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REVIEW

Alpha 1 “Hereditary Emphysema” Experience: A Patient–Physician Perspective

Katie Moyer · Kamyar Afshar

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ABSTRACT

This article is co-authored by a patient living with alpha-1 antitrypsin deficiency, and her treating physician. The commentary article describes the patient’s experience of the diagnosis and treatment process. The physician then discusses alpha-1 antitrypsin deficiency diagnosis and management in the context of the patient’s experiences.

Keywords: Hereditary emphysema; Patient; Physician

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ALPHA 1: PATIENT PERSPECTIVE

Katie Moyer

Suddenly, out of nowhere, at 49 years old, I couldn’t breathe! One flight of stairs left me fighting for breath. I had never been in great physical shape, but I knew this was extreme and it scared me. Worse yet, I also started experiencing bronchitis and pneumonia. For the next 4 years, I saw five different doctors, looking for a reason, looking for a cure.

The doctors would prescribe antibiotics, steroids, and breathing treatments—none of which took care of the problem. Doctors had handed me inhaler samples, prescribed prednisone, and blamed my previous smoking. I just could not believe that smoking was the culprit, when I had quit a 12-year habit over 25 years previously and had been healthy ever since. My husband and I were caring for our profoundly brain damaged son in our home and I attributed my sickness to exposure to him. Working with his feeding tube and tracheostomy, I was constantly exposed to his bodily fluids.

Now frustrated, weak, chronically congested, and breathless, I felt I was an embarrassment to my family, unable to participate in any activities. My husband and I began making out our wills, as I feared I might not survive whatever was going on with me.

Finally in 2002, an internist asked me, “You say these symptoms only started in the last 4 years and you’d been okay prior to that?” When I confirmed, she said she might have a possible answer; she’d recently read in a medical journal about a liver condition that might explain what I was experiencing. A simple blood test confirmed that I did indeed have alpha-1 antitrypsin deficiency, with a ZZ phenotype, “the worst kind”. She explained that I had inherited one bad gene from my mom and one from my dad, which is the only way this condition can be passed on. She told me that alpha-1 is a chronic progressive disorder, and there is no cure. It had been damaging my lungs for many years, eventually causing my emphysema. I was finally diagnosed! She had actually listened to me!

I was immediately referred to UCSD where I was listed for a lung transplant. (I actually stayed on the list, never getting sicker, until the criteria for lung transplant changed 4 years later and I was taken off the list.)

I was also referred to the Alpha-1 Foundation and agreed to replacement therapy, which entails weekly infusions of antitrypsin. I was told that the infusions would not cure alpha-1, but could slow the damage to my lungs. I have been on this therapy ever since. I believe it works for me because I didn’t get sicker from 2002 until 2015.

For many years I was able to have the nurse who helped me care for our son deliver my infusions in our home. After our son’s death, I started receiving my infusions at a facility only 3 miles from our home.

My local pulmonologist knew almost nothing about A1AD but learned along with me through the years. He got me on the right bronchitis medications and enthusiastically directed me toward pulmonary rehab, which involves monitored exercising twice a week; walking on a treadmill, stationary bicycling, lifting weights, and doing calisthenics. I started within 2 months of my diagnosis and continued for 15 years until my local program closed down.

Pulmonary Rehab was more than an exercise program for me. It was an ad hoc support group. We were all COPD patients and we shared our

stories, our advice, and our support. We laughed and cried together, and more times than I like to remember, attended funerals together. I so often felt that, when I saw what others were going through to survive, I could make it, too.

Soon after starting rehab, I realized that I absolutely had to drop the extra weight I was carrying. For the next year, I stopped overeating, ate smaller portions, and ate them slowly: everything in moderation as they say. I lost 35 lbs. and have kept them off ever since, staying at around 130 lbs.

When my pulmonary rehab program closed down, I was lucky enough to find a therapy pool at a local senior complex. It’s a saltwater pool, maintained at 81°. I’m able to tread water, use foam weights for arm exercises, and do leg stretches and calisthenics. Using the pool has changed my life. I am happier and I do believe healthier than I would otherwise be. Even on the days that I am reluctant to go, I know I will feel better afterwards, so I go.

When I was diagnosed, I also took advantage of a program that provides monthly contact from a peer counselor wherein I receive information and encouragement from a fellow alpha-1 who shares my experience. He or she checks on my health and provides support. I can also just pick up the phone, call my coordinator, and get, if not an answer, a referral to available resources. I have to admit that most of the calls involve just plain conversation and venting with laughter and tears included.

In 2011, after receiving peer counseling for 9 years, I was offered a position as an AlphaNet coordinator, which would mean I would be making those calls to Alphas throughout the country. I did this job for 4 years and learned more than I could possibly have done otherwise. A1AD affects everyone differently. Some Alphas are extremely debilitated and need oxygen and help just getting around. Others are relatively healthy, enjoying a somewhat active, if monitored, lifestyle. I absolutely believe that the difference between most COPD patients and Alphas is the education and support we receive from the Alpha community.

My husband and I have attended seven annual National Alpha Conferences throughout the years. They are weekend affairs that provide

education resources and access to Alpha doctors and experts throughout the world.

In 2015, even with almost no exacerbations, my lungs had deteriorated to the point that I needed to use oxygen. It did not stop me. I continued my pool exercise, tethered to a 7-ft cord attached to my portable oxygen concentrator that sat at the side of the pool. Again, I felt empowered.

By 2017, at 68 years old, I was a candidate for a lung transplant, as my O₂ levels continued to drop and the trapped air in my lungs was increasing. I did not want to end up as some of the Alphas I knew did, becoming sicker and weaker and eventually unable to qualify for a transplant.

I had started seeing the pulmonology team again at UCSD, whose transplant program was growing. My left lung was replaced in October 2017. I started my recovery well and was able to restart my pool therapy soon thereafter. I also restarted replacement therapy almost immediately, continuing to today. I've had some complications, which I know to be commonplace after transplant, as the doctors try to adjust my anti-rejection, anti-viral, anti-fungal, anti-bacterial, etc., medications. I've been hospitalized twice and kidney issues are becoming a problem. I now regularly also see a UCSD nephrologist. I do feel as though as I am in good hands and I'm being compliant, with weekly labs, frequent pulmonary function tests, and transplant clinic appointments. And, as importantly, I get my weekly infusion of alpha-1 antitrypsin, which I will do for the rest of my life.

Note 1

I did not address the financial issues involved with treating alpha. From diagnosis on, our employer-covered insurance premiums rose from \$2600 to \$3700 a month for my coverage. My husband negotiated the premiums into his pay raises from 2002 through retirement in 2014 when we qualified for Medicare. We were broke, but I was covered!

All transplant and infusion costs have been covered by Medicare and our supplements with

prescriptions having copays totaling under \$3000 annually.

Note 2

Another difficult result of this diagnosis was that I needed to tell my six siblings of the hereditary nature of my alpha, forcing them to face the reality that this could be a possibility for them, too. Some got tested immediately, others resisted. They finally all did and we found that only one brother was an MZ Alpha, and was asymptomatic. We also know that our children are MZ Alphas. They are 34 and 33, with no symptoms, but are very aware of their need to be scrupulous with their health maintenance, knowing that they may face future problems. We are thrilled that our two young grandchildren, tested almost at birth, have not inherited an alpha phenotype.

ALPHA-1: PHYSICIAN PERSPECTIVE

Kamyar Afshar, DO

Alpha-1 antitrypsin deficiency (A1ATD) continues to be an underappreciated contributing factor for the development of COPD, even though 3–4% of people with COPD have been confirmed to have A1ATD [1, 2]. Reasons for this include biases that individuals with A1ATD are young non-smokers with bibasilar disease. This bias arose from initial case series [3, 4]. An additional bias for some physicians is that A1ATD is a rare phenomenon and there is no effective treatment. What Mrs. Moyer has experienced with the delays in recognition and the number of physicians seen over the course of the years until a diagnosis is made is a very common occurrence. All these are biases and patient challenges that are being addressed through the Alpha-1 and COPD Foundations with the assistance of alpha-1 specialists. Observational studies highlight that COPD is not the only clinical feature for individuals with confirmed alpha-1 antitrypsin deficiency. Evidence shows that A1ATD can be associated with a spectrum of clinical diagnoses, including

asthma, chronic bronchitis, emphysema, and bronchiectasis [5]. The guidelines from the American Thoracic Society recommend testing for (1) all adults with symptomatic COPD, regardless of smoking history, (2) all adults with symptomatic asthma whose airflow obstruction is incompletely reversible after bronchodilator therapy, (3) adults with bronchiectasis without evident etiology, (4) asymptomatic patients with persistent obstruction on pulmonary function tests with identifiable risk factors, and (5) test siblings of individuals with alpha-1 antitrypsin deficiency [6]. Health care providers should also be aware that A1ATD is not only found in white patients but also in other ethnicities at lower rates [7].

Through ongoing research, there is an evolution in the understanding of A1ATD. The “deficiency” in alpha-1 antitrypsin deficiency may be a misnomer in certain patients. Having the phenotypes PiSZ, PiZZ, or Pi Null is considered the “deficiency” alleles. The deficiency in alpha-1 antitrypsin deficiency is not only the serum value but also the functionality of the proteins available [8]. Hence, individuals with Pi-MZ or those with the F or I alleles may have normal serum values, but they may have dysfunctional proteins and may warrant augmentation therapy to stabilize lung functions as in patients with confirmed PiSZ, PiZZ, or Pi Null on a case-by-case basis. Being vigilant in making this diagnosis has clear implications in natural history of lung function decline [9].

The lung treatment recommendations for patients with A1ATD and COPD are generally the same as COPD without A1ATD. These recommendations include smoking cessation, physical exercise, routine vaccinations for influenza and pneumonia, and inhaler therapies. Management for A1ATD additionally includes determining if other family members are at risk and providing genetic counseling. There will be cases where patients are feeling angst and shame. Many patients have shared their guilt and sorrows of being a burden on their loved ones due to their physical limitations as well as the knowledge that they transferred the disease to their children. The liver disease surveillance is usually not considered in general COPD guidelines, hence another

important reason to test for A1ATD for all COPD patients. Surveillance includes blood tests (liver function test) and liver ultrasound. These patients should also receive vaccinations against the hepatitis A and B viruses. Lastly, they should be monitored for skin involvement, as A1ATD patients can also develop panniculitis [6].

Patients with reduced serum A1ATD levels confirmed to have PiSZ, PiZZ, or Pi Null phenotypes and have airflow obstruction in the range of 30–65% of the predicted FEV1 are eligible for alpha-1 replacement therapy, also known as, “A1 PI augmentation therapy”. There is no recommendation for augmentation therapy in subjects that continue to smoke. Currently, A1 PI augmentation therapy is provided intravenously either at home or at an infusion center. The dose is typically 60 mg/kg iv weekly. Before getting started on A1 PI augmentation therapy, the patient should have an IgA check based on the FDA-approved package insert [10]. A1 PI augmentation therapies may contain some trace amounts of IgA. Patients with IgA deficiency can have severe hypersensitivity or an anaphylactic reaction [10]. A1 PI augmentation therapy is usually safe. In clinical trials, the side effects related to A1 PI augmentation therapy included upper respiratory infection, urinary tract infections, headaches, and joint pain [11]. None of these adverse events resulted in discontinuation of the therapy.

Most individuals have a peripherally inserted iv placed for each weekly therapy. From some, the peripheral iv sites are much harder to locate, so a centrally placed (“port”) iv is recommended. In a randomized, double-blind, placebo-controlled trial, Chapman et al. demonstrated that A1 PI augmentation slows the progression of lung disease through the use of chest imaging [12]. There was no specific patient questionnaire to indicate subjective symptom changes. Patients who I started on A1 PI augmentation therapy state that they feel better after the third or fourth infusion. Their subjective improvements are energy levels and improved skin issues. Many state they have less dry skin. These claims cannot be substantiated however.

Some patients with COPD, irrespective of A1ATD, are resistant to the idea of exercise when they are feeling short of breath and exhausted all the time. Exercise is a key component to overall health. The less active one is, the more the muscles become deconditioned, thereby contributing to further deterioration of the lung function and feelings of exhaustion [13]. As physicians, we should not accept “not wanting to go or cannot go” to pulmonary rehab as easily. Even for those patients who say they exercise at home, I still recommend pulmonary rehab. It is the benefits of learning proper breathing techniques, direct observation of patient capabilities, and peer motivation that go beyond the physical benefits. This is showcased in Mrs. Moyer’s experience as well. She was reluctant to initially go, but quickly realized the benefits and utilized the skills through many years after. There are particular cases where there truly are barriers to attending pulmonary rehabilitation. This may be due to distance from home to the center, time constraints or, financial constraints. If so, there is a new online pulmonary rehab called Pulmonary Wellness Online (<http://www.pulmonarywellnessonline.com>). This is a 6-week program to help patients with COPD and other pulmonary conditions. The other added benefit in enrolling into a pulmonary rehab program is the ability to differentiate COPD exacerbations versus shortness of breath from deconditioning or anxiety with or without panic attacks [14]. A person with anxiety and panic disorder can often encounter persistent and unanticipated panic attacks when experiencing distressful thoughts, upsetting emotion stressors, and uncomfortable physical sensations. A proactive method to monitor for symptoms has become a more reliable method to track symptoms. I recommend all my patients to find the best COPD tracking tools that best meet their needs. These tracking tools help as a daily diary, patients receiving a form of biofeedback and assists with notifying the physician to determine if there is a need for additional treatment [15].

COPD, irrespective of having A1ATD, is a progressive disease. Most of the patients my colleagues and I have treated have certain fears when they come to the clinic. These have

included, but are not limited to, wanting to know if there are changes to the lung disease (“Are my lungs worsening?”), if there is a presence of a lung cancer, if they need escalation in therapy or if they are in need of oxygen. Throughout the last few years, more patients are now overtly asking how long they have to live. There are still a large number of people who want to know, but are afraid to ask. This causes misinterpretation of intentions. Patients may yell at physicians or other health care professionals. It is more based on the fear of dying and challenges with coping strategies. These are very challenging times. These events occur more readily when patients are referred to lung transplantation. The referral to a lung transplant substantiates the notion that death is on the horizon. Lung transplant centers balance the methods to provide ample patient education and the inherent risks related to the surgery or medications, while also providing hope for a better quality of life. A large amount of time is dedicated to the ability to cope with uncertainty, complications, longer time on the active waitlist, and even death with or without lung transplantation [16].

Worldwide, approximately 30% of lung transplants were performed for patients with COPD while approximately 5% were performed for A1ATD [17]. Almost all the candidates ask what they could do to avoid the need for lung transplant and/or what they could do to improve the chances to have a successful outcome if listed. The healthier one is (from a physical standpoint) going into a transplant, the more successful they are from a recovery period. Daily exercise, adherence to medications, and other health habits will allow for a smoother transition to recovery. The demands for monitoring lung transplant recipients are substantially higher than those without the need for a lung transplant. As mentioned above, investing time to improve coping strategies will help with some un-anticipated events. Mrs. Moyer shared with you her complications and need to adjust medications that are life-saving, but can cause other complications.

The overall success for any patients is based on the partnership of the patient and the physicians. Physicians are being inundated with

tremendous amounts of information [18]. Many alpha-1 patient readers have most likely experienced this. They were the ones that took the information to their doctors for testing or treatments. A more active participation by patients in their health care is welcomed. Patients should take some caution to the sources of information however. There have been patients who have been provided some misinformation [19]. To streamline valuable transfer of information, the Alpha 1 Foundation, the alpha coordinator and the alpha-1 specialists are actively engaging in the medical community to increase the awareness of the A1ATD condition, methods for proper testing and its interpretation, as well as available treatment recommendations to improve the quality of life and longevity of patients with A1ATD. Mrs. Moyer and I hope this patient–physician perspective can assist in the dialogue in the betterment of others seeking medical treatment for A1ATD.

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