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Refractory Ascites in Patient with Liver Cirrhosis: A Case Report

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Abstract: ***Refractory ascites is a common complication of liver cirrhosis. It is associated with a significant reduction of survival to 50% at 6 months and related to various complications, even without any precipitating factors. This article reported a 48-year-old man, with history of liver cirrhosis, who presented with dyspnea and stomach enlargement. There was a tense ascites (grade 3) and distension found on abdominal examination. Patient consumed spironolactone and furosemide routinely. He had history of frequent ascites paracentesis, about four times in the last three months. During current hospitalization, paracentesis was again performed, and about 6,000 mL of yellowish fluid was evacuated. A number of modalities are available for the management of refractory ascites, including dietary sodium and fluid restriction, diuretic therapy, large volume paracentesis (LVP), insertion of a transjugular intrahepatic portosystemic shunt (TIPS), and consideration for liver transplantation. However, paracentesis is still the first-line treatment, as it can be easily performed safely.***

Keywords: chronic liver disease, liver cirrhosis, paracentesis, refractory ascites

1. Introduction

Ascites, defined as pathological fluid accumulation within the abdominal cavity, is one of the most common complications of liver cirrhosis, along with hepatic encephalopathy and variceal hemorrhage [1]. More than 50% of patients with decompensated cirrhosis develop ascites within 10 years of diagnosis [2]. Ascites in cirrhotic patients indicates a poor prognosis [1].

Nearly 5-10% of patients with cirrhotic ascites will develop refractory ascites, defined as ascites that cannot be mobilized or the early recurrence of which (i.e., after paracentesis) cannot be satisfactorily prevented by sodium restriction and diuretic therapy [2-4]. Development of refractory ascites is associated with a significant reduction of survival to 50% at 6 months, and related to the various complications, including dilutional hyponatremia, hepatorenal syndrome, spontaneous bacterial empyema, hepatic hydrothorax, spontaneous bacterial peritonitis, and umbilical hernia, even without any other precipitating factors [1], [5].

2. Case Report

A 48-year-old male patient presented to emergency department with a 3-day progressive dyspnea. Patient also reported an enlarged stomach and swollen legs. He had history of liver cirrhosis due to chronic hepatitis B and had been frequently hospitalized due to various complaints, including bloody vomiting and black stool, shortness of breath, and stomach enlargement. He had history of frequent ascites paracentesis (four times in the last three months), the last time was three weeks before.

Physical examination revealed a blood pressure of 110/70 mmHg, heart rate of 100 beats per minute, respiratory rate of 28 times per minute, body temperature of 36.5^{o}C, and oxygen saturation of 96% in room air. Both conjunctivas are pale. There was a tense ascites (grade 3) and distension found on abdominal examination, with slight pitting edema on lower extremities. The remainder of the examination was normal.

Laboratory values at admission time were as follows: WBC 4,93 x 10^3/ µL; HGB 8.0 g/dl; MCV 75 fL; MCH: 23 pg; PLT 140 x 10^3/µL, albumin 2.6 g/dL, SGOT 11 U/L; SGPT 11 U/L; BUN 55 mg/dl; SC 0,8 mg/dl; Na 130 mmol/L; K 5.0 mmol/L; Cl 90 mmol/L. No abnormalities were found on chest x-ray.

A diagnosis of refractory ascites and anemia due to chronic disease (liver cirrhosis) was made at the end of evaluation. During hospitalization, patient was treated with omeprazole 40 mg BID, sucralfate syrup 10 ml TID, lactulose syrup 10 ml TID, spironolactone 100 mg TID, furosemide 20 mg BID, and transfusion of packed red cell. Therapeutic paracentesis was performed on the 8th day of hospitalization, and about 6,000 mL of yellowish fluid was evacuated.

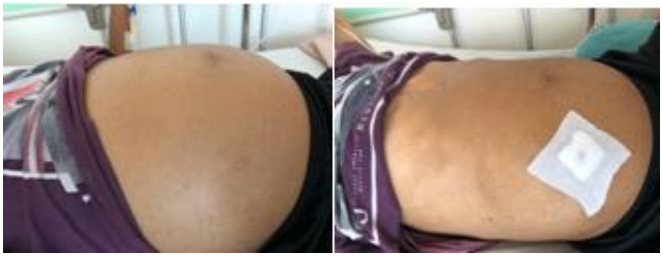

Figure 1: Before (left) and after (right) paracentesis procedure

3. Discussion

Ascites is a frequent complication of liver cirrhosis. Cirrhosis is defined as the histological development of regenerative nodules surrounded by fibrous bands in response to chronic liver injury, that leads to portal hypertension and end stage liver disease [6]. The etiology of

cirrhosis can usually be identified by the patient's history combined with serologic and histologic evaluation. Alcoholic liver disease and hepatitis C are the most common causes in the Western world, while hepatitis B prevails in most parts of Asia and sub-Saharan Africa [6], [7].

Formation of ascites in liver cirrhosis is related to two main pathogenetic mechanisms: portal hypertension and renal sodium retention [4], [8]. Ascites was recently defined into 3 groups by the International Ascites Club according to its severity: in grade 1, ascites fluid is detected only by ultrasound; in grade 2, ascites is moderate with symmetrical distention of the abdomen; and in grade 3, ascites is large or tense with marked abdominal distension [9], [10]. Five to 10% of ascitic patients per year become refractory to standard medical treatment [2-4].

According to the International Ascites Club, refractory ascites is defined as ascites that cannot be mobilized or whose early recurrence after paracentesis cannot be satisfactorily prevented by medical therapy [11], [12]. Diagnostic criteria of refractory ascites are described in Table 1. The term refractory ascites includes two different subtypes: (1) diuretic-resistant ascites and (2) diuretic-intractable ascites (Table 1). Refractory ascites is frequently associated with hepatorenal syndrome type-2, spontaneous bacterial peritonitis, dilutional hyponatremia, muscle wasting, and pleural effusion [1], [5].

The case at hand had features of recurrence ascites. Patient was treated with combination of spironolactone and furosemide, was advised to limit his dietary sodium and fluid intake, and underwent paracentesis three weeks ago, but the ascites reaccumulated rapidly after paracentesis as grade 3 ascites; so, this case can be diagnosed as diuretic-resistant refractory ascites, caused by liver cirrhosis due to chronic hepatitis B.

Table 1: Diagnostic criteria of refractory ascites [11], [12]

Diuretic-resistant ascites: ascites that cannot be mobilized or the early recurrence of which cannot be prevented because of lack response to dietary sodium restriction and maximal doses of diuretics despite compliance to therapy
Diuretic-intractable ascites: ascites that cannot be mobilized or the early recurrence of which cannot be prevented because of the development of diuretic-induced complications* that precludes the use of effective doses of diuretics
1) Treatment duration: patients must be on intensive diuretic therapy (spironolactone 400 mg/d and furosemide 160 mg/d and adherent to a low sodium diet (≤88 mmol/d) for at least one week
2) Lack of response: mean weight loss of <0.8 kg over 4 days and urinary sodium output less than the sodium intake
3) Early ascites recurrence: reappearance of grade 2 or grade 3 ascites within 4 weeks of initial mobilization
*Diuretic-induced complications: renal impairment, hyponatremia, hypo- or hyperkalemia, renal impairment, or hepatic encephalopathy

The main goal of ascites management is to improve patient's quality of life and prevent complication. Management of refractory ascites should follow a step-wise approach of dietary sodium and fluid restriction, diuretic therapy, large volume paracentesis (LVP), insertion of a transjugular intrahepatic portosystemic shunt (TIPS), and consideration for liver transplantation [8], [13].

In patient with normal renal function, combination of spironolactone (50-100 mg/day) and furosemide (20-40 mg/day) is an appropriate initial regimen and can be titrated up every 5 days as tolerated, and according to response [14], [15]. Several studies support the combination of those two diuretics, since spironolactone as a single therapy could cause hyperkalemia, and the use of furosemide alone was thought to be less effective than spironolactone. During diuretic therapy, a continuous monitoring of electrolyte is mandatory, in order to prevent electrolyte imbalance and renal dysfunction [15].

Paracentesis, the oldest treatment of ascites, is still the first-line treatment for refractory ascites. Compared to diuretic therapy, paracentesis has been shown to be more effective and safer in controlling massive ascites rapidly and shorten the hospital stay, but it has no effect on recurrence rates of ascites, the number of complications, and mortality rate [1], [5]. However, paracentesis is a local therapy that does not modify the mechanisms that lead to ascites formation; therefore, ascites will always recur in patients with refractory ascites unless there is an improvement in liver disease [1].

Patients with refractory ascites may require repeated paracentesis, which leads to poor compliance, reduces their quality of life, and increases the risk of PICD (paracentesis-induced circulatory dysfunction), bleeding, and infections [16]. The volume and intervals between two consecutive taps are widely variable, probably according to the different rates of ascites formation, compliance of the patient with dietary sodium restriction, severity of this disease, and patient's capacity to tolerate abdominal tension [1], [4]. Our patient had history of frequent paracentesis within the last three months. Grade 3 ascites and dyspnea induced by refractory ascites indicated the need of paracentesis in this patient. After paracentesis, patient was suggested to continue taking diuretic (spironolactone and furosemide) in tolerated dose, to prevent re-accumulation of ascites.

Liver transplantation is the most effective and definitive treatment modality for refractory ascites [5], [8]. The survival rate of liver transplantation is much higher compared to medical therapy. Therefore, those who develop refractory ascites ideally should be on the transplantation list already. However, liver transplantation is costly and number of donors is limited. Moreover, some patients with refractory ascites have contraindication to liver transplantation. Patients with advanced cirrhosis and refractory ascites are generally frail. Not all of them respond to medical interventions as described, nor are they liver transplantation candidates. Paracentesis plays a significant role in their end-of-life care, as it can be easily performed safely.

4. Conclusion

Refractory ascites is a common condition found in patients with liver cirrhosis. Nearly 5-10% of patients with cirrhotic

ascites will develop refractory ascites. A number of modalities are available for the management of refractory ascites; with paracentesis as the first-line treatment, as it can be easily performed safely. Adequate therapy is mandatory in order to improve patient's quality of life and prevent various complications.

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