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LIVER TRANSPLANTATION IN A LUNG TRANSPLANT RECIPIENT FOR ALPHA-1-ANTITRYPsin DEFICIENCY  |  FREE TO VIEW

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Abstract

INTRODUCTION: Alpha-1 antitrypsin is a protein with inhibitory capability over the proteolytic enzyme elastase. Since its first description in 1963, over 100 different AAT alleles have been described, each producing a different phenotypic variant of AAT. The most severe form of deficiency is the homozygous expression of the Z allele or PiZZ. When this expression occurs, it accounts for 95% of cases of severe AAT deficiency. The three organs most commonly affected by AATD are the lungs, liver and skin. Alpha-1 antitrypsin deficiency (AATD) is the most frequently recognized genetic risk factor for chronic obstructive pulmonary disease (COPD). Even though it remains underdiagnosed, its importance continues to grow in the field of solid organ transplantation, accounting for 8-9% of all lung transplants. Individuals with the PiZZ phenotype are also at risk of hepatitis as neonates and cirrhosis as adults. AATD is the most common metabolic liver disease requiring liver transplantation in children. However, in a recent population study, with self-report questionnaires, the prevalence of liver disease was 7.6% (165/2175), and severe liver disease was 1.8% (40/2175) among the participants of the Alpha-1 Foundation Registry. Furthermore, a mortality analysis found that liver disease was included as a cause of death in 21% of death certificates listing AAT deficiency, and autopsy studies have shown cirrhosis in 37% of patients with AAT. We describe a unique case of a 59 year-old woman with severe AATD who required single lung transplant and then 5 years later developed AATD cirrhosis requiring sequential liver transplantation.

CASE PRESENTATION: A 59 year-old woman ex-smoker with AATD (PiZZ) and very severe COPD (FEV1 21%) underwent single-right lung transplantation without significant complications. Her immunosuppressive regimen included tacrolimus (FK-506), prednisone, azathioprine, and opportunistic infection prophylaxis with ganciclovir, trimethoprim/sulfamethoxazole, and itraconazole. After 5 years of follow up, she was admitted to the hospital with abdominal pain, malaise, epistaxis, and thrombocytopenia. Initially, the thrombocytopenia was thought to be secondary to azathioprine. However, the lack of resolution after several months prompted a bone marrow biopsy that was non-diagnostic. Abdominal computed tomography (CT) showed splenomegaly, portal hypertension, ascites, and changes suggestive of cirrhosis. An esophagogastroduodenoscopy (EGD) demonstrated varices grade II requiring banding. Extensive search for alternative causes of liver failure included alcohol, viral hepatitis, primary biliary cirrhosis, primary sclerosing cholangitis, Wilson’s disease, non-alcoholic fatty liver disease, iron overload, and autoimmune hepatitis were all negative. A transjugular liver biopsy showed extensive AAT globules. Medical management was instituted however, progression of disease, recurrent admissions to the hospital for large volume paracentesis, and metabolic encephalopathy deemed her a candidate for liver transplantation. After 6 years and 2 months of her lung transplant, she underwent successful orthotopic liver transplant. The explanted liver confirmed the distorted architecture due to cirrhosis, and showed prominent PAS-positive, diastase resistant globules of variable sizes, as well as periseptal zonation. These combined features were diagnostic of ATD. Her follow-up at 10 months of the liver transplant she continues to do well and has a Karnofsky of 80.

DISCUSSIONS: To the best of our knowledge, this is the first reported case in the literature of ATD leading to subsequent

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lungs and liver transplantation. This case exemplifies the importance of the extrapulmonary manifestations of ATD, as well as the different pathogenesis underlying the development of severe emphysema, and liver disease in ATD patients.

**CONCLUSION:** ATD is an underdiagnosed condition that can involve the lung, liver and skin of affected individuals. Smoking is a preventable risk factor for development of emphysema in affected patients. Despite successful transplantation, extrapulmonary manifestations of ATD can occur after transplantation.

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