

TURNER'S SYNDROME AND LIVER INVOLVEMENT: IS THERE A PLACE FOR TREATMENT WITH URSODEOXYCHOLIC ACID?

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INTRODUCTION: Abnormal liver function tests (LFTs) are frequent in patients with Turner's syndrome (TS) with a prevalence between 20-80% depending on the patient's age. While the aetiology remains unclear, metabolic factors and intrahepatic biliary disease have been postulated to be significant. Moreover, some patients with TS have a predominantly cholestatic biochemical abnormality and others a hepatic picture.

Ursodeoxycholic acid (UDCA) has been shown to be a useful therapy in primary biliary cirrhosis, which is a chronic cholestatic liver disease characterised by destruction of small intrahepatic bile ducts, leading to fibrosis and cirrhosis.

CASE REPORT: A 28-year-old woman presented with a ten year history of abnormal LFTs. At six monthly follow-up, for the last decade, persistently elevated serum alkaline phosphatase (ALP), aminotransferases and γ -glutamyl transferase (GGT) were found, approximately 2-3 times the upper limit of normal (Fig. 1). Apart from experiencing biliary colic for which she underwent a cholecystectomy at 22 years of age, she remained asymptomatic.

The patient was diagnosed with TS (45X/46XrX karyotype) at the age of 6 years. She was started on growth hormone treatment and at age 13 years hormone replacement therapy (HRT) was started.

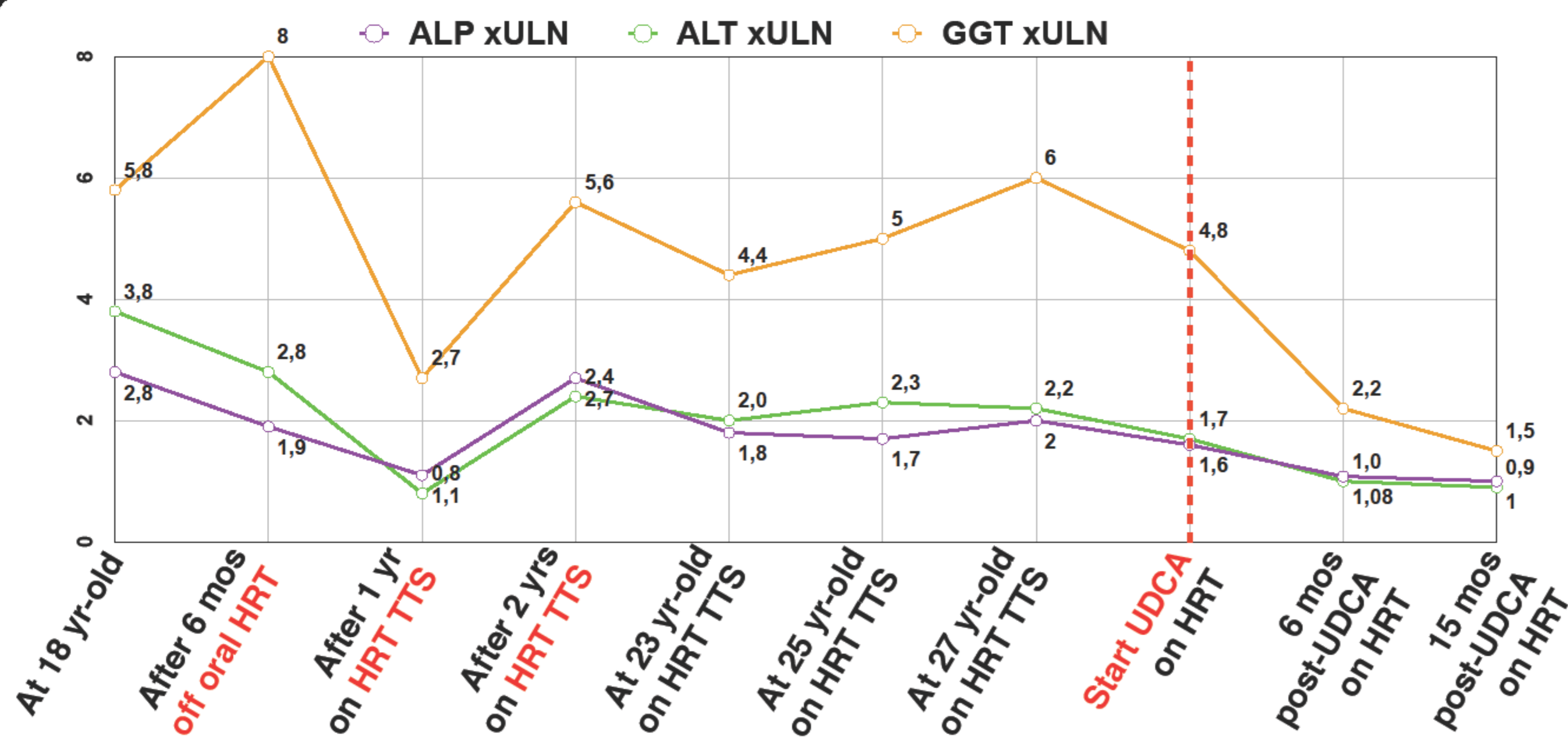


FIG.1. ALP, alkaline phosphatase; ALT, alanine aminotransferase; GGT, γ -glutamyl transferase; HRT, estrogen replacement therapy; TTS, transdermal patch; UDCA, ursodeoxycholic acid.

Abdominal ultrasound was unremarkable and no fatty infiltration was seen. Persistence of abnormal LFTs, even after a period off HRT and after switching from oral to transdermal patches, led to magnetic resonance cholangiopancreatography (MRCP) which revealed normal intra and extra-hepatic bile ducts (Fig 2).

A liver biopsy was performed and showed mild portal fibrosis and inflammation with no bridging fibrosis and no evidence of steatosis (Fig.3).

She had no history of congenital cardiac malformations or autoimmune disease. There was no history of diabetes, hypertension, dyslipidaemia, excess alcohol intake or family history of liver disease. Her weight remained stable (BMI 24.5 Kg/m²). She was clinically and biochemically euthyroid. Autoimmune markers and screening for viral hepatitis were negative.

Transferrin saturation, ceruloplasmin, copper and alpha-1 antitrypsin were all within normal limits.

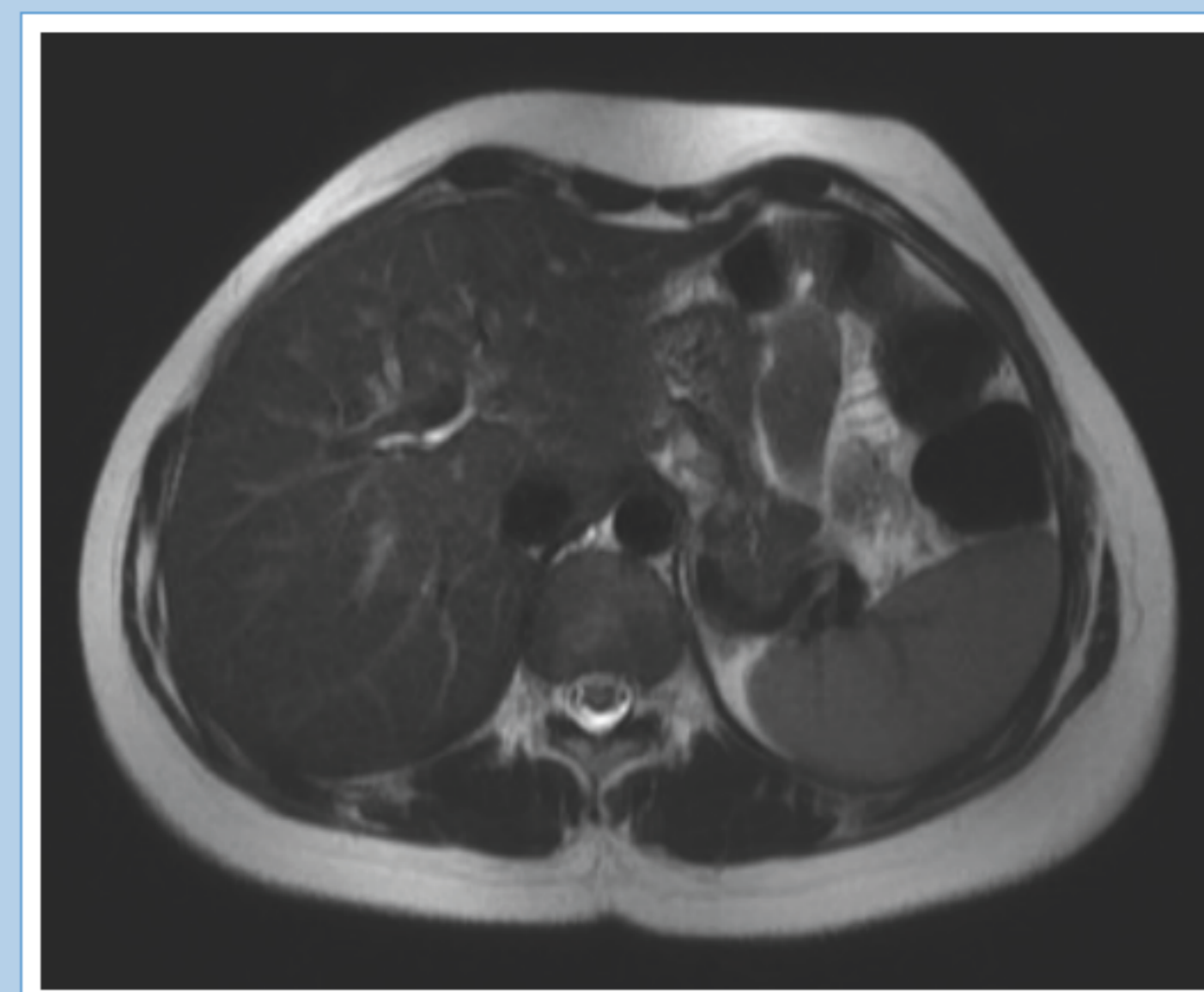


FIG.2. Magnetic resonance cholangiopancreatography (MRCP).

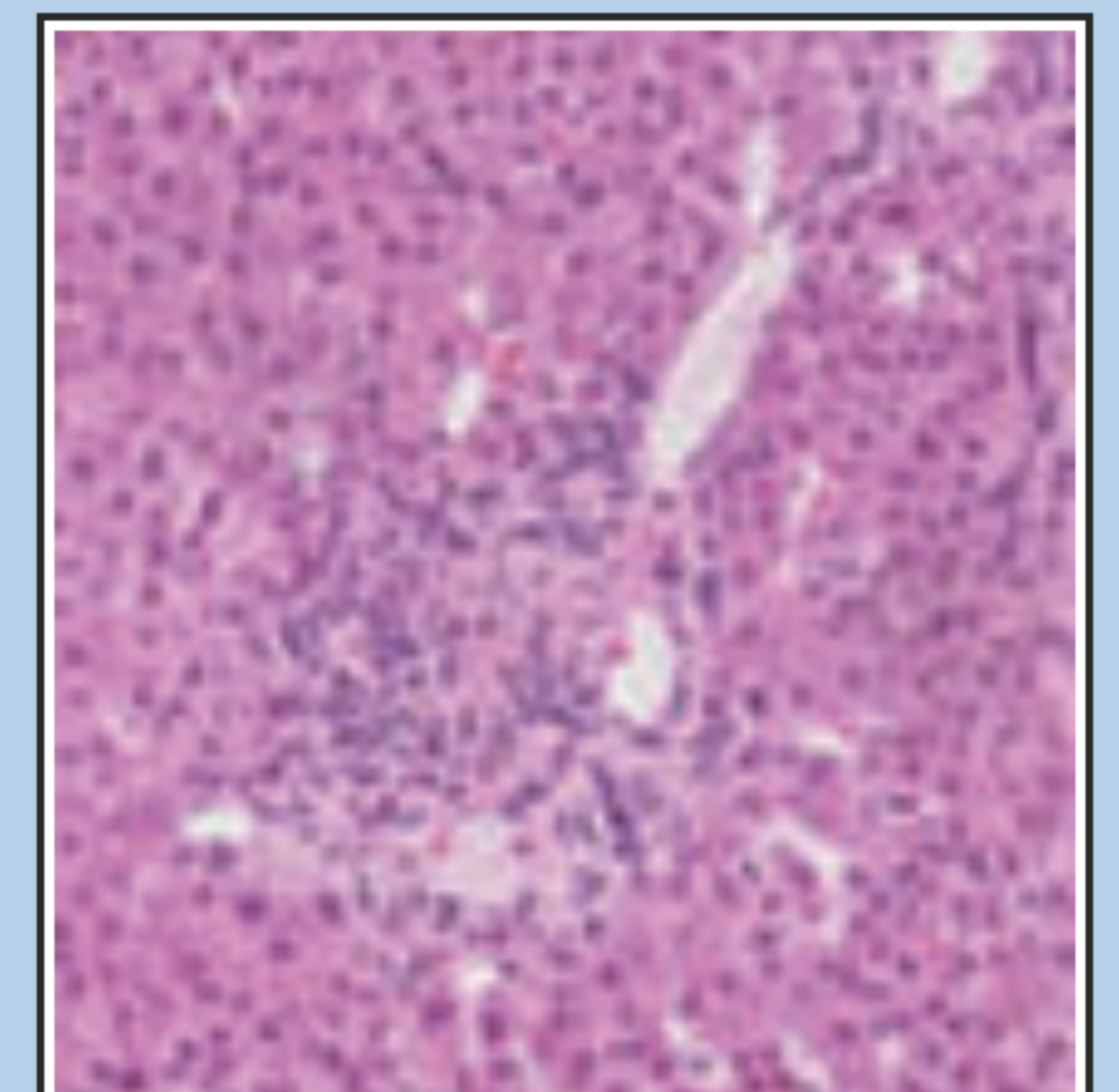


FIG.3. Liver biopsy.

The patient was started on UDCA (13 mg/kg/day) and after 6 months her LFTs had improved considerably to near normal values. UDCA was well tolerated and after 15 months of treatment her LFTs continued to improve. The percentage falls from the mean value before starting treatment and after 15 months were: ALP - 49%, ALT -60% and GGT -72%.

DISCUSSION: This case shows that UDCA treatment may be of benefit to TS patients with abnormal LFTs. In particular, in cases of cholestatic syndrome with normal liver ultrasound and without liver architectural changes, a trial of UDCA could be considered. Based on the study of primary biliary cirrhosis, serum ALP levels at 6 months can be helpful in predicting responders to UDCA. Importantly, HRT does not lead to deterioration in LFTs.

CONCLUSIONS: Due to the high prevalence of LFT abnormalities in TS, often at a young age, the use of UDCA warrants further study.

The natural history of patients with TS and elevated cholestatic liver enzymes is unclear and it is possible that the progression of biliary lesions might be also delayed by UDCA treatment.

References: Roulot D, et al. Vascular involvement of the liver in Turner's syndrome. Hepatology 2004

