Laudelino *et al.*
Surgical and Experimental Pathology (2023) 6:5
https://doi.org/10.1186/s42047-023-00131-3

Surgical and Experimental Pathology

CASE REPORT

Open Access

Pulmonary hemosiderosis secondary to mitral stenosis: a case report

Jadson Soares Laudelino[1*], Fernando Moreira Batista Aguiar[1], Filadélfia Passos Rodrigues Martins[1], Rosineli Leopoldino de Oliveira[1], Glauberto Rolim Cartaxo Bezerra Cruz[2] and Aline Lobo Ramos[1]

Abstract

Background Pulmonary hemosiderosis is a rare disease that may be idiopathic or have a secondary etiology, such as mitral stenosis. The disease is a clinical and functional consequence of iron overload in the lungs in the form of hemosiderin. The diagnosis should be considered in patients with miliary nodules on chest tomography.

Case presentation We report a case of a 30-year-old man with severe mitral stenosis who presented with chest pain and dyspnea. High-resolution chest tomography showed bilateral centrilobular micronodules. The diagnosis of pulmonary hemosiderosis secondary to mitral stenosis was suggested by transbronchial biopsy.

Conclusion The diagnosis of idiopathic pulmonary hemosiderosis requires the exclusion of other etiologies of alveolar hemorrhage, including infections and vasculitis. One possible etiology is mitral stenosis.

Keywords Hemosiderosis, Mitral valve stenosis, Miliary tuberculosis

Background

Pulmonary hemosiderosis is a rare disease characterized by the extravasation of blood from the alveolar capillaries to lung tissue. As an outcome, hemoglobin transforms into hemosiderin, which is phagocytized by macrophages, resulting in a chronic inflammatory response (Santos et al. 2012). The disease is a clinical and functional consequence of iron overload in the lungs in the form of hemosiderin (Ioachimescu et al. 2005). The clinical manifestations of hemosiderosis may include iron deficiency anemia, repeated episodes of hemoptysis and diffuse pulmonary infiltrates (Chen et al. 2008). The specific incidence and prevalence of pulmonary hemosiderosis are currently unknown (Saha 2021). The disease is reported to occur in up to 16% of patients with mitral stenosis (Agrawal et al. 2011).

*Correspondence:
Jadson Soares Laudelino
jadsonlaudelino@gmail.com
[1] Dr. Carlos Alberto Studart Gomes Hospital of Messejana, Fortaleza, Brazil
[2] Unichristus University, Fortaleza, Brazil

The diagnosis should be suspected in patients with miliary nodules on chest radiography, especially those with mitral stenosis (Agrawal et al. 2011). Being a high-prevalence country for tuberculosis, the diagnosis of miliary tuberculosis may be considered (Agrawal et al. 2011).

Macrophages with hemosiderin may be found in bronchoalveolar lavage and lung biopsy (Agrawal et al. 2011). In mitral stenosis, pulmonary parenchymal manifestations are a consequence of increased postcapillary pressures (Ioachimescu et al. 2005). Hemosiderosis may be idiopathic or secondary to a systemic disease (Agrawal et al. 2011). When an etiology cannot be determined, the diagnosis of idiopathic pulmonary hemosiderosis is suggested (Ioachimescu et al. 2004). One possible etiology is mitral stenosis (Agrawal et al. 2011).

Case report

The individual in this case study is a 30-year-old man, a farmer. The patient was admitted with atypical, intermittent chest pain and progressive dyspnea for approximately 3 years, with worsening of symptoms in the prior month. He denied hemoptysis, cough or weight loss.

There was a recent hospitalization on January third 2022 for pneumonia, when he was diagnosed with mitral stenosis and tricuspid regurgitation. The patient was still under outpatient follow-up; however, he returned to the hospital on February second 2022 due to worsening dyspnea and chest pain. Upon physical examination, the heart rate was sixty-three beats per minute, a respiratory rate was twenty-two incursions per minute, presence of fine crackles in the lung bases. The remainder of the physical examination was normal. Hemogram results were as follows: hemoglobin, 13.2 g/dL; leukocytes, 8,700/mm^3; platelets, 296,000/mm^3; electrolytes, a coagulation profile and normal renal function. The electrocardiogram showed atrial fibrillation and biventricular overload. An echocardiogram was performed, with the following findings: (1) significant mitral stenosis with a valve area of 0.4 cm^2, plus a mean gradient of the left atrium-left ventricle equal to 13 mmHg, (2) significant tricuspid regurgitation (vena contracta, 8 mm), (3) giant thrombus carpeting the roof and interatrial septum of the left atrium, (4) severe pulmonary hypertension (pulmonary artery occlusion pressure 109 mmHg, through tricuspid reflux), (5) dilation of the right ventricles, (6) systolic dysfunction of the right ventricle with tricuspid annular plane systolic excursion (TAPSE) of 13 mm and (7) left ventricular ejection fraction of 57%.

Because of the diagnosis of severe mitral stenosis of rheumatic etiology and significant tricuspid regurgitation, the following were performed: mitral valve replacement with a bioprosthesis, tricuspid repair, thrombus resection and left auricle resection. In the postoperative period, the patient developed hypoxia with 90% saturation in ambient air, and cough with little expectoration, requiring a high-flow nasal catheter and high doses of vasoactive drugs. Antibiotic therapy with piperacillin-tazobactam was initiated. Chest radiography showed bilateral micronodular infiltrate (Fig. 1), and high-resolution chest tomography showed centrilobular micronodules with a bilateral distribution (Fig. 2). Transfer to the pulmonology unit was requested for investigation of both hypoxemia and the radiological presentations.

The initial hypotheses were pulmonary vasculitis and tuberculosis. The search for anti-neutrophil cytoplasmic antibodies (ANCAs) and other connective tissue diseases was negative. For the investigation of tuberculosis, AFB (acid-fast bacillus) and rapid molecular tests using sputum were negative.

The patient was then subjected to bronchofibroscopy with cytology of the lavage and transbronchial lung biopsies on March fifteenth 2022, which showed predominantly lymphocytic inflammatory infiltrate in connective tissue with the presence of hemosiderophages (Fig. 3). The final diagnosis was pulmonary hemosiderosis secondary

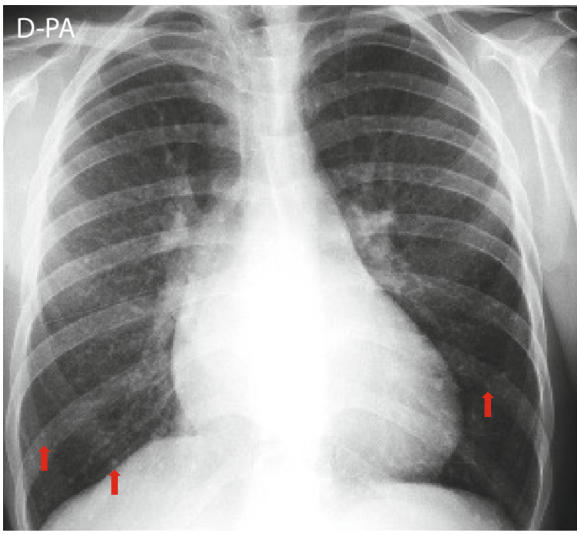

Fig. 1 Chest radiograph showing bilateral micronodular infiltrate (red arrows)

to rheumatic mitral stenosis. The patient progressed with clinical improvement after antibiotic therapy, noninvasive ventilation and respiratory physiotherapy. The patient was weaned from oxygen therapy and experienced cough recrudescence. The etiology of the clinical condition was explained to the patient, and he was discharged from the hospital with outpatient follow-up with cardiology.

Discussion and conclusion

Hemosiderosis is a term derived from the Greek hemo (blood) and sideros (iron) and is characterized by the focal or generalized accumulation of iron in the form of hemosiderin (Ioachimescu et al. 2005). Hemosiderin is a pigment that serves as a form of intracellular iron storage and appears as brownish yellow granules in Perls Prussian blue stain (Ioachimescu et al. 2005). In the lung,

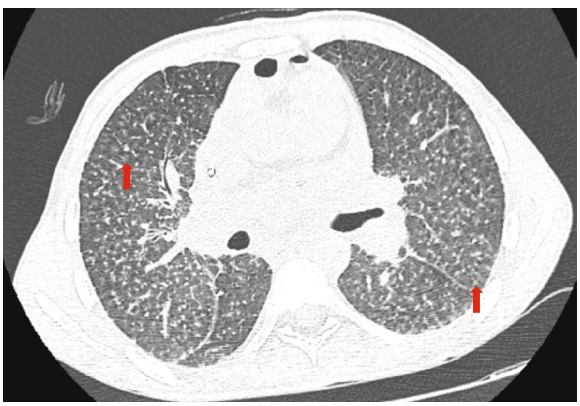

Fig. 2 High-resolution chest tomography showing bilateral centrilobular micronodules (red arrows)

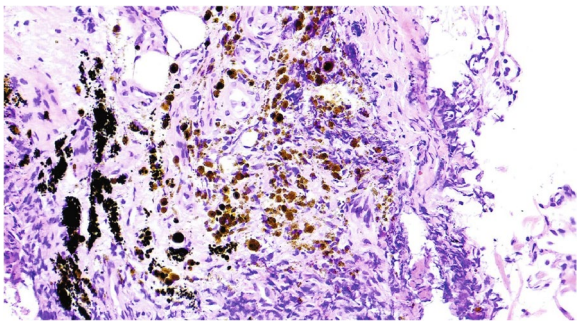

Fig. 3 Lung tissue with predominantly lymphocytic inflammatory infiltrate with hemosiderophages (200 micrometers, hematoxylin and eosin). Bronchial mucosa with ciliated columnar epithelial lining and, in the submucosa, moderate inflammatory infiltrate, predominantly lymphocytic in connective tissue with foci of anthracosis and hemosiderophages

hemosiderin accumulation seems to derive from episodes of repeated pulmonary hemorrhage due to rupture of the anastomotic channels between the lung and the bronchial artery (Chamusco et al. 1988). After a bleeding episode, alveolar macrophages convert the iron from hemoglobin into hemosiderin, but the ability of macrophages to metabolize iron quickly diminishes, and the presence of iron in the alveoli can lead to local lesions or fibrosis (Ioachimescu et al. 2005).

Hemosiderosis may be idiopathic or secondary to a systemic disease. The main secondary causes are collagen vascular diseases, coagulation disorders and cardiovascular disorders, particularly mitral stenosis (Agrawal et al. 2011). The latter was the etiological cause of pulmonary hemosiderosis in the patient reported in the study.

Mitral stenosis usually results from rheumatic heart disease but can be congenital (Woolley and Stark 1999). Rheumatic heart disease affects more women than men and is more prevalent in developing countries (Woolley and Stark 1999). Patients are usually asymptomatic until the abrupt onset of atrial fibrillation or symptoms of pulmonary venous hypertension (Woolley and Stark 1999). The patient in the study presented atrial fibrillation and pulmonary artery hypertension with overload of the right chambers.

The radiological examination of patients with hemosiderosis secondary to mitral stenosis may show multiple nodular opacities simulating those observed in miliary tuberculosis, sarcoidosis or some pneumoconiosis (Taylor and Strong 1955). However, not all hemosiderin nodules are visible on radiography, but if they are large enough, they may be seen as miliary opacities (Taylor and Strong 1955). Histologically, idiopathic or acquired pulmonary hemosiderosis is characterized by hemosiderin-loaded macrophages and variable interstitial fibrosis (Sahn and Levine 1950). The analysis of bronchoalveolar lavage showing hemosiderin-loaded macrophages is indicative of pulmonary hemosiderosis (Saha and Milman 2021). A definitive diagnosis can be provided through surgical lung biopsy or transbronchial biopsy (Saha and Milman 2021).

In the case reported here, the patient exhibited a pattern of miliary nodules disseminated throughout the lung parenchyma on high-resolution chest tomography, leading to the suspicion of miliary tuberculosis. The culture of bronchoalveolar lavage was negative for mycobacterial infections and fungi. Pulmonary hemosiderosis was suggested by transbronchial biopsy.

Biopsy samples should be analyzed in detail to exclude fungal diseases, mycobacterial infections, sarcoidosis, berylliosis and Wegener's granulomatosis (Ioachimescu et al. 2005).

The treatment of hemosiderosis secondary to heart valve disease includes valve repair and/or valve replacement (Agrawal et al. 2011). The patient in this study underwent mitral valve replacement with a decalcifying bioprosthesis and tricuspid valve repair. However, the clinical improvement was not achieved immediately because he acquired nosocomial pneumonia. After antibiotic therapy, the patient progressed with clinical improvement and was discharged with cardiology outpatient monitoring.

In conclusion**,** miliary pulmonary nodules can be seen in radiological images of patients with pulmonary hemosiderosis secondary to mitral stenosis, and this fact should be considered as a differential diagnosis of miliary tuberculosis. Establishing a diagnosis of hemosiderosis secondary to valve etiology is important because successful treatment of the disease can be achieved with valvuloplasty and/or valve replacement.

Acknowledgements
Not applicable.

Authors' contributions
Jadson Soares Laudelino, Fernando Moreira Batista Aguiar, Filadélfia Passos Rodrigues Martins, Rosineli Leopoldino de Oliveira, and Glauberto Rolim Cartaxo Bezerra Cruz were responsible for the study design, literature review, interpretation of clinical data and text review. Aline Lobo Ramos was responsible for the preparation and interpretation of the histological slides. The author(s) read and approved the final manuscript.

Funding
The authors did not receive financial support for the research, authorship and/or publication.

Availability of data and materials
Not applicable.

Declarations

Ethics approval and consent to participate
Ethics approval was obtained from the research ethics committee of Hospital de Messejana Dr. Carlos Alberto Studart Gomes, Fortaleza—Ceará. Protocol number: 59978922.4.0000.5039.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Received: 28 September 2022 Accepted: 7 March 2023
Published online: 20 March 2023

References

Agrawal G, Agarwal R, Rohit MK, Mahesh V, Vasishta RK. Miliary nodules due to secondary pulmonary hemosiderosis in rheumatic heart disease. World J Radiol. 2011;3:51–4.
Chamusco RF, Heppner BT, Newcomb EW 3rd, Sanders AC. Mitral stenosis: an unusual association with pulmonary hemosiderosis and iron deficiency anemia. Mil Med. 1988;153:287–9.
Chen CH, Yang HB, Chiang SR, Wang PC. Idiopathic pulmonary hemosiderosis: favorable response to corticosteroids. J Chin Med Assoc. 2008;71:421–4.
Ioachimescu OC, Sieber S, Kotch A. Idiopathic pulmonary haemosiderosis revisited. Eur Respir J. 2004;24:162–70.
Ioachimescu OC, Farver C, Stoller JK. Hemoptysis in a 77-year-old male with a systolic murmur. Chest. 2005;128:1022–7.
Saha BK. Idiopathic pulmonary hemosiderosis: a state of the art review. Respir Med. 2021;176:1–9.
Saha BK, Milman NT. Idiopathic pulmonary hemosiderosis: a review of the treatments used during the past 30 years and future directions. Clin Rheumatol. 2021;40:2547–57.
Sahn SH, Levine I. Pulmonary nodules associated with mitral stenosis. Arch Intern Med. 1950;85:483–9.
Santos JW, Neto ABM, Marchiori RC, Michel GT, Fagundes AL, Tagliari LG, et al. Pulmonary hemosiderosis associated with celiac disease: improvement after a gluten-free diet. J Bras Pneumol. 2012;38:412–4.
Taylor HE, Strong GF. Pulmonary hemosiderosis in mitral stenosis. Ann Intern Med. 1955;42:26–35.
Woolley K, Stark P. Pulmonary parenchymal manifestations of mitral valve disease. Radiographics. 1999;19:965–72.

Publisher's Note