New-Onset Liver Failure: Pitfalls of an Unusual Diagnosis

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Abstract

Introduction: Heart failure is the second most common cause of ascites after cirrhosis. There are cardiac and noncardiac etiologies of ascites, and the multimodality imaging approach is a rich tool to redefine the final diagnosis.

Case Presentation: We present a case-series where 3 patients were referred to our hospital for further hepatology assessment due to severe abdominal ascites and liver failure. Constrictive pericarditis was diagnosed in all of them. Nowadays, constrictive pericarditis is a well-known disease, but sometimes its clinical presentation may delay the treatment and worsen the prognosis. Our 3 cases had similar clinical scenarios and hemodynamic patterns when undergoing right-heart catheterization, but they had different anatomical pericardium-compromise, requiring different surgical strategies.

Conclusions: Nowadays, multimodality imaging, especially cardiac magnetic resonance imaging and cardiac computed tomography, allows us to study a wide spectrum of the same disease in terms of anatomical compromise and cardiac physiology in order to stratify different prognosis and treatment options. We describe 3 unusual clinical cases where the initial differential diagnosis denoted noncardiac etiologies. The level of serum NT-proBNP proved pivotal to the redefinition of the clinical scenario and differentiation between the cardiac and noncardiac etiologies of new-onset ascites. A multidisciplinary approach in this setting between internists, hepatologists, and cardiologists was helpful to establish the final diagnosis in all the patients.

Keywords: Constrictive Pericarditis, Liver Failure, Cardiac MRI, Cardiac CT, Pericardiectomy

1. Introduction

Heart failure is the second most common cause of ascites after cirrhosis. We present a case-series where 3 patients were referred to our hospital for further hepatology assessment owing to severe abdominal ascites and liver failure. All the patients presented with progressive dyspnea, abdominal ascites, neck vein distention, painful hepatomegaly, and significant weight loss within no more than 1 year. Constrictive pericarditis was the answer to the clinical setting.

Constrictive pericarditis represents the end stage of an inflammatory disease involving the pericardium, and it usually takes years to develop, although it may begin several weeks after a given insult. This process results in the thickening, dense fibrosis, calcification, and adhesions of the parietal and visceral pericardium.

Among multimodality imaging tests, echocardiography is the first-line test, followed by magnetic resonance imaging (MRI) and/or computed tomography (CT). Each of the tests can be useful in the evaluation of the structure and hemodynamic or functional disturbances of pericardial diseases. For example, echocardiography with respirometric recording is deemed the first-line modality to evaluate physiological features of constrictive pericarditis. MRI and CT are regarded as second-line tests to further assess the degree of increased pericardial thickness, functional effects of the constrictive process, and inflammation as well as the distribution of calcium in the pericardium (1). It is important to note that all these 3 tests are rarely necessary in the diagnosis of constrictive pericarditis unless there are technically poor or diagnostically uncertain transthoracic echocardiographic studies: there is mixed constrictive pericarditis and restriction, there is a need for assessment regarding pericardiectomy, or there is a concern for transient constriction with ongoing inflammation. Sometimes, an invasive hemodynamic study is necessary to evaluate myocardial versus pericardial diastolic heart failure, especially in the setting of atrial fibrillation (2).

We now present 3 cases with similar clinical scenarios and hemodynamic patterns when undergoing right-

heart catheterization but with dissimilar anatomical pericardium-compromise scenarios, requiring different surgical strategies.

2. Case Presentation

2.1. Case 1: Calcific Constrictive Pericarditis

A previously healthy 22-year-old man was admitted to our hospital because of abdominal distention, severe ascites, and progressive dyspnea, without fever or cough. His laboratory tests showed unconjugated hyperbilirubinemia with a threefold increase in liver enzymes and an NT-proBNP serum level of 676 pg/mL (normal < 450 pg/mL). An electrocardiogram showed sinus rhythm with signs of left atrial dilation and negative T waves in the precordial leads.

An initial chest X-ray was interpreted as normal (Figure 1A). An abdominal paracentesis showed a serum ascites albumin gradient (SAAG) > 1.1 mg/dL, which initially supported a hepatic disorder with portal hypertension. A transjugular intrahepatic catheterization was performed: It showed a 3 mm Hg portosystemic gradient, ruling out portal hypertension and primary liver disease. Consequently, the hepatologists requested an abdominal CT scan, which revealed marked hepatosplenomegaly without liver masses. However, thoracic CT slices unmasked a diffuse and markedly calcified pericardium (Figure 1B). An echocardiographic examination was performed, and it demonstrated septal bouncing and respiratory variations in left ventricular outflow tract, with a preserved left ventricular ejection fraction and normal tissue Doppler velocities (> 8 cm/seg). All the tests were negative for tuberculosis. Right-sided cardiac catheterization pressure-waveform tracing showed mild pulmonary hypertension, low cardiac output, and equalization of right ventricular and left ventricular wedge pressures. Also, the square-root sign or dip plateau was observed, with a significant increase in diastolic filling pressures (Figure 1C). Clinical assessment showed no improvement in right-heart failure after an administration of intravenous loop diuretics. Calcific idiopathic constrictive pericarditis was diagnosed, and complete pericardiectomy was performed (Figure 1D). Histological analysis showed a markedly thickened pericardium with extensive calcification and fibrosis. The postoperative course was benign, with serial measurements of NT-proBNP showing an initial rise followed by a gradual decline after intravenous loop diuretics.

2.2. Case 2: Effuse Constrictive Pericarditis

An 18-year-old man was admitted to our hospital because of a subacute onset of an edematous-ascitic syndrome of around 4 months' duration. He presented with marked ascites associated with bilateral neck vein distention and hepatomegaly. His laboratory tests showed unconjugated hyperbilirubinemia with slightly elevated liver enzymes and an NT-proBNP serum level of 520 pg/mL (normal < 450 pg/mL). Several paracenteses were required with a SAAG > 1.1 mg/dL but an ascetic protein level > 2.5 mg/dL, supporting a cardiac etiology.

Initially, the patient was referred to the hepatology department with a suspicion of a primary liver disease. An electrocardiogram showed sinus rhythm with signs of left atrial dilation. No bundle-branch block was evident. A chest X-ray showed marked cardiomegaly without pleural effusion evidence. All the tests were negative for tuberculosis, and the patient did not have a previous history of thoracic surgery or chest irradiation. An abdominal ultrasound was normal. All the serological tests for hepatotropic viruses were negative. A transthoracic echocardiogram showed a normal ejection fraction with moderate regional pericardial effusion and areas of an echo-bright, thickened pericardium. Septal bouncing was also observed. Finally, Doppler analysis revealed an accentuation of respirophasic changes in tricuspid flow, compatible with a constriction pattern (Figure 2A). In light of these results, the cardiologists were asked for a second opinion. Constrictive pericarditis was a differential diagnosis to take into account, so a cardiac MRI was performed. T1 sequences illustrated a pericardial thickness of 6 mm with moderate pericardial effusion. Cine sequences demonstrated increased ventricular coupling with early inspiratory flattening of the interventricular septum in diastole. No late gadolinium enhancement was observed (Figure 2B). Also, right-heart catheterization pressure-waveform tracing illustrated the typical dip plateau sign with increased filling pressures. In this case, effuse constrictive pericarditis was diagnosed and partial anterior pericardiectomy was performed. The patient had a good postoperative course. Remarkably, the NT-proBNP level behaved in the same way after releasing the heart from the external constriction (Figure 2C).

2.3. Case 3: Localized Asymmetric Constrictive Pericarditis

A 69-year-old patient was admitted to our hospital due to a 1-year clinical course of severe ascites, dyspnea on exertion, neck vein distention, and weight loss as well as eosinophilia. A markedly increased erythrocyte sedimentation rate was observed. He had no previous history of cardiovascular disease. In order to rule out a possible unknown primary tumor, we performed a total corporal CT scan. Only mildly enlarged mediastinal lymph nodes were observed. During the preceding year, the patient had required several right pleural effusion drainages and a video-assisted thoracoscopy with a lymph node biopsy without evidence of atypical cells or tuberculosis. An electrocardiogram showed sinus rhythm with signs of left atrial dilation. No bundle-branch block was evident. A chest X-ray re-

vealed marked cardiomegaly with severe right pleural effusion. At presentation, the laboratory tests revealed unconjugated hyperbilirubinemia with a threefold increase in serum liver enzymes and an NT-proBNP measurement of 469 pg/mL. The erythrocyte sedimentation rate of 120 mm suggested an infectious or rheumatologic etiology. Marked hepatomegaly as was described before was patent. A transthoracic echocardiogram was performed, which illustrated septal bouncing and a localized, echo-bright pericardium. The tissue Doppler velocities of the mitral annulus were normal, making it possible to differentiate between patterns of constriction and restriction (Figure 3A). After ruling out primary liver disease, as well as oncological or rheumatologic active disease, we had an interconsultation with the cardiology service to investigate primary cardiac compromise. Right-heart catheterization and cardiac MRI allowed us to establish the final diagnosis.
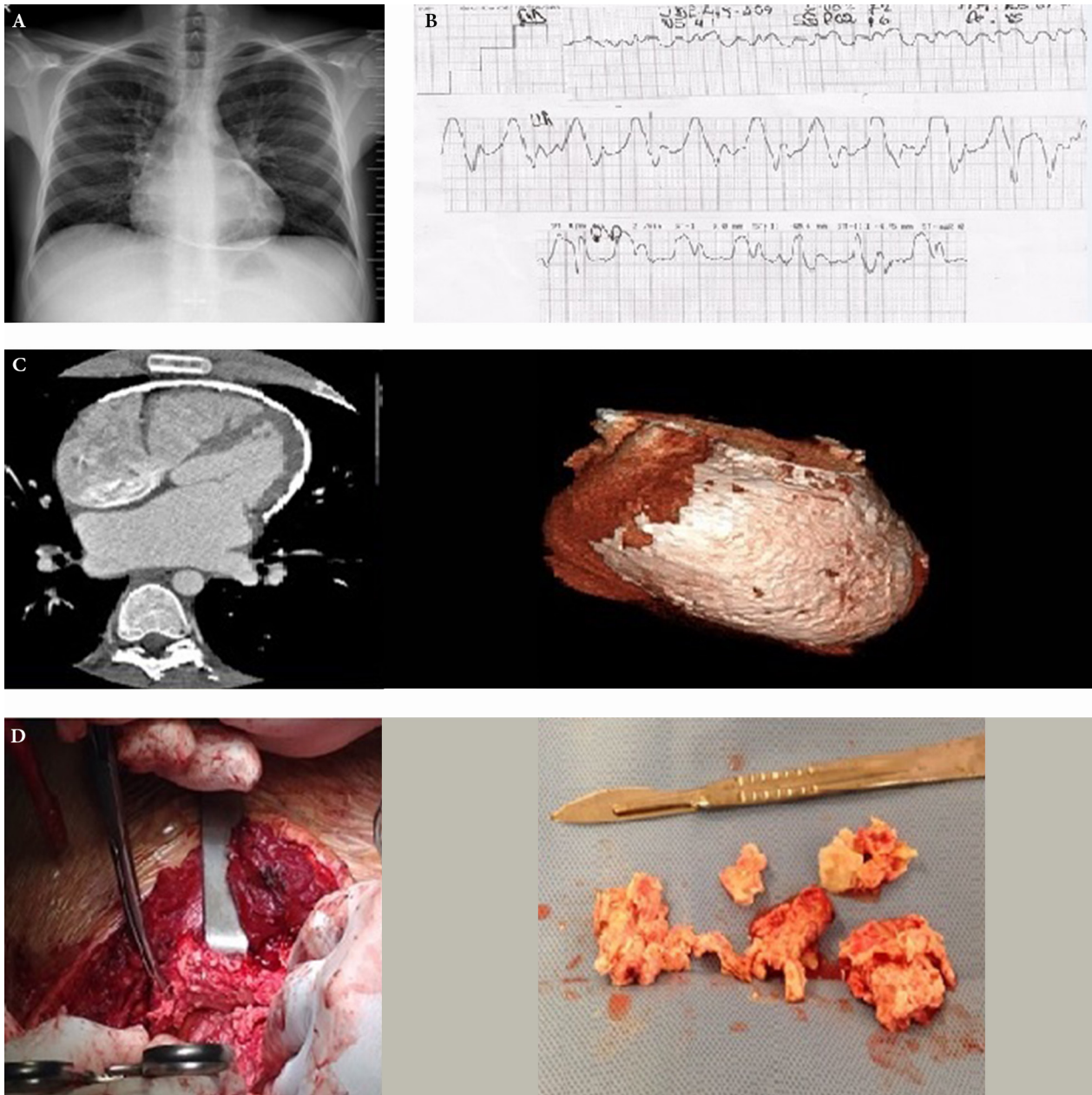

Figure 1. A, Chest X-ray shows a diffuse calcified pericardium; B, right-heart catheterization pressure-waveform tracing shows increased end-diastolic filling pressures with the typical dip-plateau sign; C, cardiac computed tomography shows calcified, diffuse, and extensive pericardial thickening associated with biatrial dilation; the 3-dimensional volume-rendering technique reconstruction also helps the cardiac surgeon plan pericardiectomy in terms of defining the cleavage plane; D, macroscopic surgical findings after pericardiectomy where pieces of a calcified pericardium are observed.

The former showed the typical square-root sign, whereas the latter demonstrated only a 4 mm focally thickened pericardium associated with constrictive physiology on cine series. Neither pericardial effusion nor calcium deposit was observed (Figure 3B). Localized asymmetric constrictive pericarditis was diagnosed after the multidisciplinary approach, and total pericardiectomy was finally performed. What ensued was a severe post-pericardiectomy low-output syndrome, necessitating high doses of inotrope agents and intra-aortic balloon counterpulsation in order to maintain a normal cardiac index. Five days later, the patient was satisfactorily weaned from the intra-aortic balloon pump and inotropes. His ejection fraction improved, albeit slightly.
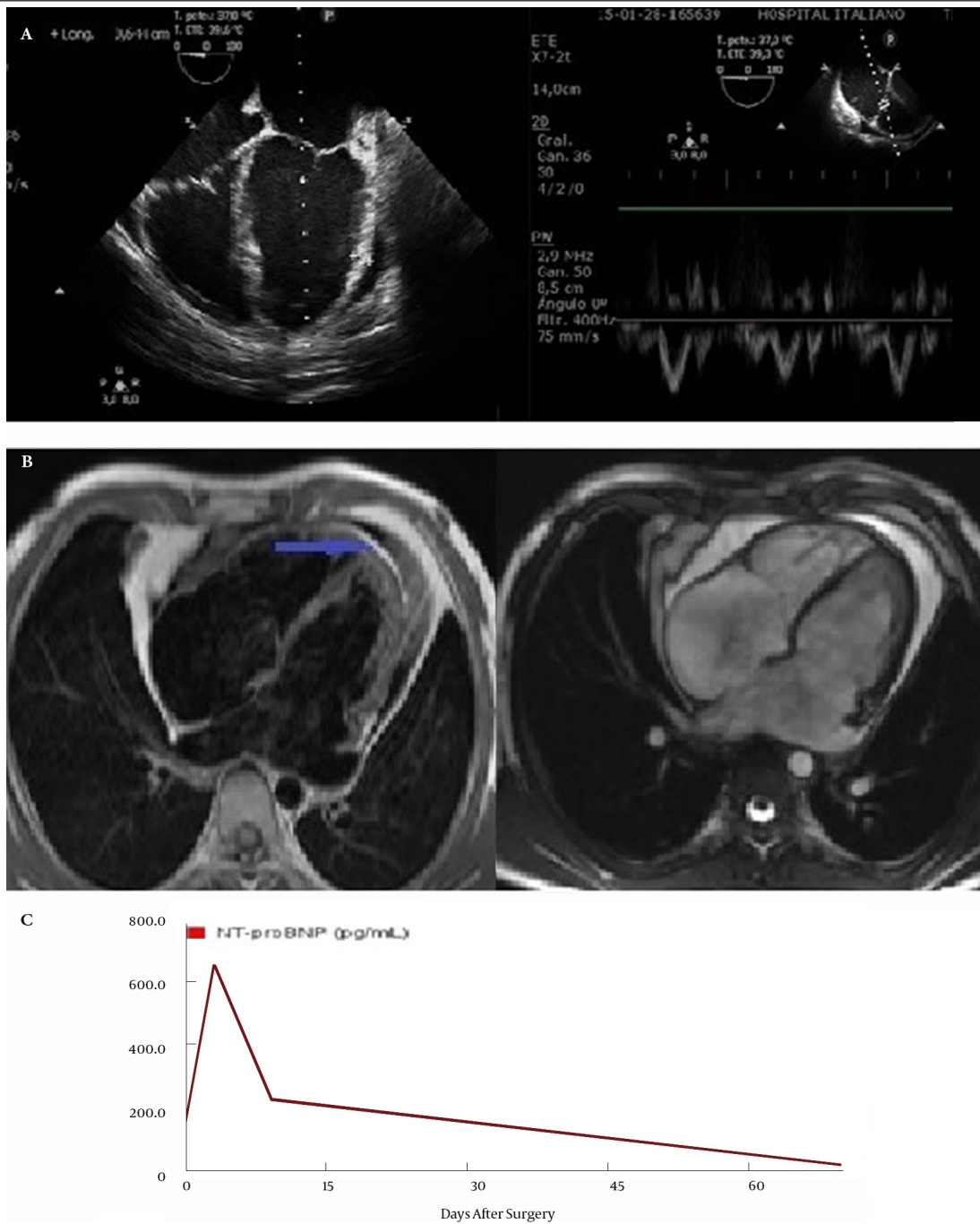
Figure 2. A, Transthoracic echocardiogram shows moderate regional pericardial effusion and areas of an echo-bright, thickened pericardium; septal bouncing is also observed; doppler analysis shows the accentuation of respirophasic changes in tricuspid flow, compatible with a constriction pattern; B, cardiac magnetic resonance imaging; T1 sequences show a pericardial thickness of 6 mm (arrow) with moderate pericardial effusion; cine sequences demonstrate increased ventricular coupling with early inspiratory flattening of the interventricular septum in diastole; no late gadolinium enhancement is observed; C, serial NT-proBNP measurements show an initial rise followed by a gradual decline after releasing the heart from the constricting pericardium.
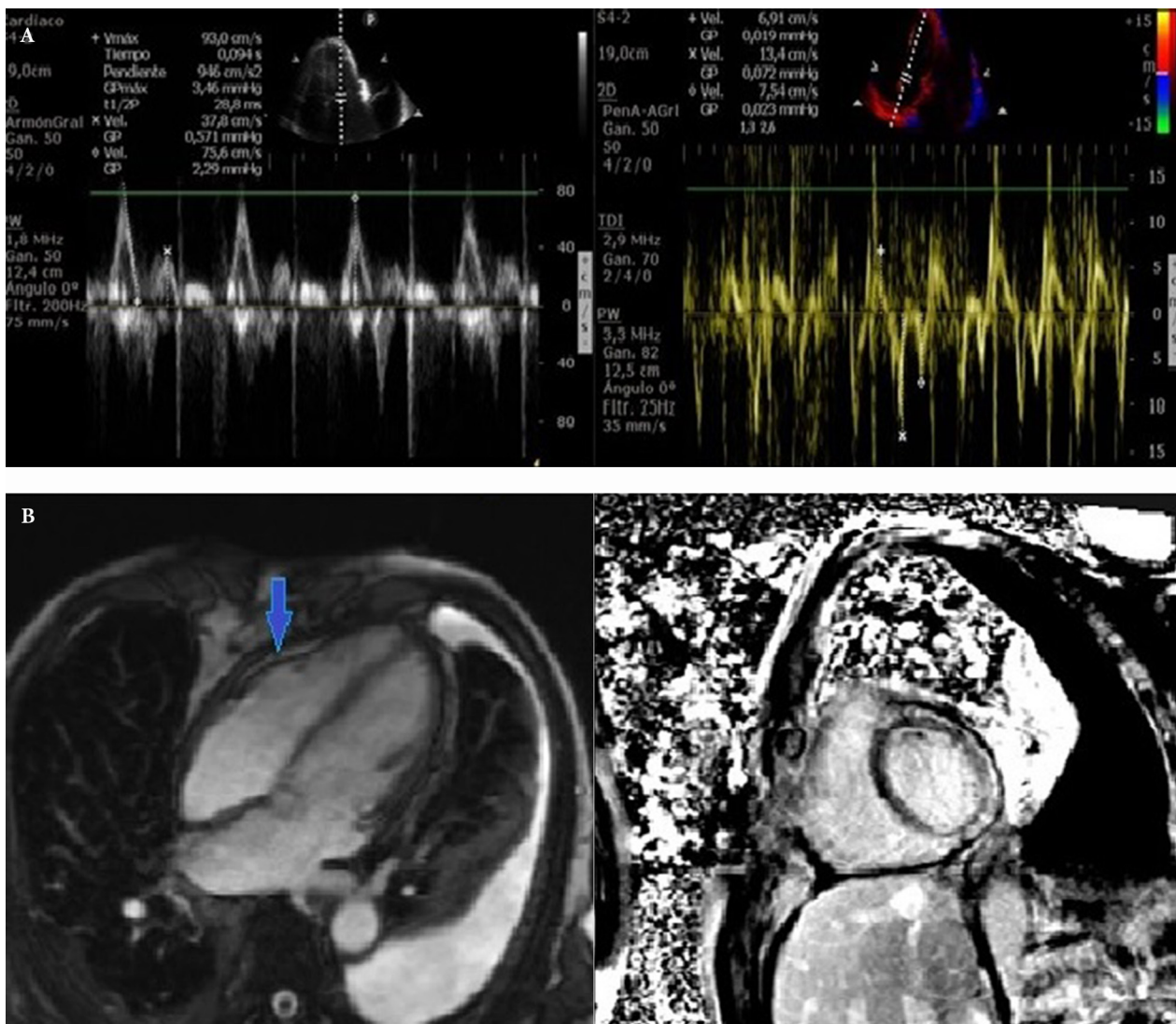
Figure 3. A, Cardiac echocardiography shows mitral flow respiratory variability; septal tissue Doppler is as follows: Sm = 6.91 cm/seg, Em = 13.4 cm/seg, and Am = 7.54 cm/seg; B, cardiac magnetic resonance imaging (4-chamber view) demonstrates a 4 mm focally thickened pericardium (arrow); neither pericardial effusion nor calcium deposit is seen; on the right, a late gadolinium enhancement sequence shows little intramyocardial fibrosis.

3. Discussion

Nowadays, constrictive pericarditis is a well-known disease; nevertheless, sometimes its clinical presentation delays its diagnosis and correct treatment worsening the prognosis. We focused on the role of cardiac multimodality imaging in terms of not only the diagnosis of constriction pericarditis but also the special features of each additional imaging testing. In situations where echocardiographic findings are equivocal, additional imaging testing (CT or MRI) is needed to arrive the diagnosis with more confidence. In some patients, hemodynamic cardiac catheterization may be necessary to establish the diagnosis. Even when the diagnosis of constrictive pericarditis is certain after echocardiography, other imaging tests are often necessary to evaluate pericardial inflammation, coexisting myocardial disease, or comprehensive pericardial as well as cardiovascular anatomy for subsequent management decisions (e.g. guiding surgical options such as total vs. partial pericardiectomy).

Regarding biomarkers the patients described here initially presented with almost normal NT-proBNP values, ascites, and neck vein distention. A recent study demonstrated that the level of serum NT-proBNP is more accurate than is the level of SAAG or ascites protein for the establishment of the etiology of new-onset ascites (3). Our patients all presented with near normal level of NT-proBNP in tandem with an elevated level of ascites protein, hinting at cardiac ascites etiology.

A quick diagnosis should be made in order to avoid long-term constriction and myocyte atrophy (4). That is what happened to our third patient, who consequently developed the post-pericardiectomy low-output syndrome, also called "the bird-in-cage phenomenon", together with severe hypervolemia.

At our hospital, CT scan proved integral to the revelation of severe calcified pericardium in our first patient. In contrast, cardiac MRI may confer other features for further pericardium compromise by providing not only morphological evidence of an abnormally thickened pericardium but also information about constrictive physiology, as was the case in our third patient (5). Regarding pericardium compromise illustrated on cardiac MRI, usually the pericardium appears hypointense and measures < 2 mm in thickness. Indeed, sometimes it may not even be visible on MRI. In addition, free-breathing real-time cine cardiac MR can depict 2 important features: increased ventricular coupling with early inspiratory flattening of the interventricular septum in diastole and dilation of the inferior vena cava, which shows little change in size during respiration. These findings may help differentiate constrictive pericarditis from restrictive cardiomyopathy (6). The use of tagged cine imaging can aid in identifying the nonadherence of the visceral and parietal pericardium throughout the cardiac cycle. Finally, the presence of pericardial delayed gadolinium hyperenhancement (DHE) on MRI is known to be associated with histological features of organizing pericarditis, whereas patients without DHE on MRI have more pericardial fibrosis and calcification, as well as lesser degrees of pericardial thickening, which of course has implications in terms of prognosis, medical management, and guiding surgical treatment (7).

We herein described 3 unusual clinical cases where the initial differential diagnosis denoted noncardiac etiologies, rendering a multidisciplinary approach necessary. Sometimes clinical and imaging data such as neck vein distention or the Kussmaul sign, together with a chest radiography, may offer enough information to establish constrictive pericarditis in the differential diagnosis of a wide spectrum of patients presenting initially with right-heart failure or new-onset ascites.

Footnote

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