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Editorial

Diagnosis of Alpha-1 Antitrypsin Deficiency (AATD) in Primary Care

Diagnóstico del déficit de alfa-1 antitripsina en atención primaria

Alpha-1 antitrypsin deficiency (AATD) is a congenital autosomal codominant condition which predisposes to the development of pulmonary emphysema and liver disease, and it is characterized by low plasma levels of alpha-1 antitrypsin (AAT) in the blood and tissues. Severe AATD is one of the most common congenital disorders with an estimated prevalence between one in 2175 and one in 5164 in Spain.[1] It is also the only known genetic factor for the development of COPD, accounting for approximately 2% of the COPD.[2]

The World Health Organization and respiratory societies such as the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR)[3] and the European Respiratory Society (ERS)[4] recommend testing of all COPD patients. Due to its great variability in the clinical expression of pulmonary disease, they also recommend testing for AATD adults with non-completely reversible asthma or with bronchiectasis of unknown etiology.[4] Despite these recommendations, AATD remains a disease significantly underdiagnosed and underrecognized, with a considerable diagnostic delay interval which often takes place after several contacts with health care providers.[5]

As primary care physicians (PCP) are the first and main contact of the patient with the health-care system, they play a crucial role in AATD case-finding. However, the picture is somewhat discouraging.[6] An epidemiological study in the United Kingdom using primary care (PC) data from the Optimum Patient Care Research Database (OPCRD) showed that only 2.2% of patients diagnosed with COPD before the age of 60 years were tested for AATD.[7] A similar study performed in Spain[8] found a low number of AAT determinations performed in PC in relation to the prevalence of COPD. Additionally, the indication to perform the test was not always clear and only 13.5% of the individuals had a previous established diagnosis of COPD or emphysema.

Altogether, the reality is that PCP usually do not include AAT testing as part of the evaluation of the COPD patient.[9] The main reason for the low testing in PC seems to be lack of awareness, either of the disease itself or of the diagnostic techniques or algorithm. In this line, an online survey on physicians in Spain and Portugal suggested that a knowledge gap may be contributing to the underdiagnosis of AATD. In the survey, the PCP included declared a low knowledge on AATD, and indeed, less than 20% were aware of the recommendation to test all COPD patients.[10] One of the most frequent reasons for not testing for AATD was the misbelief of the high economic cost of testing, but also for some physicians is the certainty or belief that there is no specific or effective treatment. This misunderstanding completely ignores the relevance of family studies, which allow to carry out interventions and prevention of emphysema in individuals diagnosed at an early age or stage, mainly with intervention on smoking habits. In view of this situation, different strategies such as detection programs[11] or pilot studies[12] have been performed in PC. However, to improve not only the screening of AATD, but also the integral care of patients with COPD and AATD there is a need to enhance and optimize the circuits and relationship between primary and other levels of healthcare.

In this sense, the document "Chronic obstructive pulmonary disease referral criteria. Continuity of care"[13] aims to fill this gap. This multidisciplinary document is meant to be a practical guide made to facilitate and improve the management and control of patients with COPD between different levels of care, and conveniently, it also addresses AATD screening and referral.

Following the recommendations of SEPAR,[3] the document advises to screen for AATD all COPD patients (and individuals with a clinical suspicion, regardless of COPD) by measuring AAT levels, a test accessible to all healthcare levels and also very affordable. Additionally, when requesting AAT levels is not possible, the diagnostic circuit of the REDAAT (Spanish Network of patients with alpha-1 antitrypsin deficiency)-Progenika can be used, sending a buccal swab or dried blood spot sample. The test detects the 14 most frequent allelic variants, but does not measure AAT levels. If AAT levels are reduced, and depending on the availability and protocol of each reference center, the next step would be the determination of the phenotype or the genotype. The genotype also is the test of choice if there is a discordance between AAT levels and the phenotype. The diagnosis of AATD or AAT levels < 110 mg/dl with the impossibility of continuing the diagnostic algorithm are indicators of referral to the pneumology clinic (Fig. 1). Although it is out of the scope of this editorial, the document addresses also relevant topics such as follow-up of the COPD patient between the different levels of care, the role of the nurse, community pharmacy or telemedicine.

Even though PC is a key piece for detecting AATD individuals, the management of patients with rare diseases should be centralized in reference centers that can provide multidisciplinary specialized care and advice to the affected individuals and their families. This centralized approach not only contributes to the accumulation of knowledge[14] but also facilitates inclusion in registries, such as the international registry of AATD EARCO.[15] This step is crutial in order to increase the knowledge on the natural history of the disease and promote multi-center international studies. Consequently, initiatives such as the document "Chronic obstructive pulmonary disease

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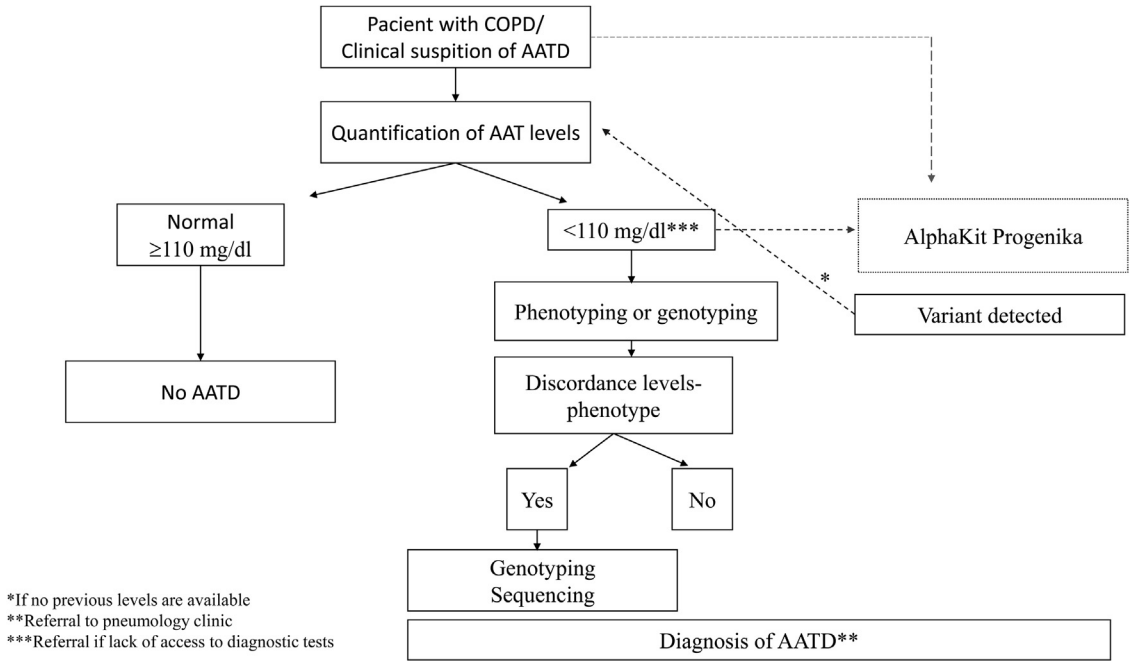

Fig. 1. Diagnostic algorithm of AATD. Footnote: COPD: chronic obstructive pulmonary disease; AATD: alpha-1 antitrypsinn deficiency; AAT: alpha-1 antitrypsin. *Adapted from 13.*

referral criteria. Continuity of care" pave the way to achieving effective coordination between the different levels of care, ensuring optimal care for the patient and resource optimization.

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