LETTER TO THE EDITOR
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Extramedullary Hematopoiesis Causing Massive Pleural Effusion in a Chronic Lymphocytic Leukemia Patient: A Rare Case

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To the Editor,

Extramedullary hematopoiesis (EMH) refers to the production and maturation of blood cells outside the bone marrow, sometimes referred to as "myeloid metaplasia [1, 2]. EMH is a compensatory response to many hematologic diseases, including myelofibrosis, thalassemia, and sickle cell anemia [3]. The pathophysiology of EMH remains poorly understood. EMH is thought to be caused by several substances, including cytokines, chemokines, adhesion molecules, and proteases, which promote the growth and differentiation of bone marrow stem cells. Any location can be affected by EMH, however, the liver and spleen are the most frequently affected. In contrast to the lungs, para-vertebral areas are rather typical locations for intrathoracic EMH [2]. The posterior mediastinum, or para- or intra-vertebral locations, is the most often affected EMH site in thorax. Paravertebral EMH patients typically don't have any symptoms. On the other hand, it is uncommon to observe individuals with pulmonary-EMH in the alveolus, alveolar septum, pleura, or pleural effusion; these patients often exhibit coughing, dyspnea, and, less frequently, chest discomfort [4]. In this report, we will present a very rare chronic lymphocytic leukemia (CLL) patient who was hospitalized with a 10 cm EMH in the lung and massive pleural effusion. This patient accepted to have his case published in a journal. A 55-year-old male patient was admitted to the neurosurgery department with difficulty in walking. Magnetic resonance imaging (MRI) detected a mass in the thoracic paravertebral region, and the patient underwent biopsy of this mass. The biopsy taken from the patient's paravertebral region was reported as compatible with EMH. Since the patient's leukocyte count was $90x10^9$/L during follow-up, the patient was referred to the hematology clinic. Lymphocyte-predominant leukocytosis was seen in the patient's peripheral smear. The patient was diagnosed with CLL based on bone marrow biopsy and flow cytometry results. The patient's CLL-IPI score at diagnosis was evaluated as 3, intermediate risk. The patient's thoracic computed tomography (CT) reported bilateral hemothorax and multiple masses, the largest of which was 82x60 mm. Thoracic CT revealed bilateral hemothorax and multiple retropleural masses. In addition, multiple lymphadenopathy was seen in the parailiac and presacral regions on abdominal CT. The patient was started on rituximab and bendamustine treatment. Chemoimmunotherapy was initiated due to the need for urgent treatment without waiting for the genetic result, due to the patient's clinical

condition, with current findings, and walking difficulty for to treat the underlying disease. At the initiation of treatment, TP53 mutation, del(17p), and IGHV mutation status were unknown; ZAP70 and CD38 were detected as negative in flow cytometry. No positive mutation was detected in the genetic results reported during follow-up. After the second course, the patient was hospitalized with dyspnea and massive pleural effusion covering almost the entire left lung. The patient's thoracic CT showed that the 82x60 mm mass had increased to 100x80 mm. A biopsy was taken from the mass. The patient's left lung lower lobe biopsy was reported to be immunohistochemically CD13, CD33, MPO, Glycophorin-A, and CD61 positive, findings consistent with pulmonary extramedullary hematopoiesis. Sampling and drainage thoracentesis were performed.

The effusion was found to be transudative. Many mature lymphocytes were observed in the pleural fluid smear preparations. The patient was consulted with thoracic surgery, and a thoracic tube was inserted. When the fluid from the tube decreased, the patient underwent pleurodesis with bleomycin. The patient was consulted with radiation oncology for low-dose radiotherapy (RT) and is being followed up in the hematology department. The paravertebral space inside the posterior mediastinum, the ribs, and the lung parenchyma are the most often seen sites for intrathoracic EMH, an uncommon but well-described occurrence [5]. Usually, it is discovered incidentally in a patient with a recognized hematological disorder [6]. EMH foci are extremely susceptible to radiation therapy (RT), the usual treatment approach [6], therefore, low-dose RT may be the preferred treatment in symptomatic cases. In conclusion, as in our case, EMH findings should be kept in mind in the presence of pleural effusion and masses refractory to treating primary hematological disease. RT is the recommended treatment method for those with symptoms, because EMH tissue is extremely sensitive to radiation.

Keywords: Chronic lymphocytic leukemia, extramedullary hematopoiesis, radiotherapy, pleurodesis

Informed Consent: The patient provided written informed consent for publication.

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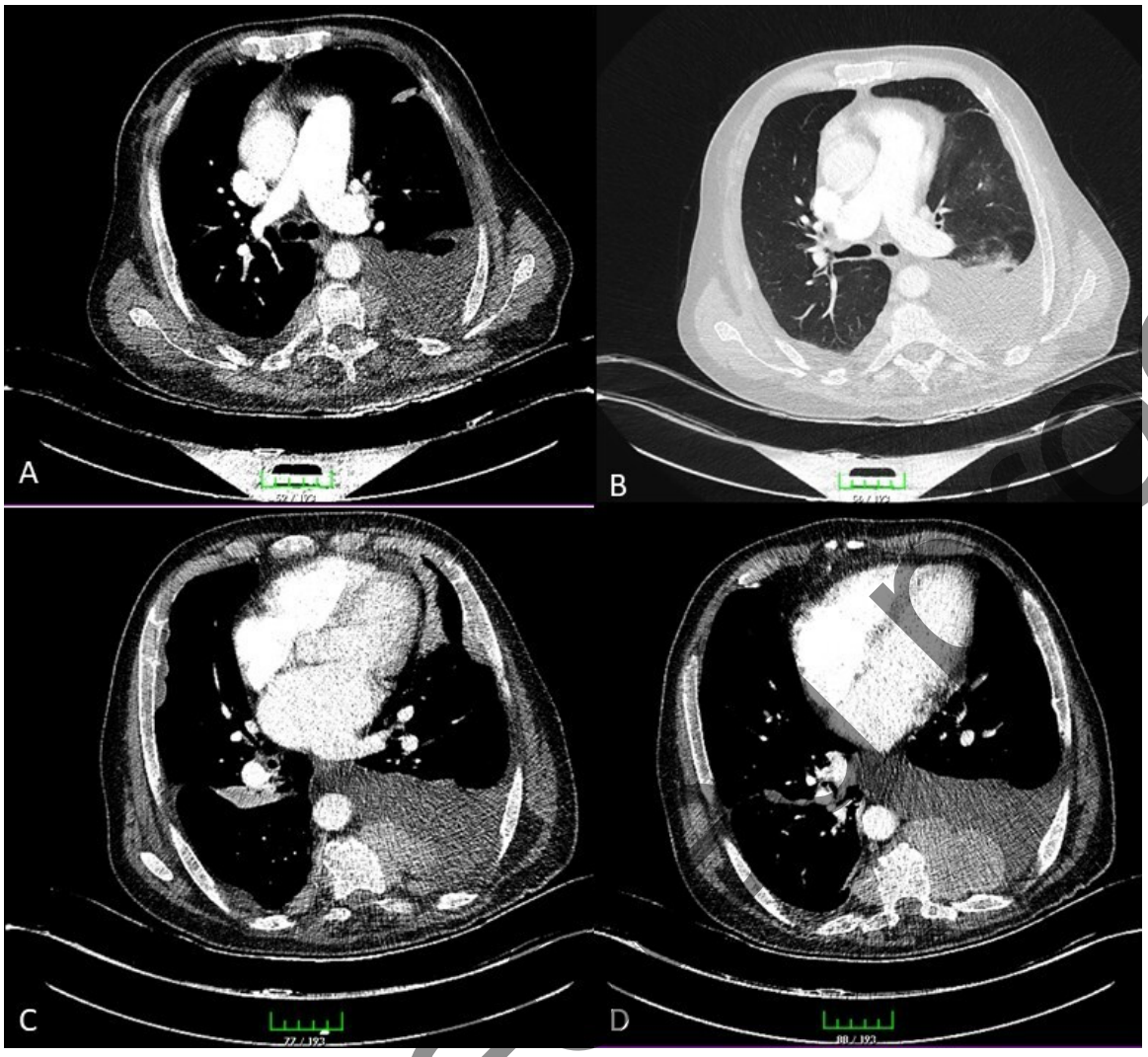

Figure 1. Pleural effusion in the left lung and dilatation of the left pulmonary artery (A), pleural effusion in the left lung (B), multiple pleural lesions, the largest in the left lower pleura (C), and lesion in the left lower lobe (D).