CASE REPORT

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# Alström syndrome with liver cirrhosis: First case from Turkey

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*Alström syndrome is a rare autosomal recessive genetic disorder characterized by cone-rod dystrophy, hearing loss, childhood truncal obesity, insulin resistance and hyperinsulinemia, type 2 diabetes, hypertriglyceridemia, short stature in adulthood, cardiomyopathy, and progressive pulmonary, hepatic, and renal dysfunction. Alström syndrome is a very rare cause of liver cirrhosis. Post-mortem biopsies of patients with Alström syndrome show relevant fibrosis in multiple organs especially in the liver, kidneys, heart, and lungs. We report the case of a patient with Alström syndrome who presented to emergency department with esophageal variceal bleeding and who was not known to have hepatic cirrhosis before.*

**Key words:** Alström syndrome, hepatic fibrosis, liver cirrhosis, variceal bleeding

## Türkiye'den bildirilen ilk karaciğer sirozlu Alström vakası

*Alström sendromu çocukluk çağında trunkal obezite, insülin direnci ve hiperinsülinemi, tip 2 diyabet, hipertrigliseridemi, yetişkinlikte boy kısalığı, kardiyomyopati ve ilerleyici akciğer, karaciğer ve böbrek fonksiyon bozukluğu, işitme kaybı, gözde koni-çomak distrofisi ile karakterize otozomal resesif geçişli genetik bir hastalıktır. Alström sendromu karaciğer sirozunun oldukça nadir bir sebebidir. Alström sendromlu hastaların post-mortem biyopsilerinde karaciğer, böbrek, kalp ve akciğerler gibi birçok organda fibrosis gösterilmiştir. Bilinen karaciğer sirozu olmayan ve acil servise özofagus varis kanaması ile başvuran Alström sendromlu bir vaka sunmaya çalıştık.*

**Anahtar kelimeler:** Alström sendromu, hepatik fibroz, karaciğer sirozu, varis kanaması

## INTRODUCTION

Alström syndrome (AS) is a very rare autosomal recessive genetic disorder first described in 1959 by Alström and characterized by cone-rod dystrophy (early nystagmus, blindness) in infancy, hearing loss, childhood truncal obesity, hyperinsulinemia and insulin resistance, type 2 diabetes mellitus, hypertriglyceridemia, short stature in adulthood, dilated cardiomyopathy, progressive pulmonary, hepatic and renal dysfunction, and fibrosis in multiple organs (1). Usually, symptoms appear in infancy with great variability in age of onset and severity of clinical symptoms, also in families having identical mutations. There is no specific therapy and affected individuals are treated for specific symptoms. Clinical features are usually sufficient for diagnosis, since AS is caused by mutations in the ALMS1 gene, molecular genetic tests can be used for confirming diagnosis (2). ALMS1 gene encodes a large protein with implicated roles in ciliary function, cellular quiescence, and intracellular transport. Affected fibroblasts show cytoskeleton abnormalities and migration impairment, expression and production of collagens are up-regulated hence multiple-organ fibrosis occurs (3).

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Hepatic dysfunction in AS was first described by Connolly in 1991 (4). We report the case of a AS patient who presented to emergency department with esophageal variceal bleeding and who was not known to have hepatic cirrhosis before.

## CASE REPORT

A 19-year-old male was born at full term with a weight of 3700 grams. There was no parental consanguinity. During his early childhood, the patient was noticed to have poor visual acuity and obesity. Five years ago, he was diagnosed as AS in our pediatric endocrinology outpatient clinic because of deafness, central vision loss, type 2 diabetes mellitus, acanthosis nigricans, truncal obesity, and short stature. He was admitted to emergency department with hematemesis and melena. On his physical examination, blood pressure was 90/60 mmHg, pulse 96 beats/min, and hepatosplenomegaly and acanthosis nigricans were observed. Laboratory evaluation revealed hemoglobin of 11.9 g/dL, platelet 58 000/µL, glucose 240 mg/dL, aspartate aminotransferase (AST) 76 u/L, alanine aminotransferase (ALT) 98 u/L, gamma glutamyl transferase (GGT) 122 u/L, alkaline phosphatase (ALP) 67 u/L, international normalized ratio (INR) 1.46, albumin 3.3 g/dL, and total bilirubin of 1.1 mg/dL. Hepatobiliary ultrasonography of the patient showed nodularity in the liver edge, parenchymal heterogeneity, caudate lobe hypertrophy, splenomegaly (approximately 19 cm in the longitudinal axis), and portal vein diameter of 13 mm. On upper gastrointestinal system endoscopy, grade 3 esophageal varices with active bleeding were seen, and band ligation was performed. Searching for etiology of cirrhosis, infectious agents including hepatitis B and C, cytomegalovirus, Epstein-Barr virus, and autoimmune markers were found to be negative. Serum ferritin, copper, ceruloplasmin, and alpha-1-antitrypsin levels were normal. There was no thrombus on his portal doppler ultrasonography. We performed a liver biopsy that revealed nodular parencyhma, fibrosis, fatty degeneration areas, and lymphocyte infiltration. The limiting plate was irregular (Figure-1).

## DISCUSSION

Hepatic dysfunction in AS is variable and ranges from mildly elevated transaminase levels to cirrhosis. Liver involvement in AS was first described by

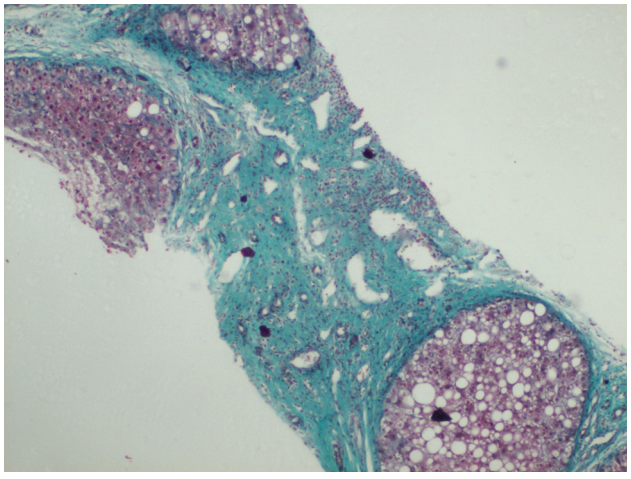

**Figure 1.** Large fibrous bands and noduler parencyhma of liver (Mason Trichrome x40).

Connolly in 1991 (4), and the liver disease was diagnosed when the patient was eight years of age, with pathological findings of chronic active hepatitis. No viral, autoimmune, or metabolic etiology was found. Four other patients have been described with AS, and evidence of liver disease was demonstrated during the third decade of life by Awazu in 1997 (1); three patients had cirrhosis and one had steatosis. In 2001, acute liver failure in AS at 8 years of age was reported by Quiros-Tejeira et al (5). In 2008, liver fibrosis with hepatocellular adenoma in AS was demonstrated by Morgan et al (6). It is not yet known why some patients with AS develop serious liver disease, while others do not. Fatty liver may progress to significant fibrosis, cirrhosis, and portal hypertension in AS.

The possibility that hepatic dysfunction is an incidental complication in patients with AS cannot be ruled out, but the association of a rare syndrome with liver cirrhosis at younger ages without known causes suggests that liver dysfunction is a part of systemic manifestations of AS. Post-mortem biopsies of patients with AS show relevant fibrosis in multiple organs especially in the liver, kidneys, heart, and lungs, which involvements are closely related with complications and prognosis. There is no specific treatment of the liver involvement in AS, and also the effectiveness of liver transplantation has not been proven. Since AS is a very rare condition, we should consider the possibility of hepatic cirrhosis development and carefully follow up hepatic function tests.

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