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Editorial

Alpha 1 Antitrypsin Deficiency: Rare or Under-Diagnosed Disease?

Myriam Calle Rubio*, José Luis Álvarez-Sala Walther, Juan Luis Rodríguez Hermosa

Service of Neumology, Hospital Clínico San Carlos, Madrid, Spain

***Corresponding Author:** Myriam Calle Rubio, Service of Neumology, Hospital Clínico San Carlos, Madrid, Spain.

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Alpha-1 antitrypsin (AAT) deficiency is a rare inherited condition due to the existence of mutations in the serpin gene and clinically manifested by the existence, though not in all cases, of pulmonary emphysema, chronic liver disease and, less frequently, systemic paniculitis or vasculitis.

The review published by the European Respiratory Society in 2017 on the situation of alpha-1 antitrypsin deficiency (AATD) highlights the importance of screening for the diagnosis of this disease in anyone with chronic respiratory disease [1].

The detection of cases allows for the implementation of genetic counselling, the screening of blood relatives and, in selected individuals, the application of substitution therapy. However, despite the current recommendations of good clinical practice guidelines, underdiagnosis is very important because many physicians are unaware of the existence of this disease and, therefore, its diagnosis and treatment.

The underdiagnosis of the AATD is a very important problem, as could be demonstrated in the EPOCONSUL study, carried out in Spain during 2015. It was an audit that evaluated the care that had been performed in pneumology outpatient consultations carried out by patients with COPD. In this audit, only in 22.1% of the cases had the blood levels of AAT been determined at some point during the follow-up of the patients, which reached an average of 4 years in the consultation [2].

The situation is similar for general practitioners; thus, in a study carried out in Spain in 2007-2008, only 5.559 AAT determinations had been carried out in a population of 5.8 million inhabitants, and 6.850 during the years 2010 - 2011 [3].

This also causes a significant diagnostic delay, more than 7 years delay from the onset of symptoms to the correct diagnosis [4].

In Spain, the allelic frequencies of S and Z (expressed as per thousand) have been estimated at 104 for PiS and 17 for PiZ, which means, according to the Spanish population, that 12,000 people have a ZZ phenotype and some 145,000 have an SZ phenotype [5]. These data place Spain as the second country with the highest number of serious AAT deficits in Europe after Italy.

Neonatal screening and detection of genetic alteration have been shown to reduce the incidence of smoking in these subjects when they reach adolescence, thus preventing them from developing pulmonary emphysema in adulthood or, at least, delaying its appearance for several decades. On the negative side, we could attribute the psychological effects on parents and children of the detection of this deficit, but these aspects must be saved with correct genetic advice.

Although the DAAT was classically associated with young patients, with severe obstruction and with predominant emphysema in the lower lobes, in clinical practice this is not the case, since the clinical presentations are diverse.

For this reason, the determination of this protein in the blood must be carried out at least once in a lifetime for all patients suffering from a chronic airway disease, since it is a simple, cheap test and, in addition, we have an effective treatment indicated in serious cases.

Another aspect to consider is the cutting point to consider normality. Although the normal value of the blood protein is set at 90 mg/dL, it should be noted that AAT is an acute phase reactant and increases in any inflammatory process. In cases with only one affected allele, either S or Z, blood concentrations of AAT up to 110-120 mg/dL are described, so it seems advisable to set these values for disease screening.

The European Respiratory Society document recommends the creation of centers of reference or excellence to improve the quality of care in this disease[1]. Spain has 5 centers of excellence for the AATD, located in Barcelona (Hospital Vall d´Hebrón), Madrid (Hospital Clínico San Carlos), Galicia (Hospital Álvaro Cunqueiro de Vigo) and two in Andalusia (Hospital Clínico Universitario San Cecilio de Granada and Hospital Virgen del Rocío in Seville).

Research and dissemination of knowledge of this disease among the physicians who care for these patients can improve case detection and prevent the development of the disease, as well as earlier treatment of severe cases.

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