JGG Online First 2022;Mar 1
doi: 10.36150/2499-6564-N479

Dyspnea as a symptom of progressive chronic myeloproliferative disease: a rare case of hemorrhagic alveolitis and pulmonary fibrosis, due to extramedullary erythropoiesis

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We report the case of a 75-year-old man, who was admitted to the General Medicine Ward of the San Raffaele Hospital for asthenia, and worsening dyspnea, in July 2020. The patient had a diagnosis (2008) of polycythemia vera (PV), which had been treated with phlebotomies, and since 2010, with hydroxyurea. Evolution from PV to secondary myelofibrosis was demonstrated in December 2017. His comorbidity burden was high, due to hypertension, ischemic heart disease, relapsing transient ischemic attacks, recurrent episodes of supraventricular tachycardia, and right bundle branch block. In January 2020, he was diagnosed with interstitial lung disease of undetermined etiology (bronchoalveolar lavage negative for tuberculosis, Pneumocystis Jirovecii, Aspergillus, and malignant cancer cells; spirometry: restrictive pattern; diffusing lung capacity for carbon monoxide: reduced).

To investigate the etiology of dyspnea, the patient underwent an echocardiogram, which revealed severe pulmonary hypertension, (PAPs 75-80 mmHg) and a chest computed tomography, (CT) which showed ground glass areas with an inflammatory aspect, involving almost all-lung parenchyma, and diffuse lymphadenopathies (Fig. 1). Therefore, the patient was further investigated with a second bronchoalveolar lavage cytology, which showed abundant macrophages and hemosiderin pigments. ANCA-related vasculitis was excluded.

Based on his clinical history, imaging, and cytologic findings, it was made a probable diagnosis of hemorrhagic alveolitis, secondary to extramedullary hematopoiesis. The patient continued cytoreductive therapy with hydroxyurea, in association with corticosteroids, but progressed to end-stage respiratory failure in a few months.

Lung involvement by myeloproliferative diseases is extremely rare, though its incidence could be higher than the one reported in case series [1]. It occurs, mainly, in advanced fibrotic stages, when bone marrow haematopoiesis is significantly impaired [1]. Marrow fibrosis displaces pluripotent hematopoietic stem cells, which are homed and sequestrated in other organs, where they proliferate, and differentiate to make extramedullary haematopoiesis (EMH) [2].

In addition, myeloproliferative neoplasms can induce peribronchiolar fibrosis, and interstitial lung fibrosis [3,4]. This can lead to pulmonary vascular remodeling [5], with a sustained elevation in pulmonary pressure [6]. Older patients seem to be at higher risk of developing pulmonary hypertension, (PH) because of a higher comorbidity burden, and/or a longer hematologic

Received: November 17, 2021
Accepted: December 7, 2021

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How to cite this article: Frangi C, Damanti S, Bozzolo EP, et al. Dyspnea as a symptom of progressive chronic myeloproliferative disease: a rare case of hemorrhagic alveolitis and pulmonary fibrosis, due to extramedullary erythropoiesis. Journal of Gerontology and Geriatrics Online First 2022;Mar 1. https://doi.org/10.36150/2499-6564-N479

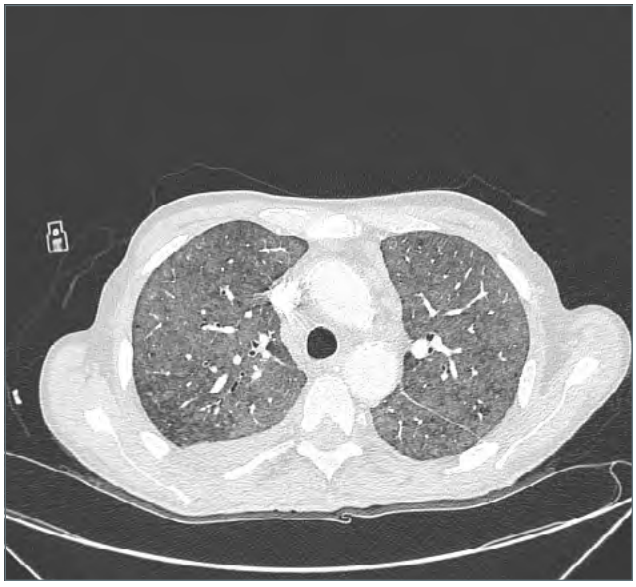

Figure 1. Computed tomography scan of the patient showing ground glass areas with an inflammatory aspect involving almost all-lung parenchyma.

disease duration [7]. The development of pulmonary hypertension could worsen the prognosis [8].

Patients with pulmonary EMH and PH, frequently, manifest dyspnea. Chest CT is one of the main radiologic tools to detect pulmonary EMH. Radiologic aspects of EMH can be heterogeneous: diffuse ground-glass opacity, pulmonary nodules, multilobulated masses, interstitial thickening, and interstitial fibrosis [2,9]. Lung biopsy, which would be the gold standard for the diagnosis of pulmonary EMH, is seldom performed, because of high hemorrhagic risk. A presumptive diagnosis based on clinical history and radiologic findings is frequently sufficient to set up an appropriate clinical management, which is mainly directed to the treatment of the hematologic disease. Pulmonary extramedullary hematopoiesis should be taken into account in any patient with chronic myeloproliferative neoplasms, developing progressive respiratory failure and lung infiltrates.

Ethical consideration
Not required

Acknowledgement
Not required

Conflict of interest
The Authors declare no conflict of interest.

Funding
This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Informed consent
Obtained from the patient

Author's contribution
All Authors made substantial contributions to all of the following: (1) the conception and design of the case report, or acquisition and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, (3) final approval of the version to be submitted.

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