is often excluded through microbiological and laboratory testing such as culture, gram staining of sputum and PCR. *Pneumocystis jiroveci* pneumonia (PJP) in particular should always be investigated (9).

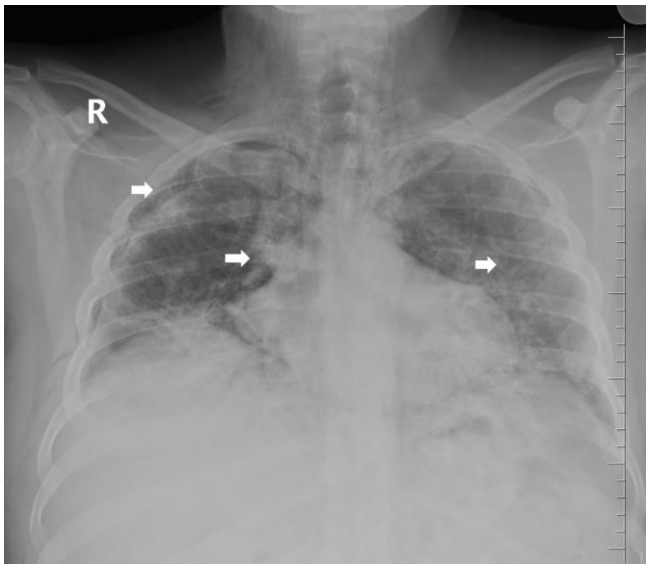

Figure 1: *Chest X-Ray showing volume loss in the right lung, increased reticular opacities in the upper and lower zones, left lung multifocal scattered opacities in the perihilar region (arrows)*

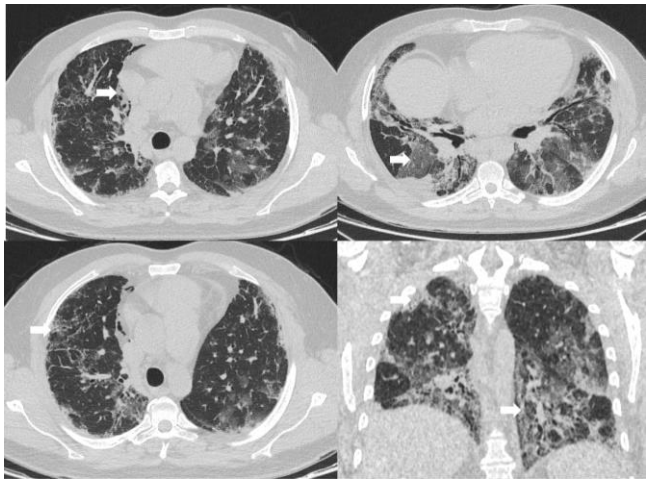

Figure 2: *Chest CT scan revealing bleomycin induced lung toxicity, diffuse lung fibrosis, multifocal ground glass opacities with peribronchial cuffing, and cylindrical bronchiectasis (arrows). This CT scan showed no pneumothorax or pneumomediastinum*

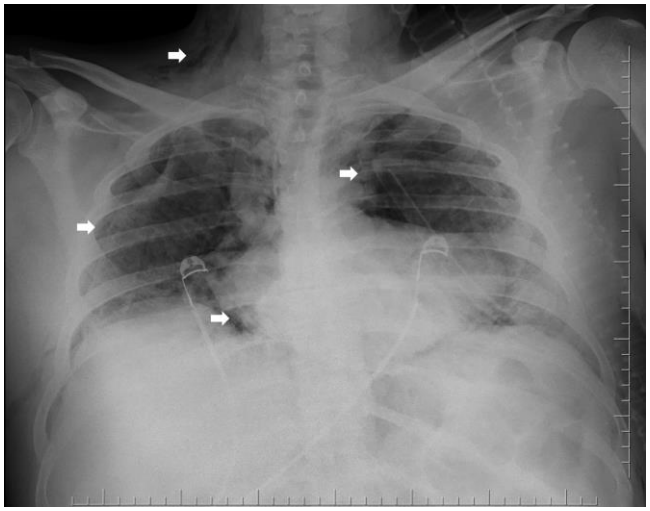

Figure 3: *Chest X-Ray showing bilateral pneumothorax and pneumomediastinum. Cardiac contours are clearly identified by pneumomediastinum. Subcutaneous emphysema seen in the right neck region*

Bleomycin lung toxicity is well established, and can be detected as bleomycin-induced pneumonitis (10). In chest high resolution computed tomography (HRCT) it can appear as diffuse alveolar damage, pulmonary fibrosis, organizing pneumonia pattern (OP) or nonspecific interstitial pneumonia pattern (NSIP). The HRCT features that imply underlying pulmonary fibrosis are a honeycomb pattern, traction bronchiectasis and reticulation. Diffuse alveolar damage is associated with ground-glass opacities and consolidations. The OP pattern manifests as bilateral multifocal ground glass opacifications and/or consolidations with peribronchial or subpleural distribution (9). CT findings of COVID-19 have enabled the diagnosis of the most common pattern-resembled OP (11).

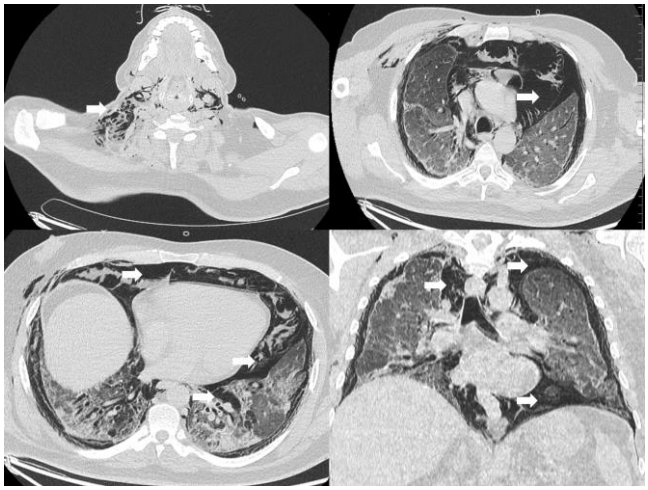

Figure 4: *Chest CT scan showing extensive subcutaneus empyhsma in the neck, bilateral extensive pneumothorax and pneumomediastinum. Bilateral pulmonary emphysema seen in the lower lobes (arrows)*

COVID-19 typically presents with ground glass opacities with or without consolidation, with a peripheral, posterior, and diffuse or lower lung zone distribution. Crazy paving pattern, reverse halo sign and other findings of OP patterns seen later in the disease are also typical signs (12). Primary or secondary organizing pneumonia, such as drug toxicity, connective tissue disease, some viral pneumonias and acute lung injury patterns are the main differential diagnoses of COVID-19 pneumonia.

The mortality rate associated with BILT is 1–2% (13). Spontaneous pneumomediastinum, pneumothorax and pulmonary interstitial emphysema are very rare fatal complications of the treatment, as identified in our case study, as well as in a few studies in literature (14-17).

CONCLUSION

The radiology of BILT can be confusing, and so patients may be misdiagnosed as COVID-19. During the ongoing pandemic, the history and follow-up of the patient, as well as the radiological images, must serve for correct diagnoses, as in our case.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - M.K., Y.C.G.; Planning and Design - M.K., Y.C.G.; Supervision - M.K., Y.C.G.; Funding -; Materials -; Data Collection and/or Processing -; Analysis and/or Interpretation -; Literature Review - Y.C.G.; Writing - M.K., Y.C.G.; Critical Review - M.K.

YAZAR KATKILARI

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