Case Report

Refractory Hepatic Hydrothorax: A Rare Complication of Systemic Sclerosis and Presinusoidal Portal Hypertension

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Received 19 February 2018; Accepted 22 March 2018; Published 30 April 2018

Academic Editor: Julio M. F. Chebli

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We report on a rare case of refractory hepatic hydrothorax in an individual with Scleroderma/CREST syndrome and noncirrhotic portal hypertension. Portal pressure measurements revealed a normal transjugular hepatic venous portal pressure gradient, mild pulmonary hypertension, and an unremarkable liver biopsy except for mild sinusoidal dilatation. Pulmonary hypertension, cardiac diastolic dysfunction, and chronic kidney disease were determined to be the causes of his refractory pleural effusions and ascites. Over the year, he underwent 50 thoracenteses and 20 paracenteses averaging 10–12 liters/week. Repeat pulmonary evaluation determined his pulmonary pressures to be normal and a secondary review of the “unremarkable” liver biopsy noted mild venous outflow obstruction and possibly Nodular Regenerative Hyperplasia (NRH). Repeat portal pressures indirectly and directly confirmed the existence of presinusoidal portal hypertension that has been associated with NRH. A transjugular intrahepatic portal systemic shunt (TIPS) was placed and he has not required thoracentesis or paracentesis over the past 18 months.

1. Introduction

Idiopathic noncirrhotic portal hypertension (INCPH) has many etiologies, but a common denominator is vascular resistance at various locations that include the intrahepatic sinusoidal and presinusoidal as well as extrahepatic portal and hepatic veins [1]. Schistosomiasis is a common worldwide illness and the most frequent cause of INCPH [2]. Nodular Regenerative Hyperplasia (NRH) was first described in 1959 [3]; however this is a histological diagnosis that can often be overlooked. We describe a complicated rare case of refractory right-sided pleural effusions and ascites due to NRH and presinusoidal portal hypertension that was successfully treated with a transjugular intrahepatic portal systemic shunt (TIPS).

2. Case Report

A 59-year-old Caucasian male was referred to our liver center for refractory right-sided pleural effusion and abdominal ascites. His history is significant for Scleroderma/CREST syndrome and chronic kidney disease (CKD). He had 12 paracenteses in 2015 and starting from February 2016 was undergoing thoracentesis 3 times weekly (about 8-9 liters/week) and a single weekly paracentesis up to 5 liters. Medications included Spironolactone 50 mg and Furosemide 20 mg, which were limited dosages due to CKD. In February 2016, prior to our visit, he underwent a liver transplant evaluation: Na 138 mg/dL, Cr 4.4 mg/dL, eGFR 31 mL/min, INR 1.0, Hb 13 g/dL, Platelets 342 × 10^3/mm^3, TB 0.5 g/dL, AlkPhos 278 IU/L, ALT/AST 46/40 IU/L, albumin 2.7 mg/dL, negative viral serology, ANA 1:320, SMA and AMA negative, C282Y/H63D, and MELD-Na score 14. Abdominal ultrasound revealed a heterogeneous liver and ascites. A thoracentesis demonstrated a SAAG 1.9 and total protein 3.3 g/dL suggesting posthepatic portal hypertension. A right heart catheterization was notable for RA 5 mmHg, PA 31/15 mm/Hg, mean 22 mmHg, normal Echo LV function, and grade 1 diastolic dysfunction. At this juncture, the etiology of his presumed cirrhosis had not been determined and a liver biopsy with portal pressures was to be scheduled but he wanted a second opinion and presented to us in March.
The physical exam revealed a pleasant frail appearing gentleman with stable vital signs: B/P 87/58, HR 80, and BMI 24.5 kg/m^2; labs demonstrated TB 0.5 mg/dL, AlkPhos 462 IU/L, ALT/AST 62/65 IU/L, total protein 5.7 IU/L, albumin 3.2 mg/dL, and Cr 2.4 mg/dL (spironolactone had been discontinued one month earlier). A large right-sided-pleural effusion with moderate abdominal ascites was noted on examination. He underwent a transjugular intrahepatic portal systemic shunt study (TIPS) and liver biopsy after 100 g of IV albumin (given for renal dysfunction) with the following results: RA 13 mmHg, FHVP 16 mmHg, WHVP 17 mmHg, and HVPG 1 mmHg (Table 1). The TIPS was aborted due to the normal sinusoidal portal pressure gradient and elevated right-sided pressures. A right heart catheterization 5 hours later revealed RA 13 mmHg, PA 57/30 mmHg, mean 39 mmHg, PWP 20, and CO 5.5 L/min. Presumptive diagnosis was mild/moderate mixed arterial and venous pulmonary hypertension. The liver biopsy revealed mild sinusoidal dilatation, no inflammation or fibrosis, trace iron deposition and was considered unremarkable, other than mild outflow obstruction (Figure 1). The patient was subsequently referred for a pulmonary work-up as well as a dysphagia evaluation. Pulmonary function tests demonstrated a low DLco 9.33 L, vital capacity 2.75 L, and a repeat heart catheterization after a thoracentesis and paracentesis without albumin: RA 3 mmHg, PA 30/10 mmHg, mean 18 mmHg, and PWP 12 mmHg (Table 1). An EGD demonstrated trace esophageal varices (Figure 2). A second interpretation of the liver biopsy noted mild venous outflow obstruction and possibly Nodular Regenerative Hyperplasia (NRH, Figures 3 and 4). Taken together, in the setting of normal right heart pressures and a possible diagnosis of NRH, the patient could have portal hypertension due to a presinusoidal obstruction. He successfully underwent a TIPS shunt with a post-TIPS PPG of 7 mmHg. Prior to TIPS, the patient underwent 50 thoracenteses and 20 paracenteses over that past year and after TIPS he had 1 thoracentesis/paracentesis 10 days after and none over the past 18 months. Other than mild hepatic encephalopathy, controlled on medication, no other adverse effects have been reported.

3. Discussion

Idiopathic noncirrhotic portal hypertension (INCPH) has been proposed to unify the obliterated vasculopathy that links various etiologies [4]. Five diagnostic criteria must be met to diagnose INCPH: (1) clinical evidence of portal hypertension, (2) absence of cirrhosis or advanced fibrosis on liver biopsy, (3) intrahepatic etiologies of liver disease such as viral hepatitis and fatty liver disease, (4) Sarcoidosis, Schistosomiasis, and congenital hepatic fibrosis, and (5)
significant HVGP is considered
direct calculation of the portal venous system. A clinically
these indirect portal pressure measurements alone, requiring
presinusoidal portal hypertension cannot be diagnosed by
FHVP and WHVP but a normal HVPG. In comparison,
Postsinusoidal portal hypertension is defined by an elevated
than 6 mmHg, this signifies sinusoidal portal hypertension.
if the difference
of mmHg higher than the RA pressure. The WHVP indi-
hypertension [11]. The FHVP should be within a couple
pressure assessments.
will undergo a large volume paracentesis several days prior to
the development of ascites or esophageal varices and clinical
decompenstation in subjects with compensated cirrhosis [12].
The patient’s initial portal pressures were consistent with
posthepatic portal hypertension. The liver biopsy did not
reveal cirrhosis; therefore pulmonary hypertension and mild
diastolic dysfunction were determined to be the culprits
of the pleural effusions and ascites. However, a subsequent
pulmonary evaluation revealed mild pulmonary dysfunction
and normal right heart pressures. During this period he had an
EGD for dysphagia, and trace esophageal varices were
noted. Finally, a repeat interpretation of the liver biopsy
suggested NRH. Taking these together, we were suspicious of
a presinusoidal etiology for his effusions/ascites and directly
measured the portal vein along with indirect measurements.
The portal pressure was 15 mmHg and the PPG was 11 mmHg,
consistent with portal hypertension; therefore we proceeded
with TIPS placement. Ten days after TIPS he needed a single
3-liter thoracentesis and subsequently has not warranted any
further thoracentesis or paracentesis over the past 1.5 years.
A recent review investigated the outcome of TIPS in 25 subjects
with NCPIH [13]. NRH was identified in 12 subjects and
associated with Scleroderma in only 1 person in this study.
Eight of nine NRH individuals had a normal WHVP; all 12
had elevated portal pressures and 9/10 had an elevated HVPG.
Indications for TIPS included either esophageal varices or
ascites; none of the NRH subjects had hepatic hydrothorax
listed as an indication. The long-term outcome over 3 years
was very good with 80% functioning TIPS and hepatic
encephalopathy was the most common adverse effect.
An international working definition of liver nodules
defined NRH in 1995 [14]. It is postulated that the under-
lying pathogenesis for presinusoidal portal hypertension is
obliteration of the small portal venules [15] and abnormal
electron dense deposits within the hepatic microcirculation
[16]. The immunologic or immunogenetic risk factors for
these microvasculopathies are unknown. The association
of NRH and Sclerosis has been limited to case reports but
the recent systemic review does suggest common clinical
manifestations including Raynaud’s phenomenon in 19/19
individuals (as did our case), ascites in 6/8, and varices
in 10/13 of individuals [7]. Pulmonary information was
limited to only 9 subjects with dyspnea; however the exact
etiology is unclear and pulmonary hypertension or fibrosis
was mentioned. To our knowledge, there are no reported
cases of refractory hepatic hydrothorax in the literature as a
complication of Systemic Sclerosis and NRH.
In conclusion, this case highlights an unusual presen-
tation of refractory hepatic hydrothorax and ascites due to
the combination of Systemic Sclerosis/CREST syndrome
causing NRH and presinusoidal portal hypertension that
was successfully treated with a TIPS shunt. This case also
brings forth the diagnostic awareness that both indirect and
direct portal vein measurements are warranted to diagnose
presinusoidal portal hypertension.

Consent
Informed patient consent was obtained to publish all case
details and images.
Conflicts of Interest

There are no conflicts of interest related to the content or production of this paper.

Authors’ Contributions

Gary A. Abrams and Robert Chapman wrote and revised the manuscript. Samuel R. W. Horton provided the histologic pictures.

References

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