Isotopic exploration of hepatic hydrothorax: ten cases

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SUMMARY

Objective — The aim of this retrospective study was to evaluate the performance of peritoneal scintigraphy for the diagnosis of peritoneopleural communication in patients with cirrhosis and to discuss its role in therapeutic management.

Patients and methods — Ten patients with cirrhosis and pleural effusion were included in this study. Cirrhosis was due to viral hepatitis in eight patients, autoimmune disease in one patient and of unknown origin in one. The pleural effusion was right-sided in nine patients and bilateral in one. 99m-technetium sulfur colloid peritoneal scintigraphy was performed in all patients.

Results — Scintigraphy revealed peritoneopleural communication in nine patients. In four patients, radioactivity appeared in the pleural cavity within a few minutes after injection of the radiotracer. In three of them, a large diaphragmatic defect was demonstrated by ultrasonography, magnetic resonance imaging or thoracoscopy. Complete response to medical treatment was observed in four patients. Scintigraphy revealed rapid radioactivity migration in four patients; diuretic treatment led to resolution of the hydrothorax in one of them. Three patients whose hydrothorax was refractory to medical treatment were treated by pleurodesis with talc. Resolution of the hydrothorax was achieved in one of them.

Conclusion — Peritoneal scintigraphy is a simple non-invasive method enabling confirmation of peritoneopleural communication in cirrhotic patients. The importance of the diaphragmatic defect can also be evaluated, providing a significant contribution to therapeutic decision-making.

The full text of this article is available in English, free of charge, on the web on: www.e2med.com/gcb.

Pleural effusion complicating cirrhosis, also called hepatic hydrothorax, is an exceptional clinical entity. Leuallen et al. [1] studied 436 cases of pleural effusion and found only 2% due to cirrhosis. Hepatic hydrothorax affects 4% to 10% of patients with cirrhosis [2-4].

The treatment of hepatic hydrothorax is difficult in cirrhotic patients due to advanced disease and the limited efficacy of invasive therapeutic methods. The pathophysiological mechanisms underlying the development of hydrothorax in the course of cirrhosis are poorly elucidated. Several studies have demonstrated direct migration of ascitic fluid via a peritoneopleural communication. Peritoneal scintigraphy is one of several useful diagnostic methods.

We report our experience with ten cirrhotic patients who developed hydrothorax to illustrate the diagnostic contribution of peritoneal scintigraphy and its role in therapeutic decision-making.

Material and methods

From 1992 to 2002, ten patients with hydrothorax complicating cirrhosis underwent peritoneal scintigraphy to search for a
peritoneopleural communication. There were seven women and three men, mean age 47 years (range 30-63). Diagnosis of cirrhosis was established 2.7 ± 2.0 years before the development of hydrothorax in nine patients. Hydrothorax was an inaugural manifestation in one patient. Cirrhosis was related to hepatitis B virus infection in eight patients, an autoimmune disease in one and an unknown cause in one. Ascites, evaluated by physical examination and ultrasonography, was considered to be significant in the presence of major abdominal distension and minimal if ultrasonography was required to demonstrate its presence. Pleural effusion was right-sided in nine patients and bilateral in one (table I). Samples were obtained for biochemistry and bacteriology tests in all patients. Peritoneal scintigraphy was performed after intra-peritoneal injection of 5 mCi 99m-technetium-labeled sulfur-colloid particles using a gamma camera (DSX, Sopha Medical, France) to detect pleural radioactivity. The point of injection was situated on the mid-third of a line drawn between the umbilicus and the left anterosuperior iliac spine. While in the supine position the patient was turned to the left and right two or three times to achieve homogeneous distribution of the radioactivity in the ascitic fluid. The patient was then returned to the dorsal supine position for image acquisition. The gamma camera was placed in front of the patient, the acquisition field covering the thorax and the upper part of the abdomen. A series of images was acquired over a 15-minute period. If no sign of pleural radioactivity was noted at this time, static images were acquired every 15 to 30 minutes up to the 4th hour after injection of the radiotracer. If pleural activity appeared within one hour of injection, migration into the pleural cavity was considered to have occurred early. Abdominal and diaphragmatic ultrasound explorations were performed in all patients. One patient underwent thoraco-abdominal magnetic resonance imaging.

All patients were advised to follow a low-salt diet and were given diuretics (spironolactone 50-100 mg/d ± furosemide 40-80 mg/d for 4 days).

Results

Pleural effusion was clinically significant in all patients. Mean protein level in the pleural fluid was 9 ± 4 g/L. The bacteriological examination of pleural fluid was negative in all patients. Cardiac or pulmonary disease was ruled out in all patients on the basis of clinical, biological and radiological findings. Ascites was significant in six patients (table I). Peritoneal scintigraphy revealed a peritoneopleural communication in nine patients (figure 1). Pleural radioactivity was detected early in eight of them (table II), very early in four (< 15 minutes after injection of the radiotracer). Pleural activity occurred late in only one patient (4 hours after the injection).

A wide breach in the diaphragm was identified in three of the four patients who had very early pleural radioactivity, by ultrasonography in one (figure 2), by ultrasonography and magnetic resonance imaging in one (figure 3), and by thoracoscopy in one. Ultrasonography also demonstrated a large diaphragmatic defect in one patient in whom pleural radioactivity appeared one hour after injection of the radiotracer.

Peritoneal scintigraphy was negative in only one patient. This patient had undergone abdominal paracentesis several days before the examination and another aspiration the day before the scintigraphy.

Table I. – General patient characteristics.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Etiology</th>
<th>Ascites</th>
<th>Site of the hydrothorax</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>49</td>
<td>F</td>
<td>Hepatitis B virus</td>
<td>Minimal</td>
<td>Right</td>
</tr>
<tr>
<td>2</td>
<td>63</td>
<td>F</td>
<td>Unknown</td>
<td>Moderate</td>
<td>Right</td>
</tr>
<tr>
<td>3</td>
<td>54</td>
<td>M</td>
<td>Hepatitis B virus</td>
<td>Significant</td>
<td>Right</td>
</tr>
<tr>
<td>4</td>
<td>54</td>
<td>F</td>
<td>Autoimmune hepatitis</td>
<td>Minimal</td>
<td>Right</td>
</tr>
<tr>
<td>5</td>
<td>33</td>
<td>F</td>
<td>Hepatitis B virus</td>
<td>Significant</td>
<td>Bilateral</td>
</tr>
<tr>
<td>6</td>
<td>30</td>
<td>M</td>
<td>Hepatitis B virus</td>
<td>Significant</td>
<td>Right</td>
</tr>
<tr>
<td>7</td>
<td>43</td>
<td>F</td>
<td>Hepatitis B virus</td>
<td>Moderate</td>
<td>Right</td>
</tr>
<tr>
<td>8</td>
<td>52</td>
<td>M</td>
<td>Hepatitis B virus</td>
<td>Significant</td>
<td>Right</td>
</tr>
<tr>
<td>9</td>
<td>40</td>
<td>F</td>
<td>Hepatitis B virus</td>
<td>Significant</td>
<td>Right</td>
</tr>
<tr>
<td>10</td>
<td>53</td>
<td>F</td>
<td>Hepatitis B virus</td>
<td>Significant</td>
<td>Right</td>
</tr>
</tbody>
</table>

Fig. 1 – Peritoneal scintigraphy: Anterior image of the thorax 30 minutes after intraperitoneal injection of 99mTc sulfur colloid showing significant migration of the radioactivity into the right and the left pleural spaces. Note the visualization of thoracic lymph nodes.

Sintigraphie péritonéale: Image antérieure du thorax, 30 minutes après injection intra-péritonéale de sulfo-colloïdes marqués au technétium 99m, montrant un important passage de la radioactivité dans les espaces pleuraux droit et gauche. Noter la visualisation de ganglions lymphatiques thoraciques.
Diuretic treatment led to resolution of the pleural effusion in four of the ten patients (table II). Diuretic treatment failed in three of the four patients who displayed very early pleural radioactivity. For the patient with a negative scintigraphy, the volume of the ascitic fluid decreased and pleural effusion resolved after diuretic treatment.

Thoracoscopy was performed for pleurodesis with talc in three patients who did not respond to diuretics. Pleural radioactivity had appeared early on the scintigrams in all three of these patients and one had a large diaphragmatic defect. Pleurodesis with talc led to resolution of the pleural effusion in one patient (table II).

Discussion

Hepatic hydrothorax is a term introduced by Morrow et al. [5] in 1958 to designate pleural effusion observed in a cirrhotic patient free of cardiac or pulmonary disease. Hydrothorax may develop in all patients with cirrhosis, irrespective of the etiology [2, 3]. Among patients reported in the literature, alcoholic cirrhosis has largely predominated with only a few cases of post-hepatitis cirrhosis [6-9]. Most of these reports were from Europe or North America where alcohol consumption is the principal cause of cirrhosis. Viral hepatitis was the cause of cirrhosis in eight of our ten patients.

The presence of hydrothorax and the volume of effusion are not correlated with the volume of generally associated ascitic fluid [2]. Hydrothorax can occur without ascites [10-14].

The pathogenesis of hydrothorax has been the subject of much debate in the past, but the present hypothesis is that ascitic fluid passes into the pleural space through breaches in the diaphragmatic barrier. Defects measuring only a few millimeters have been demonstrated intraoperatively [12], at thoracoscopy [14, 15] or at autopsy [16, 17]. When a diaphragmatic defect is present, the hydrostatic pressure gradient forces the ascitic fluid to flow into the pleural cavity. Several studies have demonstrated the role of this pressure gradient in the genesis of hydrothorax. Inversion of the pressure gradient by positive pressure assisted ventilation can lead to resolution of the hydrothorax [4]. Leveen et al. reported two cases of hepatic hydrothorax where movement of fluid into the pleural cavity occurred only after an evacuating pleural aspiration reduced the intra-pleural pressure [18]. One-way fluid movement has also been suggested since injection of radioactive particles into the pleural fluid does not lead to passage of the radioactivity into the peritoneal cavity [11, 12, 19].

Pleural effusion is constituted by the effect of two opposing flows: inflow from the abdomen and outflow corresponding to the

<table>
<thead>
<tr>
<th>Patient</th>
<th>Scintigraphy</th>
<th>Appearance of pleural radioactivity</th>
<th>Diagnosis of diaphragmatic defect</th>
<th>Effect of diuretics</th>
<th>Pleural symphysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>+</td>
<td>Very early</td>
<td>Ultrasound</td>
<td>Failure</td>
<td>Failure</td>
</tr>
<tr>
<td>2</td>
<td>+</td>
<td>Early</td>
<td>ND</td>
<td>Failure</td>
<td>Failure</td>
</tr>
<tr>
<td>3</td>
<td>+</td>
<td>Late (&gt; 4 hours)</td>
<td>ND</td>
<td>Failure</td>
<td>nd</td>
</tr>
<tr>
<td>4</td>
<td>+</td>
<td>Early</td>
<td>ND</td>
<td>Resolution</td>
<td>nd</td>
</tr>
<tr>
<td>5</td>
<td>+</td>
<td>Early</td>
<td>ND</td>
<td>Failure</td>
<td>nd</td>
</tr>
<tr>
<td>6</td>
<td>+</td>
<td>Early</td>
<td>Ultrasound</td>
<td>Resolution</td>
<td>nd</td>
</tr>
<tr>
<td>7</td>
<td>—</td>
<td>None</td>
<td>ND</td>
<td>Resolution</td>
<td>nd</td>
</tr>
<tr>
<td>8</td>
<td>+</td>
<td>Very early</td>
<td>Ultrasound + MRI</td>
<td>Failure</td>
<td>nd</td>
</tr>
<tr>
<td>9</td>
<td>+</td>
<td>Very early</td>
<td>ND</td>
<td>Resolution</td>
<td>nd</td>
</tr>
<tr>
<td>10</td>
<td>+</td>
<td>Very early</td>
<td>Thoracoscopy</td>
<td>Failure</td>
<td>Resolution</td>
</tr>
</tbody>
</table>

ND: non diagnosed; nd: not done.

Table II — Results of peritoneal scintigraphy, radiographic studies and treatment.
Résultats de la scintigraphie péritonéale, des explorations radiologiques et du traitement.

Fig. 2 — Abdominal ultrasonography showing a large diaphragmatic defect (†). The diaphragm appears as a hyperechoic band (D) separated from the liver (F) by the ascitic liquid.
Echographie abdominale montrant une large brèche diaphragmatique droite (†). La coupole diaphragmatique apparaît sous forme d’une bande hyperéchogène (D) dont elle est séparée du foie (F) par du liquide d’ascite.

Fig. 3 — T1-weighted coronal MR image demonstrating a large diaphragmatic defect (†).
IRM en coupe coronale pondérée en T1 montrant une large brèche diaphragmatique (†).
Generally, the patient is frail and has advanced disease. No endoscopic repair is suspected, unless a very wide opening which could be closed by surgical or demonstrating a diaphragmatic defect is not particularly con-
difficult task because most defects are very small. Furthermore, the abdominal fat contrasts well with the low-intensity T2 signal can be used to obtain a precise exploration of the diaphragm. rapid magnetic resonance imaging sequences and multiple slices structures formed by the pleural and abdominal fluids. Ultra-
techniques. Only a few cases have been reported in the literature [25-28]. The hemi-diaphragm is seen as an arciform hyper-
phragmatic defect in a cirrhotic patient with classical imaging
defect and to a lesser extent on the peritoneopleural pressure
pleural cavity depends basically on the size of the diaphragmatic
ratio here. Several methods have been proposed [9, 14, 18-20]. Noninvasive peritoneal scintigraphy may be preferred for its simplicity and high diagnostic sensitivity [21-23]. 99m-
technetium scintigraphy using sulfuro-colloid particles is particu-
larly attractive. These 500 nm particles are excellent carriers for the radioactive tracer because they are easy to manipulate and dose and do not enter the bloodstream after intra-peritoneal injection [23]. Presence of a diaphragmatic defect is proven by appearance of pleural radioactivity after intra-peritoneal injec-
tion of the radiotracer. No radioactivity is observed in the pleural cavity after the intra-peritoneal injection if the effusion arises from a cardiac or pulmonary condition in a cirrhotic patient [12, 24]. Generally, radioactivity is detected very early after the injection if there is a diaphragmatic defect, usually within one hour. Longer delays of up to 24 hours have however been reported [24]. Presence of high pressure in the pleural cavity, inhibiting inflow of abdominal radioactivity, is the principal cause of false negative peritoneal scintigraphy. To avoid this problem, the pleural cavity can be evacuated before or just after the intra-peritoneal injection [18]. Our patients had a voluminous hydrothorax and the scintigraphy was negative in only one patient. This negative result may have resulted from an inverted trans-diaphragmatic pres-
sure gradient due to evacuation of the ascitic fluid the day before scintigraphy.

The quantity of labeled colloid particles which enter the pleural cavity depends basically on the size of the diaphragmatic defect and to a lesser extent on the peritoneopleural pressure gradient [3]. Appearance of pleural activity within minutes of the injection is generally a sign of a large breach [19, 21].

In routine practice it is exceptional to demonstrate a dia-
aphragmatic defect in a cirrhotic patient with classical imaging techniques. Only a few cases have been reported in the literature [25-28]. The hemi-diaphragm is seen as an arciform hyper-
echoic band contrasting well with the adjacent hypoechoic structures formed by the pleural and abdominal fluids. Ultra-
rapid magnetic resonance imaging sequences and multiple slices can be used to obtain a precise exploration of the diaphragm. The abdominal fat contrasts well with the low-intensity 12 signal produced by the diaphragm. Identifying a defect is however a difficult task because most defects are very small. Furthermore, demonstrating a diaphragmatic defect is not particularly con-
tributive to diagnosis (apart from exceptional doubtful situations) unless a very wide opening which could be closed by surgical or endoscopic repair is suspected.

Treatment of hepatic hydrothorax is a difficult challenge. Generally, the patient is frail and has advanced disease. No ideal treatment has been defined and several approaches are proposed. Medical management with low-salt diet, diuretics, and thoracocentesis can provide initial relief. Medical treatment can generally control pleural effusion, especially if it is not abundant [2, 29, 30], but is rarely successful in the presence of a large breach [12, 13, 19]. Looking at our four patients who displayed very rapid pleural radioactivity, only one responded to medical treatment. This high rate of failure was undoubtedly related to the size of the breach since ascites has to be perfectly controlled to obtain resolution of the hydrothorax [2, 12, 13]. Nevertheless, high-dose diuretics are often required to achieve this result, with an important risk of adverse effects. Peritoneal-venous shunts have been proposed as a therapeutic alternative in the event of failure or complication after medical treatment in patients with an associated voluminous ascites.

Some authors [8, 15, 18, 30] have been successful with pleurodesis achieved by intra-pleural injection of sclerosing agents (tetracycline, talc, nitrated mustard). This method is generally well tolerated. The sclerosing agent remains localized in the pleural cavity. The rate of failure is however high, reaching 50% in certain reports [15]. The failure rate is particularly high if the defect is large because the sclerosing agent dilutes in the voluminous pleural fluid and is further diluted by inflowing abdominal fluid preventing contact between the two pleural membranes [18, 30]. In order to reduce fluid inflow, Leveen et al. used chemical pleurodesis in association with peritoneal-venous bypass. They were able to treat 80% of their patients with refractory hydrothorax [18]. Drouhin et al. [8] also reported successful chemical pleurodesis in five out of six patients on continuous positive pressure assisted ventilation. When the diaphragmatic defect can be identified, surgical or endoscopic repair is the treatment of choice [3, 29, 31] but may not be possible because of the patient’s precarious general and biologi-

Transjugular intrahepatic portosystemic shunt (TIPS) has also been recently proposed for refractory hydrothorax [6, 32-36]. In a series of 40 patients treated by TIPS, Siegerstetter et al. [32] reported improvement in the hydrothorax in 81%, with complete resolution of the pleural effusion in 71%. These authors also noted an improved Child-Pugh score and serum albumin in 17 patients followed more than 12 months. Another report of 24 patients gave similar results [6]. TIPS has the advantage of not compro-
mising future liver transplantation and of providing simultaneous treatment for other consequences of portal hypertension [35, 36]. Complications are nevertheless frequent, with a significant risk of encephalopathy and poor liver function in patients with severe liver disease (Child-Pugh > 10) [6, 32, 33, 35]. To our knowledge, there has been no report on the effect of size of the diaphragmatic defect on TIPS efficacy.

Liver transplantation, when possible, is the only definitive cure for hepatic hydrothorax and the causal condition [36].

Conclusion

Peritoneal scintigraphy is a simple non-invasive method providing proof of the abdominal origin of hydrothorax in cirrhotic patients as well as quantification of trans-diaphragmatic flow. Rapid appearance of pleural radioactivity is well correlated with the size of the diaphragmatic defect. Our results suggest that peritoneal scintigraphy could play an important role in decision-
making. Further prospective study would be useful.

REFERENCES
