ARCHIVES OF HELLENIC MEDICINE: ISSN 11-05-3992

CASE REPORT
ΕΝΔΙΑΦΕΡΟΥΣΑ ΠΕΡΙΠΤΩΣΗ

Esophageal varices
Not always due to liver disease

ARCHIVES OF HELLENIC MEDICINE 2021, 38(2):248–251
ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2021, 38(2):248–251

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An 82-year-old woman presented with blood-stained regurgitation, an episode of melena and exertional dyspnea during the preceding month. She had a history of hypertension and aortic stenosis, for which she was receiving medication. Gastrointestinal endoscopy revealed esophageal varices, but clinical examination and routine laboratory testing showed no features of liver cirrhosis or hepatitis of viral or autoimmune etiology. Abdominal computed tomography (CT) scan showed findings of liver congestion but no signs of liver cirrhosis. Shearwave elastography confirmed the presence of liver fibrosis. Transthoracic echocardiography revealed remarkably elevated pulmonary artery systolic pressure (PASP) >100 mmHg, severe tricuspid regurgitation, moderate mitral regurgitation, mild aortic stenosis, and moderate aortic regurgitation. Based on the combination of the findings of the transthoracic echocardiogram, abdominal CT and shearwave elastography, we attributed this patient's portal hypertension to congestive liver fibrosis (CLF), which was a consequence of pulmonary hypertension due to left-sided multivalvular heart disease. She was treated with diuretics with quick relief of her symptoms.

Κιρσοί οισοφάγου χωρίς πρωτοπαθή βλάβη του ήπατος

Περίληψη στο τέλος του άρθρου

Key words

Esophageal and gastric varices
Fibrosis
Heart failure
Liver cirrhosis
Portal hypertension

Submitted 9.11.2020
Accepted 14.12.2020

Esophageal varices are among the major complications of portal hypertension. Although liver cirrhosis is the cause in approximately 90% of cases of portal hypertension, in the remaining 10% portal hypertension is not associated with cirrhosis (non-cirrhotic portal hypertension, NCPH). The causes of NCPH are classified into prehepatic, hepatic (presinusoidal, sinusoidal, postsinusoidal), and posthepatic. Cardiac causes, including restrictive cardiomyopathy, constrictive pericarditis and congestive heart failure, are well-defined causes of posthepatic portal hypertension. When cardiac causes of portal hypertension persist, they may lead to frank liver disease, i.e., congestive hepatopathy, in the form of either congestive liver fibrosis (CLF) or cardiac cirrhosis (CC).

We report the case of a patient in whom left-sided valvular heart disease presented with bleeding esophageal varices, in order to remind readers that, apart from liver cirrhosis, a variety of other causes may lead to portal hypertension.

CASE PRESENTATION

An 82-year-old woman presented at the emergency department reporting blood-stained regurgitation during her sleep for the last two days, and an episode of melena some days earlier. She reported no nausea, vomiting or abdominal pain, but had experienced similar regurgitation episodes in the recent past, for which she had not been investigated. Systems review disclosed that the patient had exertional dyspnea during the preceding month. Her medical history included hypertension, treated with furosemide and amiloride, and aortic valve stenosis. She reported no alcohol use or smoking and she did not use any other medications. She had no history of hepatitis and she had never received a blood transfusion.

On clinical examination, her blood pressure was 140/60 mmHg, and the rest of her vital signs were normal. There was no dyspnea at rest or tachypnea. No peripheral edema was present. Clinical findings included jugular vein distention, a crescendo-decrescendo systolic murmur and an early diastolic murmur at the aortic auscultation site. Abdominal examination was unremarkable.

Digital rectal examination did not reveal the presence of blood or melena. There were no other significant clinical findings suggesting liver cirrhosis.

The routine laboratory testing showed normochromic normocytic anemia: Hematocrit (Ht) 27.5%, hemoglobin (Hb) 8.7 mg/dL, mean corpuscular volume (MCV) 92.9 fL, and a low ferritin level, 21 ng/mL. There was slight prolongation of prothrombin time (PT) of 14.5 sec, with international normalized ratio (INR) 1.32 and raised gamma-glutamyl-transferase (γGT), 57 U/L. Serum albumin was 3.9 mg/dL, serum protein electrophoresis was normal, and the inflammation markers erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were within the normal range. Hepatitis serological tests and autoimmune hepatitis antibodies were negative.

The patient underwent gastrointestinal endoscopy, which revealed grade 2 and 3 esophageal varices and esophagitis grade A, based on the Los Angeles classification.[1] There were no signs of recent bleeding.

Chest X-ray revealed a cardiothoracic ratio of 66%. The electrocardiogram (ECG) showed normal axis, sinus rhythm and no ST abnormalities. Transthoracic echocardiogram showed dilation of the right ventricle and right and left atria, remarkably elevated pulmonary artery systolic pressure (PASP) (>100 mmHg), severe tricuspid regurgitation (TRVmax: 4.72 m/sec), moderate mitral regurgitation, mild aortic stenosis and moderate aortic regurgitation.

Chest computed tomography (CT) scan showed small bilateral pleural effusions and dilatation of the cardiac chambers and the pulmonary artery. Abdominal CT scan showed findings of liver congestion, dilatation of the inferior vena cava (IVC) and the hepatic veins, and symmetrical thickening of the terminal ileum, cecum and ascending and transverse colon wall. There were no imaging signs of liver cirrhosis, and no splenomegaly or ascites was detected.

Shearwave elastography measured liver stiffness at 13.3 kPa, defining F3 liver fibrosis, according to cut-offs commonly used in clinical settings, as cut-offs vary according to the underlying disease and special cut-offs for congestive liver fibrosis are not available.[2] Doppler ultrasound (US) showed normal portal vein diameter, but the portal mean flow velocity was 11 cm/sec, suggesting portal hypertension, as values <12 cm/sec are considered diagnostic.

Coronary angiography revealed no significant coronary stenosis. Aortography demonstrated mild stenosis of the aortic valve with moderate regurgitation. Left ventriculography demonstrated moderate mitral regurgitation, left ventricular hypertrophy, an ejection fraction of 70%, and high end-diastolic pressure of the left ventricle (20 mmHg).

Perfusion lung scanning excluded thromboembolic lung disease as a cause of pulmonary hypertension. As other causes were excluded, the pulmonary hypertension was attributed to left-sided heart disease.

Based on the findings of the transthoracic echocardiogram, coronary angiography and ventriculography, we attributed this patient's portal hypertension to CLF as a consequence of left-sided multivalvular heart disease.

The patient was started on omeprazole 20 mg qd, furosemide 60 mg qd and spironolactone 25 mg qd. During her hospitalization, she received 1 g of ferric carboxymaltose intravenously (iv). After the administration of diuretics and correction of the anemia with iv ferric carboxymaltose, the symptoms of dyspnea on exertion were relieved. At follow-up one month later, the patient was in very good clinical condition and reported no symptoms of bleeding, dyspnea or right heart failure. The hematocrit had risen to 37%. She was advised to attend for close follow-up and occasional laboratory examinations.

DISCUSSION

Esophageal varices are the main manifestation of portal hypertension. Portal hypertension can be caused by several diseases other than liver cirrhosis, which is the commonest cause. Etiologies can be divided into prehepatic, hepatic (presinusoidal, sinusoidal, postsinusoidal), and posthepatic causes. Common prehepatic causes are splenic or portal vein thrombosis and splenomegaly. Common hepatic causes are schistosomiasis, granulomatous and infiltrative diseases, biliary diseases, and idiopathic non-cirrhotic portal hypertension. Posthepatic causes include obstruction of the IVC or the hepatic veins (Budd-Chiari syndrome) and cardiac diseases.[3]

Liver disorders due to heart disease include mild alterations of liver function tests in heart failure, cardiogenic ischemic hepatitis, CLF and CC.[4]

Our patient presented with esophageal varices, i.e., one of the prominent features of portal hypertension. We concluded that her portal hypertension was due to CLF, as a result of left-sided multivalvular heart disease.

The main causes of CLF and CC are ischemic heart disease (31%), cardiomyopathy (23%), valvular heart disease (23%), restrictive lung disease (15%), and pericardial disease (8%).[5]

Many patients with congestive hepatopathy (CLF or CC) remain asymptomatic. When present, the predominant symptoms are due to right heart failure, rather than liver disease. The most prominent features are right heart failure, hepatomegaly and ascites.[6] In a large series of 175 patients with either acute or chronic congestive heart failure, hepatomegaly was present in 90–95%, ascites in 17–25%, and splenomegaly in 7–20%.[7] Esophageal varices can also be present.[4] Until cirrhosis develops, signs of portal hypertension or portosystemic shunt are usually not present. Patients may experience dull right upper quadrant

pain due to stretching of Glisson's capsule or, uncommonly, jaundice. A pulsatile liver may present in the setting of tricuspid regurgitation.[6]

The laboratory findings are usually unremarkable, with normal levels or slight elevation of aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), γ-GT, alkaline phosphatase (ALP) and total bilirubin. The PT and albumin levels are usually normal, due to the preserved hepatic synthetic function.[4,9] The cardio-hepatic syndrome presents with a cholestatic pattern, while a rise in serum transaminases is more evident in acute heart failure.[10]

Treatment of congestive hepatopathy is based on treatment of the underlying heart disease, including angiotensin-converting enzyme (ACE) inhibitors, digoxin, warfarin, amiodarone, statins (if serum transaminases are below three times the upper limit of normal), angiotensin II receptor blockers (ARB), β-blockers and diuretics.[11] The outcome in patients with congestive hepatopathy depends on the underlying heart disease. It has been proposed that cardiac cirrhosis itself does not indicate a poor prognosis. With prompt treatment, the early histological changes of the congestive liver may resolve.

Data regarding the incidence of esophageal varices in heart failure are conflicting.

Luna and colleagues published an autopsy series of 74 cases with congestive heart failure. Esophageal varices were present in 5 patients, while 12 showed congestion of the esophageal veins but did not fulfill the criteria for varices, and none of the patients had liver cirrhosis. In a literature review of 886 cases of esophageal varices, 73 (8.2%) were attributed to congestive heart failure.[12] On the other hand, in Sherlock's series of 28 autopsies performed in patients who died from heart failure, esophageal varices were not seen, and superficial abdominal veins were not distended. Spleen size and mean ascitic volume was not significantly different between groups with and without cardiac cirrhosis. These findings suggest that cardiac cirrhosis does not add portal hypertension to the clinical or post-mortem picture.[13] A possible explanation for the inconsistency of findings might be the lack of specific criteria for varices.

There have been case reports of esophageal varices in the absence of cirrhosis. Ozaki and colleagues published a case report of a 51-year-old woman with congestive heart failure on a basis of mitral valve replacement for mitral regurgitation, and progressive anemia. Endoscopy revealed esophageal varices. After the patient died, autopsy revealed severe congestive liver but no cirrhosis.[14]

Another case, resembling ours, was published by Almadani and colleagues. A 43-year-old woman was diagnosed with pulmonary arterial hypertension, and after non-compliance to treatment, she experienced progressive dyspnea on exertion and hematemesis. Endoscopy revealed esophageal varices.[15]

ΠΕΡΙΛΗΨΗ

Κιρσοί οισοφάγου χωρίς πρωτοπαθή βλάβη του ήπατος

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Αρχεία Ελληνικής Ιατρικής 2021, 38(2):248–251

Ασθενής, 82 ετών, προσήλθε λόγω αναγωγής με πρόσμιξη αίματος, ενός επεισοδίου μέλαινας κένωσης πριν από μία εβδομάδα και δύσπνοιας στην κόπωση από μηνός. Το ατομικό αναμνηστικό της ασθενούς περιλάμβανε αρτηριακή υπέρταση και στένωση αορτικής βαλβίδας, για τα οποία λάμβανε φουροσεμίδη και αμιλορίδη. Η γαστροσκόπηση ανέδειξε κιρσούς οισοφάγου. Από το ιστορικό, την κλινική εξέταση και τον εργαστηριακό έλεγχο δεν προέκυψαν ευρήματα κίρρωσης ήπατος αλκοολικής, ιογενούς ή αυτοάνοσης αιτιολογίας. Η αξονική τομογραφία κοιλίας ανέδειξε ηπατική συμφόρηση, χωρίς εικόνα κίρρωσης, και η ελαστογραφία επιβεβαίωσε την ίνωση του ήπατος. Από το διαθωρακικό υπερηχογράφημα καρδιάς προέκυψε υψηλή PASP (>100 mmHg), σοβαρή ανεπάρκεια τριγλώχινας, μέτρια ανεπάρκεια μιτροειδούς, ήπια στένωση και μέτρια ανεπάρκεια αορτικής βαλβίδας. Βάσει του συνδυασμού των ευρημάτων από το υπερηχογράφημα καρδιάς, την αξονική τομογραφία κοιλίας και την ελαστογραφία ήπατος, η πυ-

λαία υπέρταση αποδόθηκε σε συμφορητική ηπατοπάθεια («καρδιακό ήπαρ»), λόγω πνευμονικής υπέρτασης σε έδαφος πολυβαλβιδικής νόσου αριστερών καρδιακών κοιλοτήτων.

Λέξεις ευρετηρίου: Ίνωση, Καρδιακή ανεπάρκεια, Κίρρωση ήπατος, Κιρσοί οισοφάγου, Πυλαία υπέρταση

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