CASE REPORT

Short telomere syndrome and fibrosis

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Learning Point

We are presenting a patient with dyspnea and pulmonary fibrosis who was later found to have cirrhosis with an ultimate diagnosis of telomere length disorder. Telomere shortening syndrome should be considered in the differential diagnosis of patients with cryptogenic cirrhosis, especially if they have other manifestations of organ fibrosis.

A 43-year-old man presented with progressive dyspnea on exertion over several months. He is a heavy smoker but denied exposure to chemicals, inhalants or dusts. Medications included fluticasone and albuterol inhalers.

On physical exam patient appeared significantly older than his biologic age. Chest exam showed bilateral crackles without wheezing or rhonchi. Cardiac exam was unremarkable. His liver was enlarged 1–2 cm below the right costal margin and his spleen was palpated 1 cm below the left costal margin. Skin exam revealed spider nevi but no palmar erythema.

Spirometry suggested moderate restriction with severely impaired gas exchange suggestive of interstitial lung disease. CT chest (Figure 1a) reinforced these findings. Lab work-up showed normal complete blood count and normal serum creatinine, alpha-1 antitrypsin and angiotensin-converting-enzyme (ACE).

Lung biopsy showed subpleural interstitial fibrosis, mild superimposed acute lung injury and focal bronchiectasis, confirming pulmonary fibrosis. He was diagnosed according to the American Thoracic Society/International Association for the Study of Lung Disease guidelines.

Lab work-up showed normal complete blood count and normal serum creatinine. Alpha-1 antitrypsin phenotype was MM and the level was normal. ACE blood level was within normal range. Additional lab investigation showed the following results: Serum total protein 7.2 g/dl, albumin was 3.1 g/dl, total bilirubin 1.3 mg/dl, conjugated bilirubin 0.4 mg/dl, alkaline phosphatase 190 U/l, aspartate aminotransferase (AST) 48 U/l, alanine aminotransferase (ALT) 31 U/l, international normalized ratio (INR) 1.1.

The chest CT (Figure 1a) incidentally revealed heterogeneous liver attenuation, especially in the left lobe suggestive of liver cirrhosis. The patient was not known to have liver disease nor carried any risk factors for chronic liver disease including heavy alcohol use or metabolic risk factors like obesity, diabetes mellitus and hyperlipidemia. Serological work-up for chronic liver disease, including viral hepatitis panel, autoimmune markers, iron indices and ceruloplasmin were all unrevealing.

Liver CT was done (Figure 1b) and showed cirrhosis and sequel of portal hypertension, with no focal liver lesion. No intra-hepatic or extra-hepatic biliary dilatation with patent hepatic vasculature. Corrected sinusoidal pressure was calculated to be 10 mm Hg (hepatic wedge pressure—free hepatic pressure) consistent with portal hypertension.

Porto-systemic pressure measurements revealed: right atrial pressure (~3 mm Hg), right ventricular pressure (3 mm Hg), inferior vena cava pressure (~2 mm Hg), free hepatic pressure (0 mm Hg), hepatic wedge pressure (10 mm Hg). Right hepatic venogram demonstrated no evidence for filling defects, focal stenosis or web formations.

Liver biopsy was done, it showed cirrhosis confirmed by trichrome stain; however, the etiology of liver cirrhosis was not apparent histologically.

The combination of pulmonary fibrosis and liver cirrhosis raise suspicion for a telomere disorder. Telomere shortening can be caused by genetic or environmental factors, which make the body predisposed to fibrosis and eventually multi-organ failure, such as IPF, a well-known disease of telomere maintenance and liver cirrhosis. Telomerase is an enzymatic protein...
complex which includes telomerase reverse transcriptase (TERT) and telomerase RNA component (TERC) which are used as templates to synthesize telomere DNA.²

In this patient, specific genetic testing for mutations in TERC and TERT did not show any abnormalities. However, less specific, telomere length testing showed that his telomeres were below the first percentile of telomere length for the patient age. This suggests that he has another telomerase gene mutation causing the same phenotype as the more common TERC and TERT telomerase gene deficiencies.

Herein, we presented a patient who presented with dyspnea and pulmonary fibrosis and was later found to have cirrhosis with an ultimate diagnosis of telomere length disorder. Telomere shortening syndrome should be considered in the differential diagnosis of patients with cryptogenic cirrhosis, especially if they have other manifestations of organ fibrosis.

References

Figure 1. (A) Axial high resolution image of the chest shows areas of traction bronchiectasis (white arrow) and predominantly peripheral reticular opacities in both lungs (black arrow) compatible with interstitial fibrosis. (B) Contrast enhanced CT image of the abdomen in the axial plane shows a cirrhotic liver with diffuse atrophy and lobulated contour. There are multiple portosystemic venous collaterals (black arrow) and an enlarged spleen, in keeping with portal hypertension.