COPD Secondary to Alpha Anti-Trypsin Deficiency

Rahul Jayas

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Dr. Convery / Dr. Chatwin

Abstract

Chronic Obstructive Pulmonary Disease (COPD) is a disease of recurring respiratory problems due to harmful gases, such as tobacco smoke. It is described as enlarged air spaces due to destruction in alveolar walls or by having chronic respiratory symptoms such as a cough and phlegm for greater than 3 months over consecutive years. It is classified by an individual having an airflow limitation. In terms of occurrence, COPD ranks 4th as cause of death in the United States The main cause of COPD, in most cases (almost 90%) is tobacco smoke.[1,2,3] This makes smoking cessation first line treatment and management of COPD. However, α_1-antitrypsin deficiency, is a rare genetic cause of COPD.[2,3] α_1-antitrypsin deficiency as the cause of COPD raises the clinical question how does the definition, diagnosis, treatment and management differ in a non-smoking patient with COPD? According to the literature regarding α_1-antitrypsin deficiency, α_1-antitrypsin is in lower than normal quantities, it allows elastase to build up and damage the pulmonary system. Reducing exposure to smoke is still a key in management as the combination of α_1-antitrypsin deficiency and smoke makes the COPD worse than with α_1-antitrypsin deficiency alone.[2,3] In addition to standard COPD management, in these cases, further specific testing for α_1-antitrypsin deficiency and α_1-antitrypsin augmentation therapy may be considered for a patient.[3,4]

Case Presentation

While working at the Agassiz medical centre, in Morden Manitoba many patients had varying degrees of COPD. There was one patient I encountered, a 71-year-old male, who had COPD with zero personal smoking history. They also could not account

for any personal exposure to second-hand smoke in their household. This individual had COPD due to an α_1-antitrypsin deficiency. In the past, this individual was first informed he had asthma and was treated for that with bronchodilators. A decade later it would be discovered that an immediate family member of his had α_1-antitrypsin deficiency and his diagnosis of the same followed soon after. The diagnosis was confirmed by confirmatory testing of α_1-antitrypsin. On exam, this individual has typical signs of COPD, with a prolonged expiratory phase and chronic cough. His spirometry had a FEV1 of 54% of predicted when he first came to Agassiz and over time has lowered to 41% of predicted FEV1. By the time of my first encounter of the patient, he is currently aware of his diagnosis, has seen a respirologist and taking an assortment of bronchodilators, Alvesco, Symbicort and Atrovent which is managing his COPD well.

Discussion

COPD is a disease of airflow limitation of an individual's lungs, with almost the entirety of cases caused by external environmental factors. The main factor causing COPD is tobacco smoke exposure to the pulmonary system. A rarer cause of COPD exists in the form of a genetic abnormality.[1,3] This case study will further define and discuss α_1-antitrypsin deficiency and its management.

COPD caused by α_1-antitrypsin deficiency is due to a genetic change of the normal Pi*MM genotype, instead, giving a variation of alleles. "The most common deficient allele associated with emphysema is the Z allele".[3] This alteration from the normal variant can result in α_1-antitrypsin deficiency. In the protection of the lung tissue, α_1-antitrypsin functions as a protein inhibitor. It prevents the build up and function for the

enzyme elastase, an enzyme which causes damage to the pulmonary tissue. This chronic damage leads to COPD and is the mechanism of how an α_1-antitrypsin deficient individual is susceptible to developing COPD.[3]

In the case of COPD secondary to α_1-antitrypsin deficiency, there are a few key differentiating points. The notion above of a genetic factor playing a role is one, this means symptoms of COPD are present in a non-smoker and the individual may have a family history of COPD. Another differentiation is that symptoms present and are noticed by the individual at a younger age, typically in their 40s.[3] "The onset of airflow limitation typically occurs at a younger age in AAT-deficient individuals than in non-AAT-deficient individuals, who usually present in the sixth and seventh decades of life".[3] Liver dysfunction is also a concern in α_1-antitrypsin deficient individuals. Unsurprisingly, individuals with α_1-antitrypsin deficiency also have lower serum levels of α_1-antitrypsin. A similarity of the α_1-antitrypsin deficient individual and non-α_1-antitrypsin deficient individual is in clinical presentation, both presenting possible symptoms such as, shortness of breath, chronic cough, phlegm and wheezes and lower than predicted FEV1 values.[3]

Diagnosing an individual with α_1-antitrypsin deficiency involves suspicion that is a possibility, followed by serum level testing for α_1-antitrypsin (less than 20 micromol/L is considered a reasonable threshold to differentiate between a normal variant individual) and ultimately genetic testing to know which variant alleles are present in the deficiency. A possible algorithm shared in an UpToDate article is shown in Figure 1.[3]

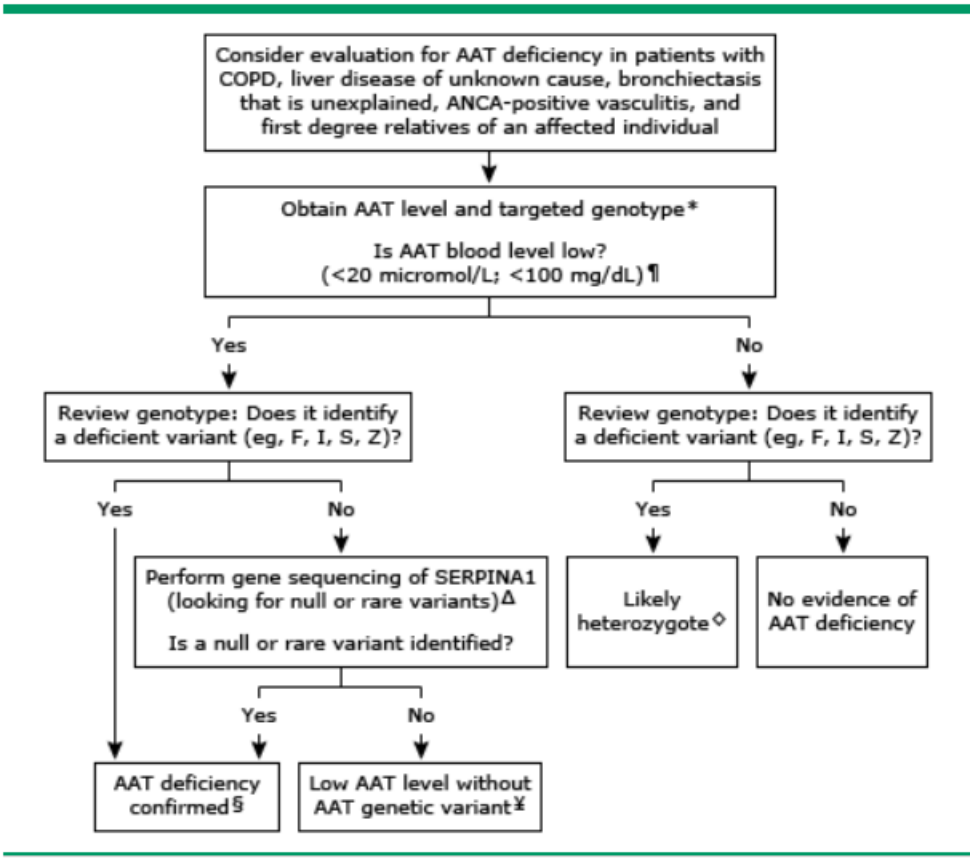

Figure 1: Algorithm of α1-antitrypsin deficiency diagnosis.[3]

The Canadian thoracic society gives the following two recommendations for testing regarding α_1-antitrypsin deficiency. “We suggest targeted testing for A1AT deficiency be considered in individuals with COPD diagnosed before 65 years of age or with a smoking history of <20 pack years. (Grade of recommendation: 2C)”[4] and “We suggest targeted testing for A1At deficiency not be undertaken in individuals with bronchiectasis or asthma. (Grade of recommendation: 2C)”.[4] Spirometry yielding low FEV1 values compared to predicted plays a role in both COPD and α_1-antitrypsin deficiency in diagnosis and assessment of severity of the airflow limitation.[3]

With regards to treatment and management of COPD secondary to α_1-antitrypsin deficiency compared to COPD secondary to smoking, the treatment and management

are largely the same. This means, even in a non-smoking individual with COPD, smoking cessation and reduction in smoke exposure of any kind is of the utmost importance. It has been shown that in an α_1-antitrypsin deficient person, smoke exposure accelerates the rate of decline of pulmonary tissue of that individual. Other management techniques include all others that are used to help a stable or acute exacerbation of any individual with COPD regardless of cause, some examples being bronchodilators, antibiotics, corticosteroids and oxygen.[3] An additional and unique treatment possible for an α_1-antitrypsin deficient individual is α_1-antitrypsin augmentation therapy. The aim of the therapy is to provide α_1-antitrypsin protein to the individual and that may improve or preserve current lung function.[3,4] The recommendation of the Canadian Thoracic Society regarding α_1-antitrypsin protein augmentation therapy is "We suggest A1AT augmentation therapy may be considered in non-smoking or exsmoking patients with COPD (FEV1 25% to 80% predicted) attributable to emphysema and documented A1AT (level ≤11 μmol/L), who are receiving optimal pharmacological and non pharmacological therapies (including comprehensive case management and pulmonary rehabilitation) because of benefits in CT scan lung density (Grade of recommendation: 2B) and mortality (Grade of recommendation: 2C)".[4]

Conclusion/Recommendation

In summary, even though COPD secondary to α_1-antitrypsin deficiency is due to a genetic abnormality and can occur in a non-smoking patient, smoking cessation and exposure reduction is still an essential part of the treatment plan because smoking makes the condition worsen faster than without the exposure. It is important to consider that a person may have and test for α_1-antitrypsin deficiency in an individual who

presents with symptoms of COPD but is either much younger than the typical age or a non-smoker. Once suspected additional testing and therapy, alongside common COPD management strategies, may be provided which may benefit the patient with regards to their lung function and overall quality of life.[3]

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