

CASE REPORT

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Transplant with MZ genotype liver: what is the clinical pulmonary picture after 30 years? a case report and review of the literature

Anna Annunziata^{1*}, Alessandra Di Perna², Ilaria Ferrarotti³, Antonietta Coppola¹, Maria Burricco² and Giuseppe Fiorentino¹

Abstract

Background Alpha-1 antitrypsin, also known as alpha1 proteinase inhibitor, is a protein 90% synthesized by hepatocytes. Alpha-1 antitrypsin deficiency should be suspected if patients have unexplained emphysema or liver disease in the absence of others recognized causes. The diagnosis is based on tests that measure the amount of the enzyme in the blood and confirm by molecular analysis.

Case presentation We present the case of a man of Caucasian ethnicity, who started experiencing difficulty in breathing 20 years after liver transplantation. After about 30 years since transplantation, an intermediate alpha-1 antitrypsin deficiency is diagnosed with evidence of air trapping, pulmonary emphysema and bronchiectasis.

Conclusion The presence of a Z-variant synthesized from the donor liver may have contribute to the onset of respiratory disease.

Keywords Alpha 1 antitrypsin, Liver transplant, Lung disease

Introduction

Alpha-1 antitrypsin deficiency is an inherited disease in which a lack of the enzyme alpha-1 antitrypsin can mainly cause lung and liver disease. Adults commonly experience emphysema, with shortness of breath, wheezing and coughing, and some even cirrhosis. Alpha-1 antitrypsin (AAT) is a protein belonging to the serpin superfamily. It is encoded in humans by the SERPINA1 gene, and is also known as an alpha-1 proteinase inhibitor

(PI) because it inhibits various proteases. Proteases fragment proteins as part of the normal repair process of lung tissue, if their action is not counterbalanced by AAT, their action can be harmful to lung tissue. More than 90% of circulating AAT is produced by hepatocytes [1].

Alpha-1 antitrypsin deficiency should be suspected if patients have unexplained emphysema, liver disease (in the absence of infection or others recognized causes), panniculitis. The diagnosis is based on tests that measure the amount of the enzyme in the blood and confirm by molecular analysis [1, 2].

Case description

We describe the case of a 73-year-old male patient, Caucasian ethnicity, never smoker, former office worker, suffering from systemic arterial hypertension and diabetes mellitus. At 43 years of age, he received liver transplant for cirrhosis, secondary to hepatitis B virus infection. At transplant time, patient did not referred pulmonary

*Correspondence:

Anna Annunziata
antonietta.coppola84@gmail.com

¹ Unit of Pathophysiology and Respiratory Rehabilitation, Intensive Care Department, Monaldi Hospital, Naples, Italy

² Unit of Pneumology, Latina, Italy

³ Pneumology Unit, Department of Internal Medicine and Therapeutics, Center for Diagnosis of Inherited Alpha1-Antitrypsin Deficiency, IRCCS San Matteo Hospital Foundation, University of Pavia, 27100 Pavia, Italy



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symptom. No signs of pulmonary disease were found at physical examination. Pulmonary functional tests were normal. CT scan did not reveal abnormalities. ABGs showed normal oxyemia and normal acid–base balance. Alpha 1 antitrypsin serum level was normal (153 mg/dl); it was dosed with a nefelometric methods (Atellica®Siemens).

The orthotopic liver transplant was performed without complications and subsequent clinical follow-up was normal.

Approximately 20 years after liver transplantation, the patient started pneumological check-ups due to the appearance of symptoms characterized by mild dyspnea on exertion and sporadic episodes of bronchitis. For many years, the patient was followed in a general practice clinic and treated with therapy as needed during exacerbations. Due to the progression of symptoms, he received a specialist visit and underwent pulmonary function tests.

Pulmonary function tests revealed mild obstruction, air trapping, with no significant bronchodilator response and reduced diffusing capacity with forced vital capacity (FVC) 4.20 L (119%), forced expiratory volume in 1 s

(FEV1) 3.01 L (112%), 8% improvement in broncho dilatory response to drug challenge, FEV1 / FVC ratio 70.6%, total lung capacity (TLC) 11.69 (180%), residual volume (RV) 7,17 L (273%), diffusing capacity (DLCO) 14.12 mL /min/mmHg (58%). The 6 min walking test showed a reduced performance and a modified Medical Research Council (MMRC) dyspnoea of 2. Chest computed tomography (CT) scan showed areas of emphysema in the left lower lobe (Fig. 1).

The serum AAT level resulted below normal (74 mg/dL with normal values 90–200 mg/dL). Therefore, suspecting an AAT deficiency, a blood sample from the patient was sent to the specialized laboratory in Pavia for further analysis. The phenotype obtained by isoelectrofocusing (IEF) was MZ, showing the presence of both M and Z proteins (Fig. 2A). This data was consistent with the plasma value of AAT previously reported, in accordance to a condition of intermediate AAT deficiency. However, SERPINA1 gene sequencing did not reveal the presence of Z variant, corresponding to a G to A transversion at nucleotide 1096 of cDNA of SERPINA 1 gene (rs28929474) (Fig. 2B) and reported the PI*MM genotype.

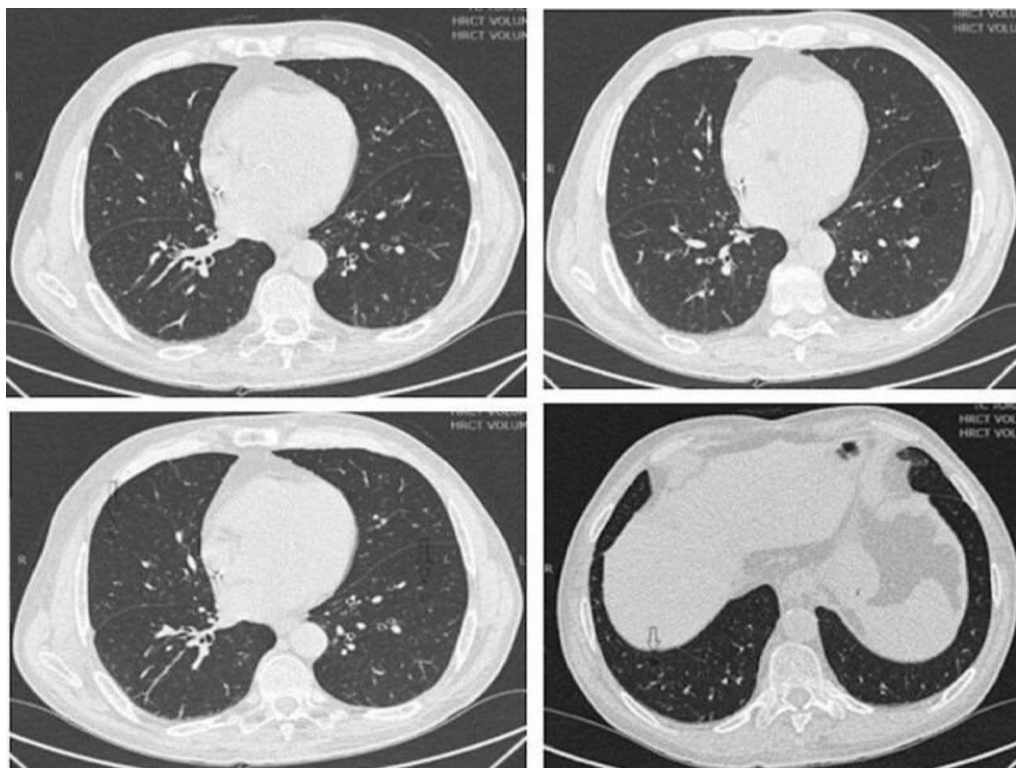


Fig. 1 There are diffuse small bronchiectasis, two centrilobular emphysema bubbles in the lateral segment of the lower left lobe, of which the largest with a diameter of about 14 mm and the more peripheral with a diameter of 9.5 mm. A small bubble of emphysema with a maximum diameter of about 7.2 mm is evident in the middle lobe in an almost peripheral location. Another small centrilobular bubble in the posterior segment of the right lower lobe of about 7 mm

the presence of impaired respiratory function, areas of emphysema in a patient who had never smoked, in the presence of a reduced serum concentration of AAT led to suspect the presence of AAT deficiency. The onset of clinical deterioration in the patient with intermediate type AAT deficiency has been the subject of debate and controversial opinions for many years. Recently, evidence of lung damage in patient with intermediate deficiency is beginning to emerge [9, 10]. In the light of current knowledge, it is possible to assume that the presence of the Z variant has slowly promoted the onset of lung damage over the years [11].

Conclusion

In conclusion, AAT deficiency is an under-recognized disorder that can have severe effects on the lungs and liver. Discrepancies in AAT quantitation, phenotype and genotype results may be caused by several clinical factors, blood transfusions, acute-phase response, or bone marrow or liver transplantation. It is therefore important for clinicians to be aware of the various clinical circumstances that can cause discordant AAT results. To the best of our knowledge this is the first case in the literature describing clinical lung disease years after a liver transplant with induction of variant Z synthesis. It is not known, due to the scarcity of data in this area, whether the presence of a Z-variant synthesized from the donor liver may have contributed, as we have hypothesized, to the onset of respiratory disease in a non-smoker.

Abbreviations

| | |
|------|--------------------------------|
| AAT | Alpha 1 antitripsin |
| FVC | Forced vital capacity |
| FEV1 | Forced expiratory volume in 1s |
| FEV1 | FVC ratio |
| TLC | Total lung capacity |
| RV | Residual volume |
| DLCO | Diffusing capacity |

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Author contributions

Conceptualization, AA and ADP; methodology, AA, ADP, IF; investigation AA, FDP, MB; data curation, ADP, MB, GF; writing—original draft preparation, AA, IF, GF; writing—review and editing, AA, MB, IF, AC; supervision, AA, GF; All authors have read and agreed to the published version of the manuscript.

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Availability of data and materials

Data supporting our findings are available at UOC respiratory pathophysiology, AORN DEI COLLI, Naples, Italy.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The authors declare no competing interests.

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