Alpha-1 Antitrypsin Deficiency—Family Study

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Abstract: According to the latest World Health Organization report 64 million people suffer from Chronic Obstructive Pulmonary Disease (COPD), 3 million people died from COPD and it is predicted that COPD will become the third leading cause of death worldwide by 2030. The alpha-1 antitrypsin deficiency is a rarely diagnosed hereditary disease caused by a genetic mutation and it is one of the most prevalent genetic disorders primarily affecting the lungs, especially in the form of COPD or emphysema, but in some cases also the liver or skin. The Global Initiative for Chronic Obstructive Lung Disease recommends all patients with COPD at a young age or significant family history to be examined for alpha-1 antitrypsin deficiency. This article presents the case of a 42 year old, female patient, Portuguese, with history of Chronic Obstructive Pulmonary Disease, 40 pack units/year smoker, with unknown family history, coming to her family doctor with breath shortness, especially during physical activities, with unsatisfying response to pharmacological prescribed therapy. Physical examination was normal. Alpha-1 antitrypsin deficiency was confirmed by blood testing. All patient’s first degree relatives were investigated showing low alpha-1 antitrypsin blood concentrations thus genetic tests were later performed. This case reinforces the need for primary care physicians to be aware of alpha1-antitrypsin deficit as an underdiagnosed clinical entity.

Key words: Alpha-1 antitrypsin deficiency, Chronic Obstructive Pulmonary Disease, family study.

1. Introduction

According to the latest World Health Organization (WHO) report 64 million people suffer from Chronic Obstructive Pulmonary Disease (COPD) and 3 million people died due to this disease. WHO predicts that COPD will become the third leading cause of death worldwide by 2030 [1, 2].

Cigarette smoking is the major risk factor for COPD but smokers show considerable variation in their risk for developing airflow obstruction [3-5]. Familial aggregation studies suggest a strong genetic component to this risk [4-6]. Severe hereditary deficiency of alfa-1 antitrypsin (AATD)—a major circulating inhibitor of serine proteases—is the best known genetic risk factor for COPD [5-7].

As pointed by The Global Initiative for Chronic Obstructive Lung Disease (GOLD), physicians must be aware for the need of systematic investigation of alpha-1 antitrypsin deficiency in a subset of patients with COPD at a young age or who have significant family history [4].

AATD is a clinically under-recognized inherited disorder that affects about one in 2000-5000 individuals [5, 6].

AATD is a rarely diagnosed hereditary disease caused by a genetic mutation affecting the long arm of chromosome 14 and it is one of the most prevalent genetic disorders [7, 9]. Primarily affects the lungs, especially in the form of COPD or emphysema, AATD can in some cases also affect the liver or the skin [7, 9, 10].

A well-acquainted family search for the disease allows for early diagnosis and will provide an increase of average age expectancy and health-related quality of life [9, 10].

2. Case Presentation

A 42 years old female, Portuguese, married, unemployed, mother of three kids, heavy smoker (40 pack/year). In presentation to her family doctor the

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patient has reported symptoms of breath shortness in the last months, including hospitalization due to the symptoms, with subsequent improvement while in the hospital. The patient maintained the symptoms while at home without improvement. Symptom worsening has reported during hard physical activities. Denied any other symptoms including pain.

The patient showed unsatisfying response to the pharmacological standard DPOC therapy: Fluticason + Salmeterol, 500 + 50 µg/dose (twice a day); Glycopyrronium Bromide + Indacaterol, 43 µg + 85 µg (once a day); Salbutamol 100 µg SOS (during 2 days).

The patient was diagnosed in 2014 with COPD, had two recent hospitalizations due to COPD exacerbation (Last Spirometry in September 2015: FEV1 After-BD 42%). No history of injuries, accidents or surgeries.

No alcoholconsume or illicit drug use was reported. Patient reported an active sexual life, adequate nutritional status, no trouble sleeping and no allergies known.

The patient was immunized according the Portuguese National Vaccination Program, with additional Influenza virus and Pneumococcus bacteria vaccines.

The lack of clinical data on the patient’s biological parents is due to her adoption during early childhood.

Physical examination was normal, including a normal cardiac and pulmonary auscultation without signs of respiratory difficulty. Patient’s body mass index was 34.

Different factors had lead us to suspect of AATD (i) the existence of COPD in a young patient, (ii) a suboptimal response to standard DPOC prescribed therapy, including increased use of short action beta agonist (SABA), i.e. Salbutamol, (iii) no additional signs of other possible causes, in the absence of family history records. Facing the clinical suspicion, blood testing to check for AATD was performed revealing low levels of AAT. Next the patient was sent to Genetic counseling where, once again, her lifestyle, diet plan and smoking cessation habits were reviewed by a Medical Genetics Department. All patient’s children were investigated, medical history was taken, physical examination showed no symptoms or signs, liver testing was negative while blood testing revealed low concentration of AAT, further genetic counseling was appointed.

3. Discussion

Cigarette smoking is the major risk factor for COPD [3], a clear indication for further investigation in our clinical case. Familial aggregation studies suggest a strong genetic component to the risk of COPD [3, 4]. The patient observed in our clinical case has heavy smoking habits. However, due to lack of family history records—while permanent heavy smoking—the diagnosis of AATD was not considered earlier.

This clinical report shows the importance of drawing attention to the need for a systematic consideration of AATD, in a subset of patients with COPD at a young age or whom have significant family history [4], such as our 40 years old COPD patient.

AATD is a clinically under-recognized inherited disorder [5, 6], often not investigated and under-diagnosed.

Primary Care is the first line health response, identifying such cases is of major importance in terms of early diagnosis, increasing average age expectancy and quality of life [9, 10], and can easily be performed by Primary Care professionals.

Important too was for family doctors knowing all the family members, be able to make interventions on primordial, primary, secondary and tertiary levels.

Intervention in primordial prevention was in this case the fact that we could intervene in lifestyles, specially smoking and physical exercise of family members as they have not yet develop the disease while two of them were already smokers. Further
primary prevention included health education and control of environmental hazards, performed also by a specialized team in secondary care who will be able to make changes on this level too.

Secondary prevention intervention was mostly in early diagnosis including screening tests.

Tertiary prevention intervention was in all the measures available to reduce or limit impairments and disabilities and to promote patient’s adjustment to immediable conditions, such as loosing weight and smoking cessation.

These patients were referred to a specialized center for further investigations, mainly for genetic studies and adequate treatment. The risk of COPD in AATD PiMZ heterozygotes is uncertain [11]. The patient’s genetic testing results are at the oment still pending and we will follow-up for a complete clinical picture of this specific patient. Meanwhile more clinical reports on this subject would improve Primary care physicians awareness on AATD.

Intravenous infusion of pooled human AAT is currently the most direct and efficient mean of elevating AAT levels in the plasma and in the lung interstitium [12]. All, the patient and affected family members will undergo this treatment as we follow-up with the interventions from Primary Care and Secondary Care services.

4. Conclusions

We report a diagnosis of an AATD in early stage of a patient’s life. Differential diagnosis was difficult as other factors could be also responsible for these clinical manifestations. Concerning to the patient’s young progeny, our timely manner approach in the absence of symptoms or clinical manifestations allowed for an early intervention in terms of pharmacotherapy and risk factors control.

Smoking cessation and therapy optimization can be simultaneously initiated trying to avoid the early onset of COPD.

This case reinforces the need for primary care physicians to be aware of AATD as an under-diagnosed clinical entity.

Reference


