



Cirrhosis in the Setting of Turner Syndrome and Alpha-1 Antitrypsin Deficiency

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INTRODUCTION

Certain genetic conditions predispose patients to liver disease, with some ultimately progressing to cirrhosis. Alpha-1 antitrypsin (A1AT) deficiency is an example with a relatively clear mechanism, whereas liver disease in Turner syndrome is not as well-elucidated. Here we present a case of a woman with both conditions who developed severe liver disease.

CASE PRESENTATION

HPI:

51 year-old female with Turner syndrome and solitary kidney was admitted with volume overload and acute kidney injury (AKI). About two months prior, she had been diagnosed with cirrhosis, which was presumed to be due to alcohol use, although she denied history of excessive drinking (previously 1-3 glasses of wine in social settings; had quit 4 months prior). She was started on diuretics and lactulose, but presented a few weeks later in decompensated cirrhosis.

Vitals: Afebrile, BP 94/60, HR 86, RR 15, SpO2 97% on RA, BMI ~38 kg/m²

Physical Exam: Notable for short stature, webbed neck, broad chest, cubitus valgus, jaundice, scleral icterus, soft bibasilar crackles, anasarca, intact mentation and no asterixis

Labs: (trend from 2.5 weeks prior included if available)

AST: 303U/L → 220U/L, ALT: 176U/L → 113U/L

Alkaline phosphatase: 834U/L → 821U/L

Total bilirubin: 20.9mg/dL → 21.4mg/dL

Albumin: 1.8g/dL → 1.5g/dL

Platelets: 126k/mm³, INR: 1.34, Ammonia: <10umol/L

Serum creatinine: 0.75mg/dL → 1.3mg/dL

MELD-Na: 26

Hospital Course:

On further evaluation, patient was found to have A1AT deficiency with PiZZ phenotype and low A1AT level. Her AKI improved with albumin infusions and withholding of diuretics. LFT abnormalities also improved. She was discharged home with plans for outpatient liver transplant evaluation.

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Image credit:

- <https://ghr.nlm.nih.gov/condition/turner-syndrome>
- https://en.wikipedia.org/wiki/Alpha_1-antitrypsin_deficiency

DISCUSSION

MECHANISMS OF LIVER DISEASE

TURNER SYNDROME¹

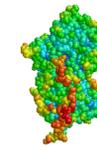


Most frequently reported: steatosis, steatofibrosis, steatohepatitis with elevated BMI.

Other proposed mechanisms include: congenital abnormality in blood vessels leading to architectural changes in the liver.

Major liver complications are rare.

A1AT DEFICIENCY²



Intrahepatocyte accumulation of A1AT molecules leading to cell death, inflammation, fibrosis, cirrhosis.

Clinical presentation varies.

~1/3 of adult patients with PiZZ phenotype (severe A1AT deficiency) develop clinically significant liver injury.

POSSIBLE INTERPLAY BETWEEN THE TWO?

Turner syndrome occurs with absence or structural alterations of one of the X-chromosomes, while A1AT deficiency stems from mutations in the *SERPINA1* gene on chromosome 14.

Prior studies on sex chromosome abnormalities and A1AT deficiency⁵⁻⁹:

Author	Year	Title
Awadalla <i>et al.</i>	1990	Alpha-1 antitrypsin and sex chromosome abnormalities
Aarskog & Fagerhol	1970	Protease inhibitor (Pi) phenotypes in chromosome aberrations
Fineman <i>et al.</i>	1976	Increased frequency of heterozygotes for alpha1 antitrypsin variants in individuals with either sex chromosome mosaicism or trisomy 21
Kueppers <i>et al.</i>	1975	Alpha-1 antitrypsin phenotypes in sex chromosome mosaicism
Mulley & Sutherland	1981	Distribution of 1-antitrypsin phenotypes in chromosome abnormalities

No definite connection was elucidated and studies were limited by small sample sizes. In more recent studies:

- Male gender has been noted as a risk factor for advanced liver disease in adults with A1AT deficiency.³
- There is some evidence that estrogen therapy improves hepatic function in women with Turner syndrome.⁴

In our patient, the co-existence of two conditions likely led to a more severe liver disease at a relatively young age.

TAKE HOME POINTS

- Patients with Turner syndrome should be screened and monitored for hepatic dysfunction.
- The connection between A1AT deficiency and Turner syndrome remains to be elucidated.
- However, when a patient with Turner syndrome presents with hepatic dysfunction, it is important to keep a broad differential that includes A1AT deficiency.
- One should avoid anchoring on alcohol abuse as the cause of cirrhosis, especially when the patient denies history of significant alcohol use.