Abstract

We report the case of a patient that developed hepatic hydrothorax as the first complication of liver cirrhosis. Due to the lack of response to diuretics, pleurodesis and TIPS, treatment with octreotide was started with resolution of hydrothorax. To the best of our knowledge, this is the third reported case of refractory hepatic hydrothorax with complete and sustained response to octreotide.

Key words: Hepatic hydrothorax. Liver cirrhosis. Ascites. TIPS. Pleurodesis. Octreotide.

Introduction

Hepatic hydrothorax is an infrequent complication of liver cirrhosis (5-10%) (1,2). It is defined as pleural effusion greater than 500 ml in patients with liver cirrhosis and portal hypertension without cardiopulmonary disease. There are many pathophysiologic theories that try to explain the mechanism of hepatic hydrothorax. Currently, the most accepted mechanism, involves the passage of ascitic fluid from the peritoneal cavity into the pleural space through diaphragmatic defects (2-4). Pleural effusion meets transudative criteria and is located in the right hemithorax in 85% of cases (2,3). It is usually associated with ascites but there are cases of isolated hydrothorax (5-7). Initial treatment is similar to that of hydroptic decompensation and it consists of fluid and sodium restriction and diuretics. Patients with hydrothorax refractory to pharmacological treatment can be managed with pleurodesis or transjugular intrahepatic portosystemic shunt (TIPS) (8-13), although liver transplantation is the definitive treatment (14). Over the last few years, two cases of successful treatment of hepatic hydrothorax with octreotide have been reported. This led us to treat our patient with this drug.

Case report

A 66-year-old woman, with a past medical history of cigarette smoking and active alcohol consumption of 70 grams per day. Premature menopause treated with estrogens for more than 20 years. She was admitted to another hospital the previous month with right hydrothorax. She was diagnosed with hepatic hydrothorax with a liver biopsy that revealed early micromacronodular cirrhosis, with moderate activity and focal steatosis. Viral, metabolic and autoimmune test were negative for the etiology of liver disease. Cardiopulmonary disease, as well as infectious disease, tuberculosis and pleural or lung cancer were excluded as the cause of the pleural effusion. Due to the absence of response to fluid and sodium restriction and diuretics she was submitted to thoracentesis and chest tube insertion to alleviate symptoms.

She was admitted to our hospital one month later with recurrent right hydrothorax. Physical examination showed decreased breath sounds over the right inferior hemithorax. Blood cell count revealed leukocytosis of 20,500/µL with 77% of neutrophils. Other laboratory values were as follows: creatinine level 1.9 mg/dl, sodium 129 mEq/liter, potassium 5.4 mEq/liter, total protein 5.68
albumin 1.82 mg/Dl, leukocytes 648 cel/mm3 with 50%
3.34 g/dl; LDH 427 UI/L; pH 7.073, glucose 62 mg/dl;
pleural fluid analysis met exudative criteria (total protein
Barr virus and syphilis were negative. On admission,
leukoprotein 6 ng/ml. Serologies for HBV, HCV, Epstein-
time 30 seconds, fibrinogen 283 mg/dl and alpha fe-
phosphatase 278 UI/L, prothrombin activity 69%, cepha-
lactate dehydrogenase 157 UI/L, total bilirubin 1.81
107 UI/Liter, glutamate pyruvate transaminase 52 U/ml,
lactate dehydrogenase 157 U/l, total bilirubin 1.81
mg/dl, gamma glutamyl transferase 370 UUI/L, alkaline
phosphatase 278 U/Il, prothrombin activity 69%, cepha-
line time 30 seconds, fibrinogen 283 mg/dl and alpha fe-
toprotein 6 ng/ml. Serologies for HBV, HCV, Epstein-
Barr virus and syphilis were negative. On admission,
pleural fluid analysis met exudative criteria (total protein
3.34 g/dl; LDH 427 UI/L; pH 7.073, glucose 62 mg/dl;
albumin 1.82 g/ml, leukocytes 648 cel/mm3 with 50%
of neutrophils) with positive culture for coagulase- posi-
tive Staphylococcus aureus sensitive to oxacillin. Tuberc-
ulos is was excluded by the determination of alcohol-
acid resistant bacilli and gamma-interferon in pleural fluid and negative mantoux. Moreover, malignancy was
ruled out by cytologic examination of pleural fluid and pleural biopsy. Doppler ultrasound revealed signs of
chronic liver disease without morphologic nor hemody-
namic signs of portal hypertension, mild ascites and right
pleural effusion. On the basis of absence of response to
fluid and sodium restriction and diuretics, a chest tube
was placed to relieve symptoms, with drainage of 2000-
2500 cc of fluid per day. Pleural effusion was complicate-
ed by acute prerenal failure due to excessive fluid loss and
hypoproteinemia with hypoalbuminemia. In an at-
tempt to control pleural fluid formation, a minithoracot-
omy with talc pleurodesis was performed without success.
After pleurodesis failure, and with hemodynamic evi-
dence of mild portal hypertension (hepatic venous pres-
sure gradient: 13 mmHg) which suggested liver disease
as the cause of hydrothorax, TIPS placement was consid-
ered. There was a transient (2-3 days) decrease in chest
drainage volume. TIPS dysfunction was ruled out by
doppler ultrasound. Due to the severity of the disease and
the absence of other therapeutical options, treatment with
intravenous octreotide was started fifteen days later, at a
dose of 25 µg/h on the first day, 50 µg/h on the second
day and then 100 µg/h for five more days. The patient
had a good response to treatment with progressive de-
crease in chest tube drainage, allowing chest tube re-
moval without recurrence of pleural effusion. Before dis-
charge, a single dose of 10 mg subcutaneous octreotide
was administered. No recurrence of hydrothorax or as-
cites has occurred within six months of discharge with a
25 mg dose of aldactone daily.

DISCUSSION

Hepatic hydrothorax is a rare complication of cirrho-
sis that is defined as accumulation of ascitic fluid in the
pleural space (> 500 ml), in a patient with liver cirrhosis and portal hypertension, in the absence of cardiopul-
monary disease. The estimated prevalence of this compli-
cation in patients with liver cirrhosis is 5-10% (1,2,14).
Its pathophysiology is unclear and it involves movement
of ascitic fluid from the peritoneal cavity to the pleural
space through micro- or macroscopic diaphragmatic de-
fects (15-18). Pleural effusion is usually a transudate. In
our case, the presence of pleural exudate with positive
culture for coagulase-positive Staphylococcus aureus
was interpreted as empyema secondary to previous pro-
cedures. Findings allowed the exclusion of tumoral and
infectious diseases and the presence of signs of portal hy-
pertension led to the diagnosis of cirrhosis as the cause of
hydrothorax.

The management of this complication is usually diffi-
cult, with few therapeutical options. The aim of the
treatment is to decrease ascites formation and/or portal
hypertension. The only definitive treatment is liver
transplantation (19,20), and it must be always consid-
ered in these patients. Initial treatment is similar to that
of ascites and consists of fluid and sodium restriction
and diuretics (16,20). Refractory hepatic hydrothorax is
defined as pleural effusion that persists despite adequate
treatment with the highest tolerable dose of diuretics.
These are the most severely ill and difficult patients.
Management is dependent on respiratory symptoms
caused by hydrothorax (16) and consist of several thera-
putic approaches: repeated thoracenteses, chest tube in-
sertion, pleurodesis and TIPS.

Patients with severe dysnea often require chest tube
placement, which is also used to treat iatrogenic or sponta-
naneous infection of pleural effusion. This procedure has
many complications such as excessive protein, fluid and
electrolyte depletion. Chest tube removal is often impos-
sible due to high volume drainage. This has led many au-
thors to contraindicate chest tube placement in these pa-
tients (16).

There are some reported cases of successful treatment
with pleurodesis. Talc is administered during thora-
coscopy, performed to repair diaphragmatic defects if de-
tected. However, this treatment has a high morbimortality
rate as it is an invasive technique and it is usually per-
formed in severely debilitated patients (16,21). We con-
sidered this option for our patient due to the absence of
response to previous treatments and with the objective of
pleurodesis and detection of diaphragmatic defects, as
well as to perform a close examination of the thoracic
cavity, taking biopsy samples to definitely exclude malig-
nancy. The procedure was unsuccessful maintaining high
chest tube drainage that did not allow chest tube removal.

According to literature, TIPS is the most effective
 treatment for refractory hepatic hydrothorax and it is con-
sidered one of the indications for this technique
(9,15,16). Apart from reducing hepatic venous pressure
gradient, it improves renal function (20). It has also been
reported to facilitate chest tube removal (15,18). Al-
though it is a safe, little-invasive and efficient procedure,
it has two major inconveniences: frequent obstruction of
the prosthesis and development of hepatic encephalopa-
thy (9). To prevent adverse outcomes after TIPS place-
ment, patients should be carefully selected, avoiding

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those with hepatic encephalopathy or with Child C cirrhosis (16). After pleurodesis failure and once excluded etiologies for hydrothorax other than liver disease, our patient underwent a hemodynamic study. Based on hemodynamic evidence of mild portal hypertension, TIPS was performed. There was an initial response after the procedure, with a decrease in chest drainage volume, that did not allow chest tube removal. This response was transient as drainage volume subsequently increased despite normal function of the prosthesis, as assessed by doppler ultrasound. Besides, she developed hepatic encephalopathy that responded to conventional treatment. There are two reported cases of treatment of refractory hepatic hydrothorax with octreotide in patients without other invasive options because of poor condition. Treatment with octreotide was justified as it has the same effect as TIPS in reducing portosystemic pressure gradient. This drug has few and minor side effects (15,20). Based on good response to octreotide treatment in these cases we considered this treatment for our patient. We administered the same doses as those reported in the literature: 25 µg/h on the first day, 50 µg/h on the second day and then 100 µg/h for five more days. In the reported cases, the effect was dose dependent since higher doses led to greater reduction of drainage volume. Our patient had progressive improvement, allowing chest tube removal after five days of treatment (Fig. 1). We decided to continue treatment for several days by subcutaneous administration before discharge. Hydrothorax has not recurred within six months of discharge.

To the best of our knowledge, this is the third reported case of refractory hepatic hydrothorax with response to octreotide. Contrary to the two previous case reports (15,20), our patient had failed to all available treatment options, including pleurodesis and TIPS. It is possible that TIPS and octreotide had a summatory effect on the decrease of portal hypertension. Based on this favorable response to octreotide, we think that splanchnic vasoconstrictors should be considered in the treatment of serious complications such as refractory hepatic hydrothorax and ascites.

![Graph](image-url)

**Fig. 1.-** Effect of different treatments on chest tube drainage volume. On 27-08-2004 talc pleurodesis was performed with minimal effect on daily drainage volume, as shown in the figure. On 2-09-2004 TIPS placement was performed with significant initial response but with subsequent increase in chest tube drainage volume. Finally, on 17-09-2004 octreotide treatment was started, allowing chest tube removal in the absence of drainage.
REFERENCES