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CASE REPORT / ПРИКАЗ БОЛЕСНИКА

Right-sided heart failure as a first presentation of portopulmonary hypertension

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SUMMARY

Introduction Pulmonary artery hypertension and right ventricular failure are potentially fatal complications that can develop in patients with portal hypertension. The objective of this case report was to report a patient with end-stage liver disease, and portal and pulmonary artery hypertension and right heart failure.

Case outline A 57-year-old man was admitted to the Cardiology Department of a tertiary referral hospital due to signs of right-sided heart failure, ascites, pleural effusions, and pretibial edema. The patient had the history of alcohol abuse, arterial hypertension, and gout. Just prior to the admission, abdominal ultrasound revealed granular liver structure, as well as ascites. Laboratory tests showed microcytic anemia, values of transaminases below referent, hypoalbuminemia, low creatinine clearance. Echocardiography revealed pulmonary hypertension, and right ventricle failure. Right heart catheterization unraveled precapillary pulmonary hypertension, but thoracic CT scan and thoracocentesis excluded underlying pulmonary illness. Treatment continued at the Gastroenterology Department of the tertiary hospital. Abdominal CT scan diagnosed cirrhotic liver, and signs of portal hypertension. The patient was treated with symptomatic therapy, but developed acute-on-chronic renal failure and eventually died.

Conclusion Multidisciplinary approach is very important to distinguish portopulmonary hypertension early in the course of liver disease, because evolution of right sided heart failure precludes these patients from adequate lifesaving therapy.

Keywords: pulmonary arterial hypertension; right-sided heart failure; liver cirrhosis

INTRODUCTION

Right-sided heart failure (RHF) clinical syndrome is associated with increased morbidity and mortality in a variety of diseases [1]. Heart failure and liver disease often coexist, because of bidirectional cardiohepatic interactions, concomitant risk factors, or diseases affecting both organs [2]. RHF in patients with liver disease can be a consequence of cirrhotic cardiomyopathy, pulmonary vascular complications, concomitant left ventricular failure, and chronic renal failure [2, 3, 4]. Patients with portal hypertension can develop increased pulmonary vascular resistance (PVR) and pulmonary artery hypertension (PAH) condition called portopulmonary hypertension (PoPH) [3–9]. PoPH is frequently underrecognized condition for a long time, with marked diagnostics and treatment variability [3, 4, 5, 8–12]. As PVR rises, right ventricle strain is raising, function declines with ultimate signs of RHF [1, 13]. Patients with advanced stage of PoPH usually have poor prognosis, frequent hospitalizations, and high mortality from progressive RHF, acute renal failure, but the majority die of complications due to underlying decompensated liver failure [4, 11, 14].

The objective of this case report was to report a patient with end-stage liver disease, portal and pulmonary artery hypertension, and RHF.

CASE REPORT

A 57-year-old man was hospitalized for the first time at the Cardiology Department of a tertiary hospital, due to clinical signs resembling biventricular heart failure and NT-proBNP above 25,000 pg/mL, referred from a pulmonologist. The patient presented with symptoms of dyspnea on minimal effort, swellings of the abdomen, scrotum, and legs, which had been deteriorating for the previous four weeks, weight loss of 10 kg, and several black stools seven days prior to admission. The patient had a history of untreated gout and arterial hypertension for the previous seven years, without medical documentation. The patient did not smoke, but consumed alcohol almost daily over the previous 10 years. Just before admission, the patient was examined by a gastroenterologist. Abdominal ultrasound showed vast amount of ascites, enlarged spleen (156 mm), small echogenic kidneys and bilateral pleural effusion; an elective gastroscopy was indicated. The patient was referred to a pulmonologist, where chest radiography and diagnostic thoracentesis with

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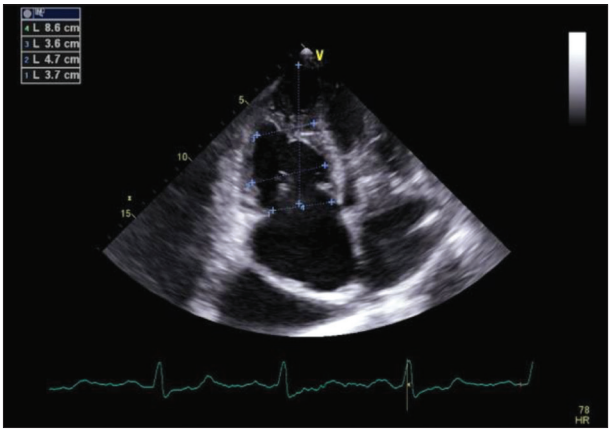

Figure 1. Dilated right atrium, the tricuspid annulus, and the right ventricle

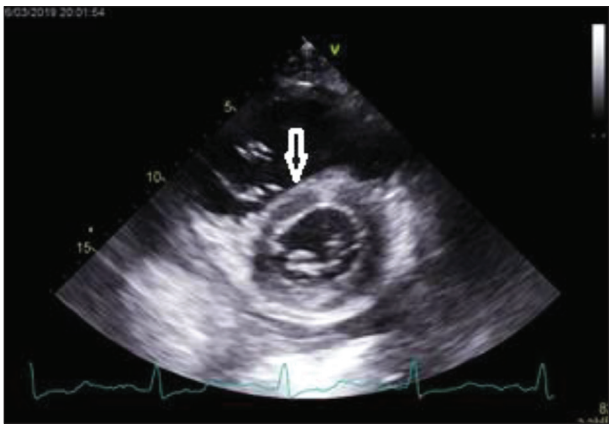

Figure 2. Flattening of the interventricular septum in systole

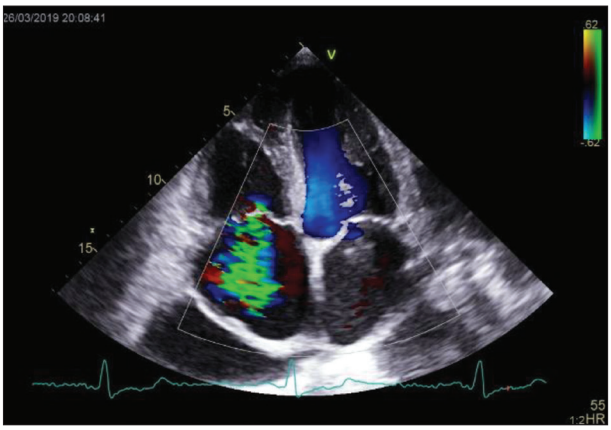

Figure 3. Severe tricuspid insufficiency

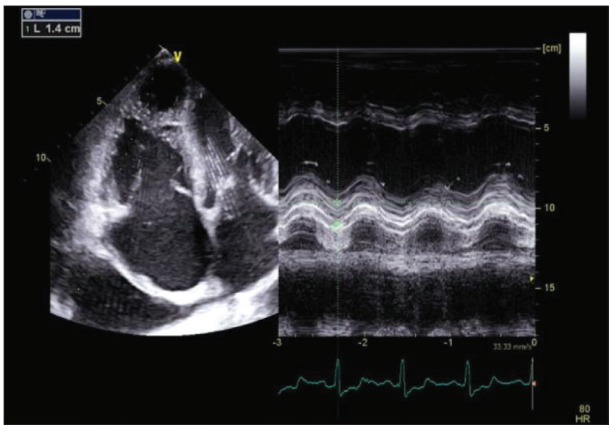

Figure 4. Low tricuspid annular plane systolic excursion (1.4 cm)

evacuation of 1000 ml of transudate was done, and the patient was referred to a cardiologist.

Physical examination on admission revealed that patient was afebrile, oxygen saturation was 93%, the skin was pale, sclera were of normal staining, hypertensive (220/120 mmHg), tachycardic (110 beats/minute), with bilateral jugular venous distention, accentuated pulmonic component of the second heart sound, tricuspid regurgitant holosystolic murmur, the right lung percussion dullness and absent breath sounds, as well as signs of ascites and pitting leg edema.

Baseline laboratory tests showed severe microcytic anemia (Hgb 73 g/l, MCV 67.9 fL), normal thrombocyte count, decreased level of liver transaminases (AST 7 U/L, ALT 13 U/L), normal bilirubin, mild direct hyperbilirubinemia (8 μmol/L), elevated gamma-glutamyl transferase (78 U/L), hypoalbuminemia (26g/L), INR value above referent (1.7), low creatinine clearance (32 mL/minute), hyperuricemia (652 μmol/L), as well as low levels of FT3 (3.73 pmol/L), normal levels of FT4 (15.04 pmol/L) and high levels of TSH (10.43 pmol/L). Serological tests for hepatitis B, hepatitis C and HIV were negative.

Transthoracic echocardiogram (TTE) revealed dilated right atrium (RAVs/BSA 43.68 mL/m^2), tricuspid annulus (3.7 cm), and right ventricle (RV1 4.7 cm, RV2 2.6 cm, RV3 8.6 cm) (Figure 1), with flattening of the interventricular septum (Figure 2), severe tricuspid regurgitation (Figure 3), high right ventricular systolic pressure (87 mmHg), peak tricuspid regurgitation velocity (4.1 m/s), low tricuspid annular plane systolic excursion (1.4 cm), and tricuspid annulus systolic velocity (0.08 m/s) (Figure 4), no mitral regurgitation, mild pulmonic regurgitation, pulmonary artery diameter (2.4 cm), and high inferior vena cava diameter (2.3 cm), without inspiratory collapsibility. Left ventricle (LV) volumes were normal, with signs of concentric hypertrophy (diameters of interventricular septum of 1.5 cm, and of posterior wall of 1.5 cm), preserved LV ejection fraction (56%). The left atrium was dilated (LAVs/BSA 38.42 mL/m^2). The ratio of peak early diastolic velocity (E) to peak velocity flow in late diastole (A) – E/A – was 1.21, tissue Doppler imaging showed low septal early diastolic velocity (es') of 0.06m/s, low lateral early diastolic velocity (el') of 0.09m/s, with normal LV feeling pressure (E/e'av = 9.3), diastolic dysfunction grade II, and minimal pericardial effusion.

The pulmonologist excluded active pulmonary disease based on the normal pulmonary parenchyma on the thorax computed tomography (CT) scan and bilateral transudative pleural effusions.

The patient was treated with red blood cells transfusion, albumin supplementation, parenteral diuretic therapy, therapeutic thoracentesis, antihypertensive therapy, and

thyroid hormone supplementation, but without improvement.

On the third day of hospitalization, right heart catheterization was performed. The values indicated severe precapillary pulmonary arterial hypertension: mean pulmonary artery pressure of 53 mmHg; PVR of 8.1 WU (703 Dynes/cm^5); pulmonary capillary wedge pressure of 15 mmHg, central venous pressure of 19 mmHg, cardiac output of 4.3 L/min, and cardiac index of 2.2 L/mL/m^2.

Given the history of untreated alcoholism in our patient, clinical signs of right heart failure, laboratory tests, TTE, abdominal ultrasound, and right heart catheterization, the diagnosis of decompensated liver cirrhosis and PoPH was suspected.

On the fourth day, the treatment was continued at the Gastroenterology Department of the tertiary hospital. Abdominal CT scan was done, revealing liver surface nodularity, portosystemic collaterals, splenomegaly, and ascites, thus confirming the diagnosis of portal hypertension and subsequent PoPH. The treatment was symptomatic, consisted of parenteral diuretics, albumins, red blood cells transfusions, several thoracenteses, and paracentesis. The patient developed acute-on-chronic renal failure, two continuous veno–venous hemofiltrations were performed, but the patient's hemodynamic status subsequently deteriorated, and he died after 35 days.

The study was approved by the Ethics Committee of the Institute for Cardiovascular Diseases of Vojvodina, and written consent was obtained from the patient for the publication of this case report and any accompanying images.

DISCUSSION

We reported on a patient with alcohol-associated decompensated end-stage liver disease and PAH who presented with right heart failure. Almost 90% of patients with cirrhosis eventually develop portal hypertension, and this condition is crucial for the majority of complications, such as PAH [4, 10, 11, 12, 15]. PoPH is most commonly observed in the setting of cirrhosis, which is alcohol-associated in almost half of the patients, as was the case in our patient [14].

Pathophysiology of PAH in the setting of portal hypertension is not clearly elucidated yet [4]. A proposed mechanism of pulmonary arterial changes are inflammation, endothelial dysfunction, smooth muscle proliferation and *in situ* thrombosis due to hyperkinetic circulation, endotoxemia, low liver clearance, and porto-systemic shunting of vasoactive peptides [4].

PoPH is usually asymptomatic for years [11]. As the disease progress and PVR rises, patients could have nonspecific clinical findings that could be mixed with signs of liver cirrhosis and include exertional or dyspnea at rest, palpitations, syncope, followed by signs of pulmonary and portal hypertension and eventually signs of RHF [11]. In our patient, signs of RHF and portal hypertension were the first noted clinical signs. In a recent retrospective analysis of patients with PoPH, the mean age at the time of death was 56 ± 8.9 years, half of the patients were males, most of them were in New York Heart Association class III or IV, and had ascites, 25% had combined precapillary and postcapillary PH, as was in our case [14]. PAH directly caused death or contributed to death in 25% of patients with PoPH, mainly from RHF [14]. Compared to patients with portal hypertension, patients with PoPH have more cardiac structural changes, like left and right atrial and ventricular enlargement, mitral and tricuspid regurgitation, pulmonary artery widening, pericardial effusion, and aortic regurgitation than those without PoPH [12, 16]. In our patient, TTE revealed PH, normal values of estimated LV filling pressures, signs of RHF, small pericardial and pleural effusions were registered on admission, which are all associated with increased mortality [13, 17, 18].

Based on the initial echocardiographic finding, and clinical signs of liver cirrhosis, in order to diagnose PAH, right heart catheterization was done [19]. Our patient had high mean pulmonary artery pressure and PVR, but had concomitant chronic renal failure and LV diastolic dysfunction leading to further volume overload. A mild elevation of pulmonary capillary wedge pressure with high level of PVR can be observed in some PoPH patients with combined pulmonary vascular disease and a post-capillary component, due to increased left ventricular stiffness in the setting of high cardiac output and fluid overload [20]. However, transpulmonary gradient greater then 10, especially above 30, is suggestive of the presence of increased pulmonary resistance, and is a predictor of poor prognosis, as was in our patient [21].

Our patient had hypothyroidism that could have been a consequence of liver cirrhosis, especially alcoholic and/or PH, and presents a predictor of severity of liver disease and mortality [1].

Chronic kidney dysfunction is common comorbidity associated with high mortality in patients with PH, and it itself may cause pulmonary vascular remodeling [22]. According to Shao et al. [12], compared to patients with portal hypertension, patients with PoPH have lower hemoglobin and higher creatinine. Our patient had pre-existing renal impairment due to long-term hypertension. Acute worsening of renal function in patients with PH is associated with RHF and mortality [23]. It has been shown that, aside systemic arterial hypoperfusion, venous congestion is a main driver for renal function deterioration in patients with RHF [23]. Our patient developed acute-on-chronic renal failure due to advanced liver disease per se, RHF, elevated intra-abdominal pressure, hypovolemia, resulting from excessive diuretic use and large volume paracentesis and contrast agent given for the CT scan.

Treatment of patients with PoPH is usually late, complex, and requires a multidisciplinary team, as was in our patient [11, 20, 24]. Mortality rate in untreated patients with PoPH is high [25]. In a retrospective analysis conducted by Sahay et al. [14], 33% of patients with PoPH were considered unsuitable for liver transplantation because of uncontrolled PAH, as was in our patient.

Deroo et al. [26] have recently showed that in patients with PoPH, vasomodulatory therapy improves pulmonary

hemodynamics and prolongs survival, but if it is followed by liver transplantation, it could further improve prognosis.

In our case with PoPH, the first clinical presentation was RHF. Early multidisciplinary approach, including transthoracic echocardiography, is very important to distinguish PoPH early in the course of the liver disease, because evolution of RHF precludes these patients from adequate lifesaving therapy.

Conflict of interest: None declared.

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Инсуфицијенција десног срца као прва манифестација портопулмоналне хипертензије

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САЖЕТАК

Увод Плућна артеријска хипертензија и инсуфицијенција десне коморе су потенцијално фаталне компликације које могу настати код болесника са портном хипертензијом. Циљ рада је приказати болесника са завршним стадијумом болести јетре, портном и плућном артеријском хипертензијом и инсуфицијенцијом десног срца.

Приказ болесника Мушкарац, стар 57 година, примљен је на Клинику за кардиологију терцијарне болнице због знакова инсуфицијенције десног срца, асцитеса, плеуралних излива и претибијалних едема. Имао је историју злоупотребе алкохола, артеријске хипертензије и гихта. Непосредно пре пријема ултразвуком абдомена утврђена је зрнаста структура јетре, као и асцитес. Лабораторијски тестови су показали микроцитну анемију, вредности трансаминаза испод референтних, хипоалбуминемију и низак клиренс креатинина. Ехокардиографија је указала на плућну хипертензију и инсуфицијенцију десне коморе. Катетеризација десног срца открила је прекапиларну плућну хипертензију, али компјутеризована томографија грудног коша и торакоцентеза су искључили постојање плућне болести. Лечење је настављено у Клиници за гастроентерологију терцијарне болнице. Компјутеризованом томографијом абдомена дијагностиковани су циротична јетра и знаци портне хипертензије. Болесник је лечен симптоматском терапијом, али је задобио акутизацију хроничне бубрежне инсуфицијенције са смртним исходом.

Закључак Мултидисциплинарни приступ је веома важан за разликовање портопулмоналне хипертензије у раној фази болести јетре, јер појава десностране срчане инсуфицијенције онемогућава овим болесницима адекватну терапију којом би се могао смањити морталитет.

Кључне речи: плућна артеријска хипертензија; десностране срчана инсуфицијенција; цироза јетре