ARCHIVES OF HELLENIC MEDICINE: ISSN 11-05-3992

CASE REPORT
ΕΝΔΙΑΦΕΡΟΥΣΑ ΠΕΡΙΠΤΩΣΗ

Hepatic hydrothorax in a HCV-positive patient with liver cirrhosis
Case report and literature review

Hepatic hydrothorax (HH) is an uncommon complication of portal hypertension. The disorder is defined as the presence of transudative pleural effusion in a patient with liver cirrhosis and no primary pulmonary or cardiac disease. The medical management of HH is often challenging, since these patients usually have advanced liver disease. The case is reported of an of HH in a 68-year-old female patient with hepatitis C virus (HCV) associated cirrhosis, without ascites, which exemplifies the many therapeutic challenges and dilemmas.

ARCHIVES OF HELLENIC MEDICINE 2012, 29(5):627–631
ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2012, 29(5):627–631

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Ηπατικός υδροθώρακας σε ασθενή με κίρρωση από ηπατίτιδα C. Παρουσίαση περίπτωσης και ανασκόπηση της βιβλιογραφίας

Περίληψη στο τέλος του άρθρου

Key words

Cirrhosis
HCV
Hydrothorax
Portal hypertension

Submitted 25.1.2012
Accepted 8.3.2012

Hepatic hydrothorax (HH) is an uncommon complication of portal hypertension. The disorder is defined as the presence of transudative pleural effusion in a patient with liver cirrhosis who has no primary pulmonary or cardiac disease.[1] Its estimated prevalence in cirrhosis is 5–12%.[2–5] Most cases are right-sided (65–87% of all reported cases), but it can be left-sided or bilateral.[6–8] Although ascites is usually present, hydrothorax can occur in its absence.[9,10]

The medical management of HH is often challenging, since these patients usually have advanced liver disease, which will often require orthotopic liver transplantation. Treatment options include dietary intervention and prescription of diuretics, therapeutic thoracentesis, creation of a transjugular intrahepatic portosystemic shunt (TIPS), chemical pleurodesis, peritoneovenous shunting, surgical repair of diaphragmatic defects and orthotopic liver transplantation.

We report a case of HH in a patient with cirrhosis associated with hepatitis C (HCV), without ascites, which exemplifies the many therapeutic challenges and dilemmas.

CASE REPORT

A 68-year-old woman presented with loss of appetite and tiredness of duration of about 1 week. She had been diagnosed five years earlier with liver cirrhosis in association with HCV. Clinical examination showed decreased breath sounds and dullness to percussion over the lower four-fifths of the right hemithorax. The

liver was palpable 5 cm below the right costal margin. There was no splenomegaly and no ascites. Heart auscultation was normal with no murmurs or extra sounds. Spider nevi were present in the neck and torso and the sclerae were slightly icteric.

Laboratory investigation on admission showed: Hemoglobin (Hb) 12.5 g/dL, hematocrit 36.5%, white blood cell count 3,900/μL, platelets 73,000/μL, International Normalized Ratio (INR) 1.25, total bilirubin 1.6 mg/dL (direct 1.15 mg/dL), alanine aminotransferase (ALT) 28 IU/L, aspartate aminotransferase (AST) 46 IU/L, gamma-glutamyltranspeptidase 28 IU/L, urea 31 mg/dL, creatinine 0.8 mg/dL.

Chest X-ray showed a massive right-sided pleural effusion (fig. 1). Abdominal ultrasound (US) failed to show ascetic fluid.

A chest drain was inserted and samples of pleural aspirate showed it to be a transudate, according to Light's criteria. Culture for Tb bacilli and other bacteria was negative. After drainage, computed tomography (CT) of the thorax and abdomen showed findings consistent with hepatic cirrhosis with portal hypertension, but no pleural or peritoneal fluid (figures 2, 3). A higher dose of diuretics was prescribed and the patient was discharged.

A week later the patient was admitted to another hospital with acute shortness of breath. Again, hydrothorax was diagnosed, without ascites, the pleural fluid was drained with the use of a catheter, and the patient was discharged.

Three days later the patient was readmitted with gastrointestinal bleeding. Laboratory findings were: Hb 6.0 g/dL, INR 1.45, urea 112 mg/dL, creatinine 0.7 mg/dL, ALT 622 IU/L, AST 582 U/L, total and direct bilirubin 3.7 mg/dL and 2.5 mg/dL, respectively. The patient was treated with intravenous terlipressin, fresh frozen plasma and packed red blood cells.

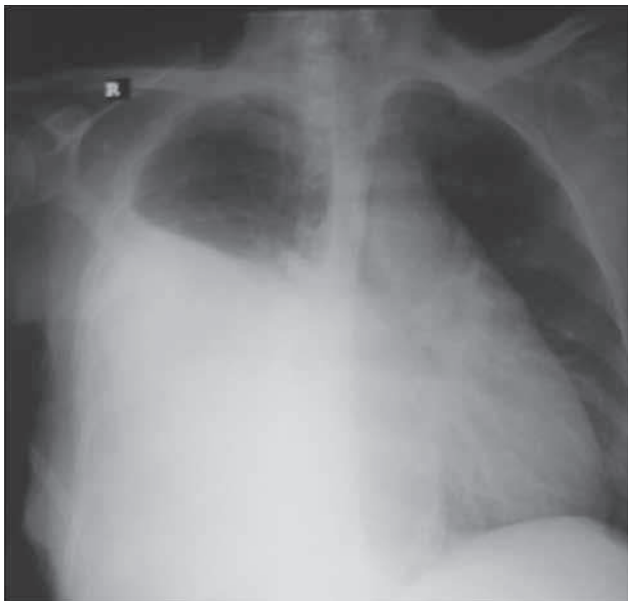

Figure 1. Chest X-ray in a 68-year-old female, showing massive right-sided pleural effusion.

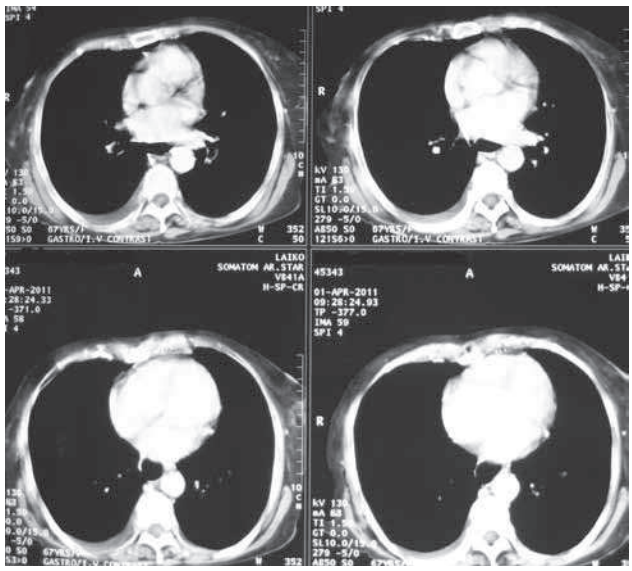

Figure 2. Computed tomography (CT) of thorax in a 68-year-old female with liver cirrhosis, showing no pleural fluid or ascites after draining of hydrothorax.

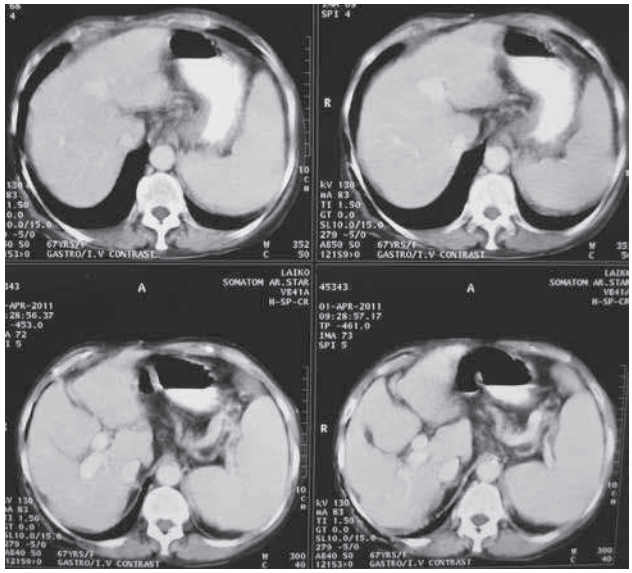

Figure 3. Computed tomography (CT) of abdomen in a 68-year-old female with liver cirrhosis, showing no pleural fluid or ascites after draining of hydrothorax.

Although the bleeding was controlled, the patient developed shortness of breath, and chest X-ray showed significant right pleural effusion completely covering the right lung (fig. 4). Oxygen saturation was 79% and emergency thoracentesis was performed, following which the saturation rose to 96%. The aspirate was once again found to be transudate according to Light's criteria. A further pleural drainage was necessary, after which the patient was once again discharged as her family refused to consider chemical pleurodesis.

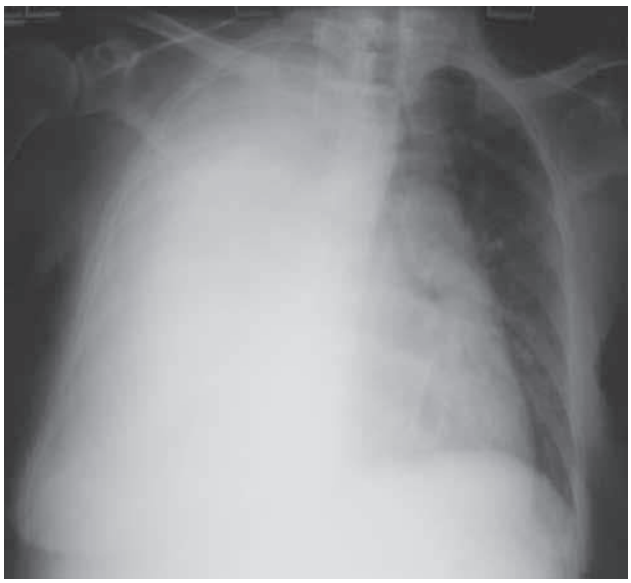

Figure 4. Chest X-ray in a 68-year-old female with liver cirrhosis, showing right sided hydrothorax covering the whole right lung.

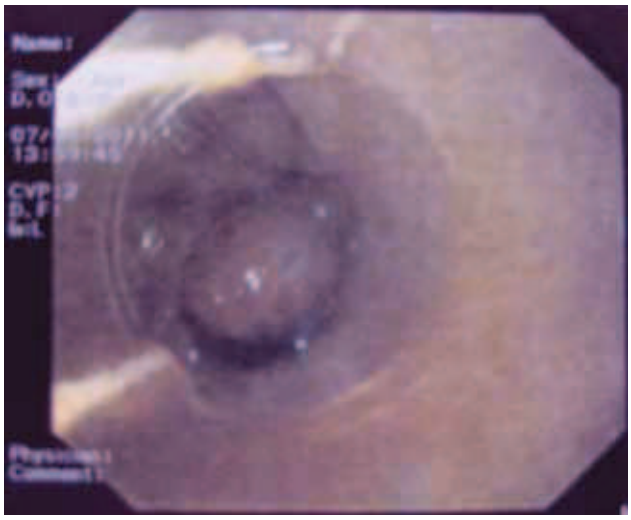

Figure 5. Successful banding of esophageal varices.

A week later the patient was readmitted with acute gastrointestinal bleeding. Banding of three esophageal varices was performed, that arrested the bleeding (fig. 5). Next day the patient developed right-sided pleural effusion with shortness of breath and we procceded with chemical pleurodesis with the family's permission. Unfortunately, the procedure was complicated by pneumothorax that necessitated a chest tube. The pneumothorax resolved and pleurodesis with talc poudrage was performed without VATS, because of the patient's poor condition. The talc pleurodesis was unsuccessful and bleomycin pleurodesis was performed, which also failed to control the hydrothorax. A large chest tube drainage was inserted but the patient died 3 days later dus to massive varial bleeding.

DISCUSSION

Hepatic hydrothorax is distinctly uncommon, being observed in 4–6% of all patients with cirrhosis and up to 10% of those with decompensated cirrhosis.[5] Its diagnosis should be suspected when a patient with established cirrhosis and portal hypertension presents with unilateral pleural effusion, most commonly right-sided.

The pathophysiology of HH involves the leakage of ascitic fluid from the peritoneal cavity into the pleural space through embryonic defects, which are more prevalent in the right hemi-diaphragm. These defects arise from the rupture of pleuro-peritoneal blebs as a result of raised intra-abdominal pressure from coughing, straining or the presence of ascites. The negative intrathoracic pressure aids the unidirectional flow of ascitic fluid into the pleural space. Hydrothorax occurs when the accumulation of fluid exceeds the absorptive capacity of the pleura.[9–16]

Other suggested mechanisms include hypoalbuminemia,[17] hypertension in the azygous or hemiazygous systems[18] and lymphatic channels in the diaphragm.[19]

In order to establish the diagnosis of HH a thorough investigation, including chest CT and echocardiography, is necessary to exclude primary cardiopulmonary disorders. In cases where the diagnosis is in doubt, in particular when the pleural effusion is left sided or ascites is absent, intraperitoneal administration of ^{99m}Tc-human serum albumin or ^{99m}Tc-sulfur colloid is a valuable test.[20–22] The migration of the radioisotope into the pleural cavity within hours confirms the presence of a communication between the pleural and peritoneal spaces. Other diagnostic modalities, including magnetic resonance imaging (MRI)[23] and thoracoscopy, might assist in the detection of the underlying diaphragmatic defects.

Almost all patients with HH reported in the literature have had clinically apparent ascites. In rare cases, including our case, hydrothorax can occur without obvious ascites,[9] in which event treating the hydrothorax is even more of a challenge, and there is no consensus about its management.

With regard to treatment, it must be kept in mind that most patients with HH have end-stage liver disease. The aim of intervention should be to relieve symptoms and prevent pulmonary complications by way of sodium restriction, administration of diuretics, and therapeutic thoracentesis.[24] Placement of a chest tube should be avoided as this leads to uncontrollable fluid loss and increased mortality.[25] In resistant cases, chemical pleurodesis with continuous positive airway pressure, videothoracoscopic repair of diaphragmatic defects[26] and creation of a peritoneovenous shunt or even

TIPS[27,28] may be considered until liver transplantation, which is the definitive treatment, can be performed.

In the case of the patient presented here, treatment was started with diuretics but this failed possibly because the patient's low blood pressure precluded the use of maximal diuretic doses. The only other option was to attempt chemical pleurodesis. Many different substances, including OK-432,[29] tetracycline and minocycline, have been used. Unfortunately, the patient was not a liver transplant candidate and because of her poor condition no VATS was feasible, so first talc poudrage and then bleomycin were injected via a thoracic tube, with poor results. Finally, a chest tube was inserted, but the patient died after a large variceal bleeding.

ΠΕΡΙΛΗΨΗ

Ηπατικός υδροθώρακας σε ασθενή με κίρρωση από ηπατίτιδα C. Παρουσίαση περίπτωσης και ανασκόπηση της βιβλιογραφίας

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Αρχεία Ελληνικής Ιατρικής 2012, 29(5):627–631

Ο ηπατικός υδροθώρακας είναι μια σπάνια επιπλοκή των ασθενών με κίρρωση και πυλαία υπέρταση. Η διαταραχή αυτή χαρακτηρίζεται από την παρουσία διιδρωματικής υπεζωκοτικής συλλογής, συνήθως >500 mL, σε ασθενείς χωρίς πρωτοπαθή πνευμονική ή καρδιακή νόσο. Ο ηπατικός υδροθώρακας πρέπει να θεωρείται πιθανός σε κάθε ασθενή με κίρρωση και πυλαία υπέρταση, ο οποίος εμφανίζει ετερόπλευρη πλευριτική συλλογή. Αν και συνήθως συνυπάρχει ασκιτική συλλογή, ο ηπατικός υδροθώρακας μπορεί περιστασιακά να εμφανιστεί μεμονωμένα. Η θεραπευτική προσέγγιση του ηπατικού υδροθώρακα είναι ιδιαίτερα απαιτητική καθώς αφορά σε ασθενείς με προχωρημένη ηπατική νόσο, με πολλούς από αυτούς σε κατάσταση αναμονής για μεταμόσχευση ήπατος. Παρουσιάζεται περίπτωση ασθενούς με ηπατικό υδροθώρακα σε έδαφος κίρρωσης λόγω χρόνιας λοίμωξης από ηπατίτιδα C, που αναδεικνύει τις πολλές θεραπευτικές προκλήσεις και διλήμματα.

Λέξεις ευρετηρίου: Ηπατίτιδα C, Κίρρωση, Πυλαία υπέρταση, Υδροθώρακας

References

1. MORROW CS, KANTOR M, ARMEN RN. Hepatic hydrothorax. *Ann Intern Med* 1958, 49:193–203
2. LAZARIDIS KN, FRANK JW, KROWKA MJ, KAMATH PS. Hepatic hydrothorax: Pathogenesis, diagnosis, and management. *Am J Med* 1999, 107:262–267
3. XIOL X, GUARDIOLA J. Hepatic hydrothorax. *Curr Opin Pulm Med* 1998, 4:239–242
4. KINASEWITZ GT, KEDDISSI JI. Hepatic hydrothorax. *Curr Opin Pulm Med* 2003, 9:261–265
5. SIDDAPPA PK, KAR P. Hepatic hydrothorax. *Trop Gastroenterol* 2009, 30:135–141
6. GARCIA N Jr, MIHAS AA. Hepatic hydrothorax: Pathophysiology, diagnosis, and management. *J Clin Gastroenterol* 2004, 38:52–58
7. CARDENAS A, KELLEHER T, CHOPRA S. Review article: Hepatic hydrothorax. *Aliment Pharmacol Ther* 2004, 20:271–279
8. GUR C, ILAN Y, SHIBOLET O. Hepatic hydrothorax – pathophysiology, diagnosis and treatment – review of the literature. *Liver Int* 2004, 24:281–284
9. RUBINSTEIN D, McINNES IE, DUDLEY FJ. Hepatic hydrothorax in the absence of clinical ascites: Diagnosis and management. *Gastroenterology* 1985, 88:188–191
10. SINGER JA, KAPLAN MM, KATZ RL. Cirrhotic pleural effusion in the absence of ascites. *Gastroenterology* 1977, 73:575–577
11. CHEN A, HO YS, TU YC, TANG HS, CHENG TC. Diaphragmatic defect as a cause of massive hydrothorax in cirrhosis of liver. *J Clin Gastroenterol* 1988, 10:663–666
12. JIMÉNEZ-SÁENZ M, VENERO J, CASTRO J, HERRERIAS JM, GARRIDO M. Hepatic hydrothorax without ascites: A rare form of a common complication. *J R Soc Med* 1990, 83:747–748
13. EMERSON PA, DAVIES JH. Hydrothorax complicating ascites. *Lancet* 1955, 268:487–488
14. FRAZER IH, LICHTENSTEIN M, ANDREWS JT. Pleuroperitoneal effusion without ascites. *Med J Aust* 1983, 2:520–521
15. SERENA A, ALIAGA L, RICHTER JA, CALDERON R, SANCHEZ L, CHARVET MA. Scintigraphic demonstration of a diaphragmatic de-

fect as the cause of massive hydrothorax in cirrhosis. *Eur J Nucl Med* 1985, 11:46–48
16. FAIYAZ U, GOYAL PC. Unilateral pleural effusion without ascites in liver cirrhosis. *Postgrad Med* 1983, 74:309, 312, 315
17. DUMONT AE, MULHOLLAND JH. Flow rate and composition of thoracic-duct lymph in patients with cirrhosis. *N Engl J Med* 1960, 263:471–474
18. ISLAM N, ALI S, KABIR H. Hepatic hydrothorax. *Br J Dis Chest* 1965, 59:222–227
19. MEIGS JV, ARMSTRONG SH, HAMILTON HH. A further contribution to the syndrome of fibroma of the ovary with fluid in the abdomen and chest: Meigs syndrome. *Am J Obstet Gynecol* 1943, 46:19–37
20. BHATTACHARYA A, MITTAL BR, BISWAS T, DHIMAN RK, SINGH B, JINDAL SK ET AL. Radioisotope scintigraphy in the diagnosis of hepatic hydrothorax. *J Gastroenterol Hepatol* 2001, 16:317–321
21. HOLT KA, OLIVIERA E, ROHATGI PK. Hepatic hydrothorax demonstration by Tc-99m sulfur colloid ascites scan. *Clin Nucl Med* 1999, 24:609
22. RAJNISH A, SUDHAKAR P. Diagnosis of hepatic hydrothorax by Tc-99m sulfur colloid peritoneal scintigraphy. *Clin Nucl Med* 2001, 26:888
23. ZENDA T, MIYAMOTO S, MURATA S, MABUCHI H. Detection of diaphragmatic defect as the cause of severe hepatic hydrothorax with magnetic resonance imaging. *Am J Gastroenterol* 1998, 93:2288–2289
24. AL-SHARIF H, SHARMA S. Hepatic hydrothorax – how would you manage it? *Can Respir J* 2005, 12:440–442
25. BORCHARDT J, SMIRNOV A, METCHNIK L, MALNICK S. Treating hepatic hydrothorax. *Br Med J* 2003, 326:751–752
26. HUANG PM, CHANG YL, YANG CY, LEE YC. The morphology of diaphragmatic defects in hepatic hydrothorax: Thoracoscopic finding. *J Thorac Cardiovasc Surg* 2005, 130:141–145
27. SPENCER EB, COHEN DT, DARCY MD. Safety and efficacy of transjugular intrahepatic portosystemic shunt creation for the treatment of hepatic hydrothorax. *J Vasc Intervent Radiol* 2002, 13:385–390
28. GORDON FD, ANASTOPOULOS HT, CRENSHAW W, GILCHRIST B, McENIFF N, FALCHUK KR ET AL. The successful treatment of symptomatic, refractory hepatic hydrothorax with transjugular intrahepatic portosystemic shunt. *Hepatology* 1997, 25:1366–1369
29. GOTO T, OYAMADA Y, HAMAGUCHI R, SHIMIZU K, KUBOTA M, AKANABE K ET AL. Remission of hepatic hydrothorax after OK-432 pleurodesis. *Ann Thorac Cardiovasc Surg* 2011, 17:208–211

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