Case Report

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Acute interstitial pneumonia associated with vinorelbine usage

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Abstract:

Vinorelbine, an analogue of vinca alkaloids, has an antineoplastic effect. Adverse effects related to vinca alkaloids are rare. A 57-year-old patient who presented to the emergency room with dyspnea and back pain was hospitalized with the diagnosis of overload related to cardiac decompensation and complicated urinary tract infection due to its acute clinical and radiological findings. While under treatment, his respiratory failure progressed. Considering his history of vinorelbine usage 2 weeks prior, it was thought to be interstitial pneumonia. High-flow oxygen treatment and 250 mg/day pulse methylprednisolone for 3 days was started; after the fourth day, methylprednisolone was reduced and continued at 1 mg/kg/day. His oxygen need decreased on the seventh day of the treatment, and the findings on the chest X-ray regressed almost completely. However, the patient died due to acute gastrointestinal bleeding.

Keywords:

Interstitial lung diseases, respiratory failure, vinorelbine usage

Introduction

Vinorelbine, an analogue of vinca alkaloids, has an antineoplastic effect. It triggers a specific cell-death mechanism called mitotic apoptosis by breaking down the microtubule proteins in the tumor cells' skeleton. It is used for numerous malignant diseases such as genitourinary cancers and lymphoma and particularly in the treatment of metastatic breast cancer and non-small cell lung cancer. The most common adverse effects are neutropenia, nausea, vomiting, constipation, diarrhea, and pain on the site of injection.[1–3] The side effects of vinorelbine making interstitial lung disease are rare.[4,5] Due to its rarity, we present a case that was thought to have developed lung involvement related to vinorelbine usage.

Case Report

A 57-year-old patient presented to the emergency room (ER) with dyspnea and back pain. He had progressive dyspnea

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for the last 2–3 days and back pain. There was no respiratory system complaint except occasional cough and shortness of breath that had worsened in the last few days. He was operated on for bladder cancer, and an artificial bladder was made. He had undergone multiple chemotherapies (mitomycin C: December 2017–2018; gemcitabine and cisplatin: March 2020–October 2020; carboplatin and paclitaxel: October 2020–April 2021; adriamyine, vincristine, and cylophosphamide: April 2020–July 2020; and Vinorelbine: December 2021–2 weeks before exitus) and last received vinorelbine treatment 2 weeks ago.

On examination, he had normal body temperature, blood pressure of 132/78 mmHg, heart rate of 99 beats/min, and respiratory rate of 20 min^{-1}, and rales were heard at bilateral bases on thoracic wall auscultation. Oxygen saturation in the room air of the patient was 86%, and with 2 L/min oxygen, it was above 90%. Other systemic examinations were considered normal.

In the blood tests at the time of admission to the emergency department, serum CRP, creatinine, procalcitonin, WBC, and proBNP levels were 16 mg/dL, 2 mg/dL, 1.2 ng/mL, 13.8×10^3 μL^{-1}, 9103 pg/mL, respectively. COVID PCR test result was negative. WBC in urinalysis was 209/HPF, and urinary leukocytes were +2. In the thorax computed tomography (CT) [Figs. 1a-d] taken while the patient was at the ER, nonhomogeneous infiltration areas limited by bilateral fissures were observed in both upper lobes. These findings, although not typical, were evaluated in favor of overload due to cardiac decompensation, considering the acute development of symptoms.

He was hospitalized at the infectious diseases service with the diagnosis of a complicated urinary tract in-

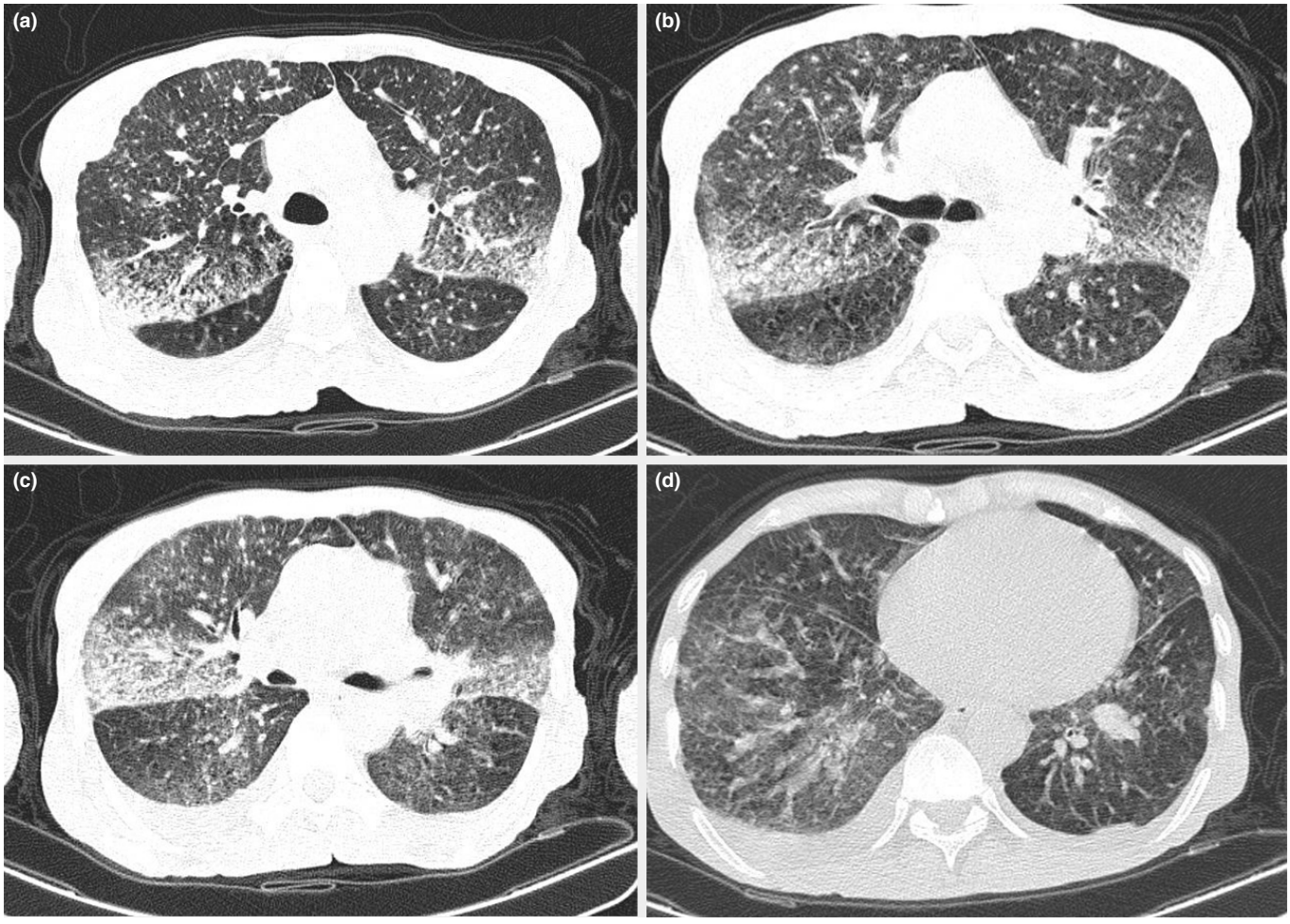

Figure 1: Thorax computed tomography (CT) section taken at the emergency room (ER)

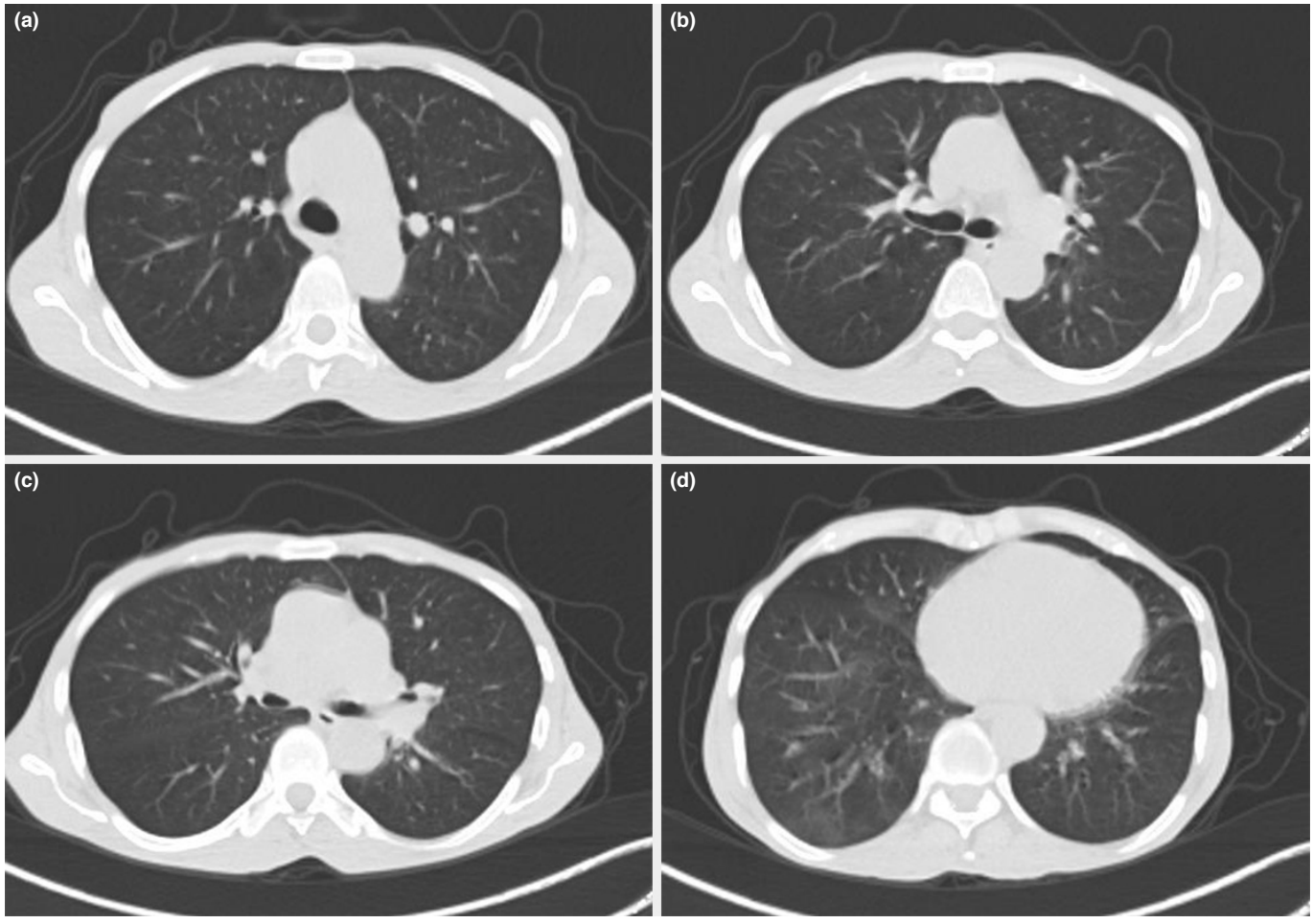

Figure 2: Thorax Thorax computed tomography (CT) section before Vinorelbine treatment

fection. Meropenem, ceftriaxone, and furosemide treatments were started. On the fifth day of follow-up, since the clinical findings did not improve and the dyspnea increased, it was thought that nosocomial pneumonia had developed. The current antibiotics were discontinued and linezolid, tazobactam–piperacillin, and fluconazole were started. With a new thorax CT, a chest disease consultation was requested. During consultation, the case was evaluated by comparing the current and before-the-admission thorax CTs. While there were not any significant pathological changes in parenchyma on the thorax CT that was taken before vinorelbine treatment was started [Figs. 2a-d], findings on the latest CT [Fig. 1c] were interpreted as a pathological state in which interstitial involvement is prominent. Cardiology consultation was recommended to rule out the possibility of cardiac overload. ProBNP control not investigated was a blood test. Echocardiography revealed an ejection fraction of 60%, normal left ventricular systolic function, minimal mitral valve failure, minimal aortic valve failure, and minimal tricuspid valve failure. Cardiological evaluation discarded

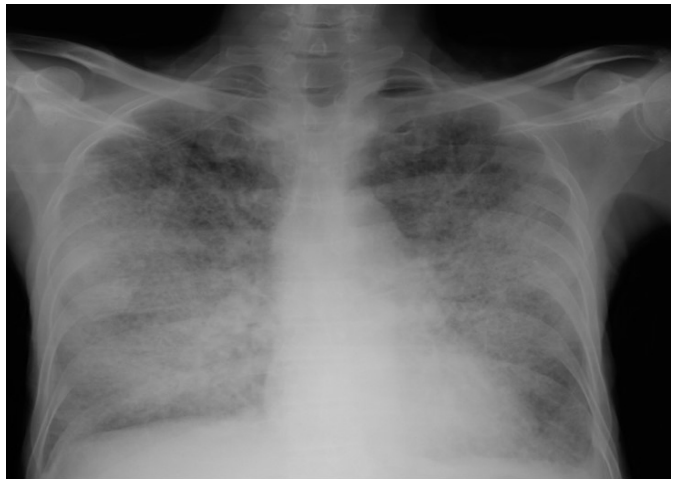

Figure 3: Chest X-ray taken while in the Infectious Diseases

the possibility of cardiac failure and cardiac overload. The respiratory specimen cultures were negative. *Legionella* and *Streptococcus pneumoniae* antigens in urine were not investigated.

On the chest X-ray taken while in the infectious diseases ward [Fig. 3], bilateral widespread reticular density increased in all zones and more prominently in the middle and lower zones, and consolidation areas with occasional air bronchograms were observed. The patient, whose saturation was 80% without oxygen support, was transferred to the chest diseases intensive care unit (ICU).

When admitted to the chest diseases ICU, the patient's saturation was 80%, his temperature was 36.6°C, heart rate was 70 min^{-1}, blood pressure was 120/88 mmHg, and respiratory rate was 33 min^{-1}. COVID PCR test was repeated, and the result was negative. Substernal retractions were present, and accessory respiratory muscles were observed to actively participate in respiration. *Auscultation* of the patient revealed *rales bilaterally* in bilateral middle and lower zones. The case was followed up with a non-rebreather mask. While being followed up with 10 L/min oxygen support with a non-rebreather mask, it was necessary to switch to high-flow oxygen therapy. Bronchoscopy could not be performed on the patient due to rapidly developing significant respiratory failure; thus, a sample could not be taken. The patient was administered 250 mg/day pulse methylprednisolone for 3 days and then continued as 1 mg/kg/day. Improvement in the symptoms and signs was observed in a short time. Oxygen saturation was 95% with non-rebreather mask oxygen support on the third day of ICU follow-up. A control chest X-ray was taken in the first week of methylprednisolone treatment. This chest X-ray was taken immediately after intubation [Fig. 4]. Significant regression was observed in the findings detected on the previous X-ray.

In the patient who was stabilized in regard to the respiratory system, melena developed on the seventh day of treatment. Gastroenterology consultation was requested, endoscopy was planned on the same day, and proton pump inhibitor infusion was started. He was intubated a few hours later with a sudden decrease in saturation and poor general condition. The patient who developed cardiopulmonary arrest did not respond to cardiopulmonary resuscitation and was accepted as exitus.

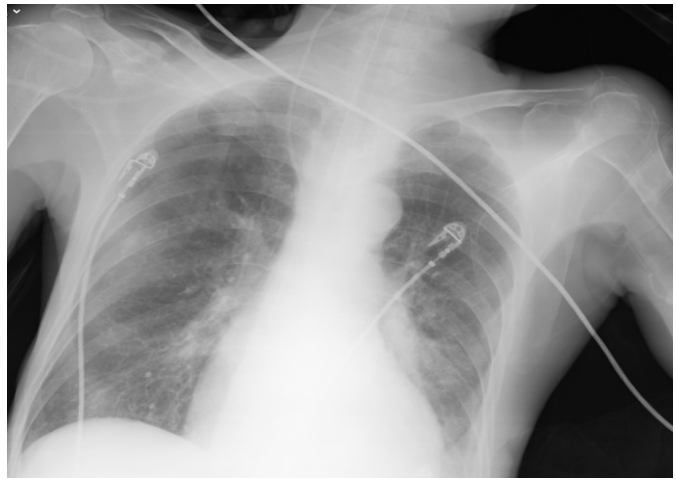

Figure 4: Control chest X-ray in the first week of methylprednisolone treatment (this is a chect x-ray belong immediately after intubation)

Discussion

Although vinorelbine is a chemotherapeutic agent with frequent adverse effects, pulmonary involvement is very rare. Interstitial lung involvement associated with vinorelbine use has been reported very rarely in the literature.[6] Therefore, we wanted to report a case of acute interstitial pneumonia with vinorelbine use 14 days ago as the only risk factor to explain it as vinorelbine-induced lung involvement. Treatment-related lung disease occurs in 5%–10% of patients receiving chemotherapy.[7] It is thought that 2.5%–3% of all interstitial lung diseases occur due to drugs.[8] Symptoms can range from cough to acute hypoxic respiratory failure. The clinical, laboratory, radiological, and histological findings of the diseases are nonspecific. In addition, the disease may occur within a few days after the use of the drug or sometimes even after years of use of the drug.[9] The diagnosis is based on the exclusion of other causes. The first goal in diagnosis is to suspect clinically and to take a good anamnesis. It should be questioned whether there are appetite suppressants, illegal drugs, and radiation therapy. While side effects such as bronchospasm due to some drugs develop rapidly, the side effects of drugs that cause lung fibrosis such as cyclophosphamide may begin within years. Abnormal radiological findings should be suspected. Infection, primary tumors, lymphangitic spread, radiation injury, pulmonary thromboembolism, and metastasis should be considered in the differential diagnosis. Also, diagnostic criteria for drug-induced lung

diseases are determined: (i) confirmation of drug use, dose, and duration; (ii) consistent clinical, imaging, and histopathological findings observed with the same drug before; (iii) exclusion of other lung diseases; (iv) improvement after discontinuation of the suspected drug; and (v) reappearance of symptoms with readministration of the drug.[10]

Multiple chemotherapy drugs were administered to our patient for 1 year after the diagnosis of bladder cancer. It was determined that there were no acute or subacute respiratory system side effects while using carboplatin, paclitaxe, adriamyine, vincristine, and cylophosphamide. It was found that vinorelbine was given 2 weeks before the onset of symptoms. When radiological and clinical findings were evaluated together with the absence of any other etiological risk factor that could be associated with interstitial pneumonia, vinorelbine-induced interstitial pneumonia was considered. In the literature, although rare, two different involvements related to the use of vinorelbine have been reported. The first is in the acute phase and is characterized by bronchospasm, fever, and pulmonary infiltrates that occur within minutes after treatment. The second is progressive dyspnea and diffuse interstitial involvement that occurs in the subacute period hours or days after treatment.[6] Treatment of drug-induced interstitial pneumonia is stopping the drug used and starting corticosteroid therapy. A complete response to corticosteroid treatment is usually obtained.[5] Thus, we applied pulse steroid to the patient for 3 days. Afterward, we continued with 1 mg/kg/day steroid. We received a response to the treatment in a short time. Although procedures such as follow-up and parenchymal biopsy are required for the diagnosis, the response to steroids in a short time supports our diagnosis. However, the patient died due to treatment complications. In addition, the fact that the radiograph taken after intubation is normal indicates that clinical worsening is due to treatment complications.

As a result, although lung involvement associated with vinorelbine is rare, it should also be considered when questioning chemotherapeutic agents in cancer cases with rapidly developing interstitial pneumonia with no other explanation. Side effects may be underreported because they are overlooked in the routine or because complaints and findings are not associated with the drug. In addition, care should be taken to not develop treatment complications, as in the case of our patient who died due to treatment complications although we received a good response to the treatment.

Informed Consent

Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

Conflicts of interest

There are no conflicts of interest.

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Nil.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept – A.A., M.Y., Z.A.A.; Design – A.A., M.Y.; Supervision – Z.A.A., F.Y.; Materials – A.A., M.Y.; Data collection &/or processing – M.Y., Z.A.A.; Analysis and/or interpretation – A.A., M.Y.; Literature search – A.A., F.Y.; Writing – A.A., M.Y., Z.A.A.; Critical review – A.A., F.Y.

References

1. Di Maio M, Gridelli C, Gallo C, Shepherd F, Piantedosi FV, Cigolari S, et al. Chemotherapy-induced neutropenia and treatment efficacy in advanced non-small-cell lung cancer: a pooled analysis of three randomised trials. Lancet Oncol 2005;6:669–77. [CrossRef]
2. de Matteis A, Nuzzo F, Rossi E, Landi G, Perrone F. Intestinal side-effects of docetaxel/vinorelbine combination. Lancet 2000;355:1098–9. [CrossRef]
3. Colleoni M, Gaion F, Vicario G, Nelli P, Pancheri F, Sgarbossa G, et al. Pain at tumor site after vinorelbine injection: description of an unexpected side effect. Tumori 1995;81:194–6. [CrossRef]
4. Zerna C, Guenther M, Folprecht G, Puetz V. Acute ischaemic stroke and myocardial infarction after chemotherapy with vinorelbine for non-small cell lung cancer: a case report. J Chemother 2017;29:49–53. [CrossRef]
5. Tanvetyanon T, Garrity ER, Albain KS. Acute lung injury associated with vinorelbine. J Clin Oncol 2006;24:1952–3. [CrossRef]
6. Kouroukis C, Hings I. Respiratory failure following vinorelbine tartrate infusion in a patient with non-small cell lung cancer. Chest 1997;112:846–8. [CrossRef]
7. Raissy HH, Harkins M, Marshik PL. Drug- induced pulmonary disease. In: Dipiro JT, Talbert RL, Yee GC et al, editors. Pharmacotherapy: A Pathophysiologic Approach. 7th ed. Mcgraw-Hill;2008. p.521–34
8. Dimopoulou I, Bamias A, Lyberopoulos P, Dimopoulos MA. The pulmonary side-effects induced by novel antineoplastic agents have not been well characterized. Ann Oncol 2006;17:372–9. [CrossRef]

9. Matsuno O. Drug-induced interstitial lung disease: mechanisms and best diagnostic approaches. Respir Res 2012;13:39. [CrossRef]
10. Bradley B, Branley HM, Egan JJ, Greaves MS, Hansell DM, Harrison NK, et al; British Thoracic Society Interstitial Lung Disease Guideline Group, British Thoracic Society Standards of Care Committee; Thoracic Society of Australia; New Zealand Thoracic Society; Irish Thoracic Society. Interstitial lung disease guideline: the British Thoracic Society in collaboration with the Thoracic Society of Australia and New Zealand and the Irish Thoracic Society. Thorax 2008;63:v1–58. Erratum in: Thorax 2008;63:1029. [CrossRef]