

Is it Asthma, is it Bronchiectasis... or is it an Alpha-1-Antitrypsin Deficiency?*

¿Es asma, son bronquiectasias... o es un déficit de alfa-1-antitripsina?

Dear Editor:

Alpha-1-antitrypsin deficiency (A1AD) is the most frequent potentially mortal congenital disease in adults. It usually presents as pulmonary emphysema at early ages.¹ A1AD is an underdiagnosed disease and one of the causes of this notable underdiagnosis is the limited frequency with which the serum concentrations of alpha-1-antitrypsin (A1AT) are determined even in COPD patients, despite the fact that the guidelines recommend it.¹ A lesser known aspect is that pulmonary disease due to A1AD can present varying symptoms and that patients with A1AD can have another respiratory disease not directly related with the deficiency. This makes diagnostic suspicion difficult and complicates the therapeutic decision about the need to initiate substitutive therapy.

We have had the opportunity of a visit with a 52-year-old woman, ex-smoker of 14 pack-years, who consulted for recurrent lobar pneumonia in different localizations and episodes of purulent bronchitis. Lung function showed: FEV1: 3.17 L (121%), FVC: 4.12 L (103%), FEV1/FVC: 76%, RV: 1.84 L (106%), TLC: 5.66 L (110%) and KCO: 96% predicted. Chest computed tomography demonstrated bronchiectasis in the right middle and upper lobes, without evidence of emphysema. On the analysis, we observed gamma globulin 9.14 g/L (normal: 8–18) and A1AT <0.19 g/L (normal: 0.9–2 g/L), with homozygous PiZZ phenotype. A study of the family detected an A1AD with PiZZ phenotype in a 49-year-old sister, with a concentration of A1AT <0.30 g/L. She had never been a smoker and presented a clinical history of intermediate mild extrinsic asthma. Spirometry showed: FVC: 3.89 L (109%), FEV1: 2.85 L (101%) and FEV1/FVC: 73%.

The index case had a conserved lung function, with no evidence of emphysema, despite being a smoker with a history of recurrent pneumonia and bronchiectasis. The US registry of patients with A1AD showed a frequency of pneumonia of 21% in their population of 1127 severe homozygous patients,² but it is not considered that recurrent pneumonia has a causal relationship with A1AD. Even more controversial is the relationship between A1AD and bronchiectasis: although there are studies that indicate a high prevalence of bronchiectasis in patients with A1AD, the series of bronchiectasis have not demonstrated a higher frequency of A1AD cases.³ In fact, the prevalence of bronchiectasis in A1AD is similar to that which can be found in series of patients with COPD

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Mediastinal Epithelioid Hemangioendothelioma Mimicking a Teratoma*

Hemangioendoteloma epitelioido mediastínico simulando un teratoma

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and similar severity.⁴ The presence of recurrent infections and bronchiectasis in patients with A1AD suggests a defect in humoral immunity.⁵ The patient presented low concentrations of immunoglobulin, even with bronchiectasis and recurring infections, which rules out a deficiency in IgG subclass or production of specific antibodies. The relationship between bronchial asthma and A1AD is also open for debate. Some studies suggest that the patients with deficient alleles, especially S, can have a greater incidence and/or severity of asthma, but there are no conclusive studies about the Z allele.⁶ Nevertheless, in the same US registry, the frequency of asthma in PiZZ homozygous subjects was 31%.² This patient should receive treatment for her mild intermittent asthma, but neither she nor her sister meet the criteria for substitutive treatment with intravenous A1AT.¹

It is striking to see such different clinical expressions in two sisters with PiZZ homozygous phenotype, which newly demonstrates the extreme clinical variability that patients with A1AD can present. We would also like to reiterate the importance of studying family members after a diagnosis of A1AD. In this manner, we can identify individuals with severe deficiency in its initial phases of evolution, when the possibilities for successful therapeutic intervention are higher, both with standard measures as well as smoking cessation and the treatment of emphysema with substitutive treatment.

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Dear Editor:

Epithelioid hemangioendothelioma is a vascular tumor of endothelial origin with an intermediate histological and clinical behavior somewhere between that of hemangiomas and angiosarcomas.¹ Its incidence is very low, and its most frequent location is at the hepatic and pulmonary level.^{2–4} Its localization in the mediastinum is exceptional, and diagnosis is usually established after surgical treatment.

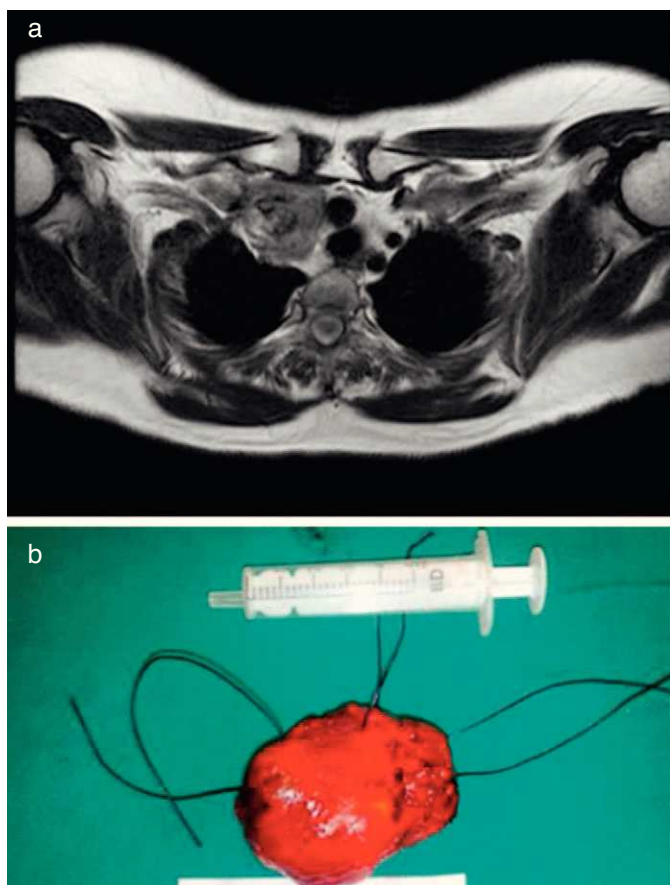


Fig. 1. (a) Thoracic MRI where the mass is observed at the anterior mediastinal level; (b) macroscopic image of the resected mass. It is a nodular formation, measuring 5 cm × 4 cm × 3.6 cm with a smooth surface and areas of brown-violet coloration.

Our patient is a 56-year-old woman with no medical history of interest who was sent to our consultation with the suspicion of a teratoma after thoracic CT performed due to pain in the right hemithorax. The CT scan revealed a 4-cm mass with fatty density and calcium in its interior located in the mediastinum. Thoracic MRI identified a 4-cm mass in the right anterior mediastinum with intralesional fatty foci and foci of hyposignal in related with calcifications. The mass was in contact with the brachiocephalic artery and with the right subclavian vein with no clear data of invasion (Fig. 1a). By means of transverse cervicotomy, we proceeded with the exeresis of the mass. Post-operative evolution was satisfactory. The histologic report of the piece described a 5 cm × 4 cm mass with different mesenchymal components: mature-looking adipose

tissue, fibroblastic fusiform cells, bone tissue with thick trabeculas in anarchic distribution and numerous capillary vessels covered with epithelioid endothelium (Fig. 1b). The epithelioid cells showed an endothelial immunophenotype (CD 31 and CD 34+). These findings supported the diagnosis of epithelioid hemangioendothelioma with an extensive metaplastic ossification. This result was confirmed by the Pathological Anatomy Department at Brigham and Women's Hospital in Boston (USA), reference center for the study of soft tissue tumors.

Epithelioid hemangioendothelioma usually presents in patients around the age of 40; the presentation is asymptomatic and is usually a coincidental radiological finding in half of patients.⁵ In our case, the radiological suspicion was for a teratoma due to the calcifications observed on the imaging studies. Although its most frequent localization is at the hepatic and pulmonary level, other localizations have been reported in the mediastinum.⁵ The histologic diagnosis with routine techniques is difficult, and it is necessary on the majority of occasions to use immunohistochemical techniques. In our case, we observed a large metaplastic ossification with positive epithelioid cells in the immunohistochemical study for CD 31 and CD 34, which coincides with the series by Suster et al. confirming the vascular origin of this type of tumor.⁵ As for prognosis and treatment, we should mention that it is a tumor with slow growth. The treatment of choice is surgical extirpation.

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