PLEURAL EFFUSION ASSOCIATED WITH CIRRHOSIS

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Pleural effusion may either herald or accompany significant disease. Usually the effusion is the result of cardiac failure, or inflammatory, or neoplastic disease, involving the pleura, lung or mediastinum. At times it is seen in association with systemic lupus erythematosus, hypoproteinaemia, or with tumours of the female pelvic organs and ascites (Meig's syndrome).[1,2] Only occasionally has a pleural effusion been attributed to cirrhosis of the liver.[3-9]

In this paper we report a patient with cirrhosis of the liver, who initially had severe ascites, and 5 months later developed massive recurring pleural effusion, at which time there was no detectable fluid in the peritoneal cavity.

CASE REPORT

The patient, H.K., a White female 62 years of age, presented on 14 May 1965, with a 10 months' history of progressive swelling of the legs and feet. This was most severe in the evenings, and subsided overnight. Three weeks before admission she noticed in addition, swelling of the abdomen, and dyspnoea on effort. There was no history of orthopnoea, angina pectoris or paroxysmal cardiac dyspnoea. The patient had received no treatment at all, and was ambulant.

Interrogation revealed a history of jaundice 2 years before this illness, but no details were available, except that the icterus had persisted for 6 weeks. She was a known diabetic of 9 years' duration, controlled on Acetohexamide and Metformin. There was no history of cardiac or pulmonary illness, and she took no alcohol. She was not exposed to hepatotoxic agents.

Physical Examination on Admission

She was an obese, elderly female, able to lie flat in bed and was not distressed at rest. Marked palmar erythema, spider naevi and alopecia capitis were present. There was no jaundice, nor evidence of impending hepatic decompensation. Lower limb oedema extended up to the mid-tibial shaft. There was no clubbing or cyanosis.

On examination of the cardiovascular system, the pulse was 80/minute and regular; the blood pressure measured 200/100 mm.Hg; the venous pressure was normal. There were no cardiac murmurs and the peripheral pulses were equal and synchronous. There was no clinical evidence of cardiomegaly. Thoracic respiration was 20/minute, but fine crepitations were present at the right posterior lung base. There was no evidence of pleural effusion, and air entry was full and equal. Central nervous system examination was normal.

Abdominal examination revealed a moderate degree of ascites with a fluid thrill, obvious shifting dullness and an underlying 5 cm., firm, non-tender hepatomegaly. There were no distended veins, and there was no other visceromegaly. Stool occult blood was negative.

Special Investigations

Haemoglobin 11·5 G/100 ml., white cell count 7,900/cu.mm., ESR 85 mm. in the first hour (Westergren); serum albumin 2·2 G/100 ml., serum globulin 5·0 G/100 ml., blood urea 25 mg./100 ml., serum alkaline phosphatase 10 KA units, thymol turbidity 2, zinc turbidity 14. The prothrombin index was normal. The SGOT was 90 Karmen units/ml.

X-ray examination of the chest showed calcification of the aortic knuckle, and mild left ventricular hypertrophy. The lung parenchyma and pleural spaces were normal. Straight X-ray of the abdomen confirmed the presence of ascites.

Liver biopsy showed 'cirrhosis of the post-necrotic type; no evidence of malignancy was detected'.

Peritoneal aspiration yielded a fluid with SG 1·013, and a protein content of 2·2 G/100 ml. No organisms were isolated, nor were malignant or other cells identified. Urinalysis was normal apart from glycosuria.

Course and Management

The patient was given a high-protein (100 G daily), low-salt diet with added vitamin B complex, and parenteral vitamin K. Furosemide, supplementary potassium and oral antidiabetic agents were given. The diuresis following the Furosemide resulted in a weight loss of 28 lb. in less than 2 weeks, and after 3 weeks' hospitalization, she was discharged.

The patient had lost most of her ascites. The 5 cm. hepatomegaly persisted, but she had no evidence of oedema and was asymptomatic. Chest examination revealed no abnormality, and her blood pressure was 165/90 mm.Hg. There was no cardiac failure.

Second Admission

The patient's second admission, on 12 August 1965, followed the gradual onset of progressive dyspnoea, and a non-productive cough.

Examination showed a dyspnoeic patient who was neither cyanosed nor anaemic. Once again she was anicteric, but had spider naevi and palmar erythema. There was minimal leg oedema.

The cardiovascular system was normal; the blood pressure measured 170/90 mm.Hg. Central nervous system was normal. Abdominal examination again confirmed a 4 cm. firm, non-tender granular hepatomegaly, but on this occasion no ascites could be detected. Respiratory system examination showed the trachea was displaced to the left by a large right-sided pleural effusion preventing any air entry into the right lung. The air entry into the left lung was normal. There were no basal crepitations.

Special Investigations

Blood urea and serum electrolytes were normal; serum albumin 2·8 G/100 ml., serum globulin 4·4 G/100 ml., total

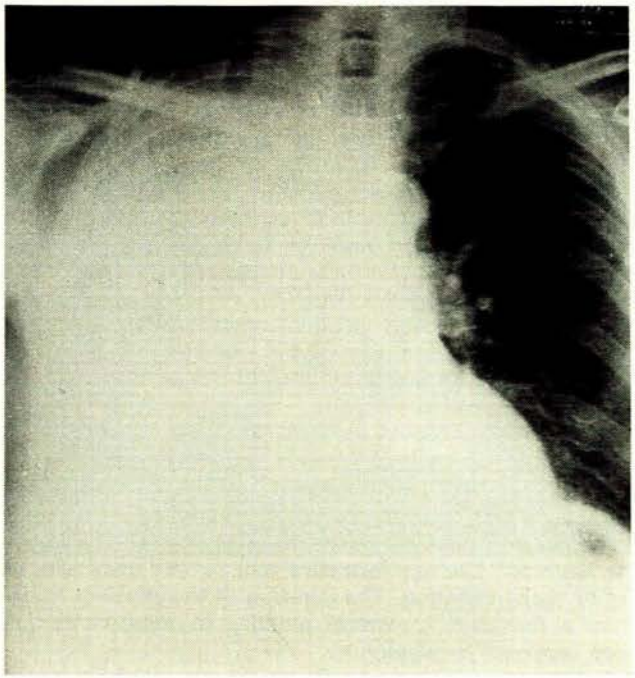

Fig. 1. PA radiograph showing large right-sided pleural effusion.

serum bilirubin 2·6 mg./100 ml., thymol turbidity 18, zinc turbidity 28, and serum alkaline phosphatase 13·2 KA units. Serum electrophoretogram showed a low albumin and a raised broad non-specific gammaglobulin peak. Repeated searches for LE cells were negative. The electrocardiogram was normal.

X-ray examination of the chest confirmed a large effusion in the right pleural cavity, with atelectasis of the underlying lung (Fig. 1). Pleural aspiration yielded a clear straw-coloured fluid with SG 1·010, a protein content of 1·1 G/100 ml., sodium content of 137 mEq./l. and potassium 4·4 mEq./l. The fluid contained no cells or pathogens.

Course and Management

Daily thoracocenteses were performed to alleviate the patient's respiratory distress, yielding a total of 10 l. of fluid over a period of 10 days. Ultimately a thoracoscopy with a view to inserting an underwater drain and obtaining relevant biopsies was performed.

At thoracoscopy, the surgeon reported: 'apart from some areas of atelectasis in the right lower and upper lobes, and a minor degree of basal fibrinous pleuritis, everything else was surprisingly normal. Multiple pleural biopsy specimens were taken.'

The results of these biopsies showed 'fibrous tissue partly lined by reactive pleural cells and some adipose tissue. Moderate numbers of acute and chronic inflammatory cells are present and there are also some iron-laden macrophages. There is no evidence of malignancy.' Four litres of pleural fluid were drained at this procedure, and the underwater drain continued to yield large volumes of fluid as shown in Table I. The patient was treated with diuretics and dietary sodium restriction. *At no time was there any clinical evidence of ascites during this admission.*

TABLE I. FLUID VALUES

Date:	*16/8/65*	*17/8/65*	*18/8/65*	*19/8/65*	*20/8/65*	*21/8/65*	*22/8/65*	*23/8/65*
Body-weight (lb.)	162	159					141	
Oral fluid (ml.)	1,370	1,550	1,140	1,280	1,230	1,170	1,560	1,200
Urine output (ml.)	1,350	1,140	1,840	745	2,050	1,180	3,370	850
Pleural drain (ml.)	4,600	840	No record	1,100	850	800	No record	900

Despite fluid replacement, the patient deteriorated rapidly and collapsed 13 days after admission. She succumbed in hyperkalaemic metabolic acidosis. Consent for autopsy was not obtained.

DISCUSSION

Incidence. Although the first description of massive hydrothorax occurring in a case of cirrhosis of the liver has been attributed to Laennec, it has since received scant clinical attention. The incidence of this complication of hepatic cirrhosis has been disputed. Vedel and Peuch[10] reported that 8% of all cases of cirrhosis of the liver developed a hydrothorax. They probably included cases in which the pleural effusion was attributable to other causes. Tinney and Olsen[5] found that 3% of their patients with cirrhosis had a pleural effusion, while McKay and Sparling[6] reported an incidence of 1% and Morrow *et al.*[7] one of 2·4%. Johnston and Loo[9] recently found the frequency to be 6% in 200 consecutive cases of cirrhosis.

Morrow *et al.*[7] coined the term 'hepatic hydrothorax' for the entity of cirrhosis of the liver and pleural effusion, and concluded that the effusion was a transudate in every case.

Site and age. In one series, 67% of effusions occurred on the right side, 17% bilaterally and only 17% solely on the left side.[9] The age incidence was 24—80 years with no sex or racial variation. The duration of the effusions varied from a few days to several months. In some cases they only occurred terminally.

Pathogenesis. The transudation of pleural fluid in cirrhosis of the liver appears to be dependent on the combined influence of 3 causative factors that produce ascites; and any one of three local factors responsible for the pleural fluid.

The 3 factors responsible for the ascites are: (*a*) hypoalbuminaemia; (*b*) water retention due to the hormonal influence including the action of antidiuretic hormone and aldosterone; and (*c*) portal hypertension.

The 3 local factors responsible for the pleural fluid are:

1. Increased pressure in the azygos vein[7] subsequent to the formation of collaterals between this system of veins and that of the portal vein ('azygos hypertension').
2. Movement of ascitic fluid through the diaphragmatic lymphatics[1] into the pleural cavity.
3. Communications between the peritoneal and pleural cavities. This may occur with congenital defects of the diaphragmatic musculature.[12] Rise in peritoneal pressure may rupture the pleuro-peritoneal membrane overlying such a defect. Alternatively, the fluid under pressure may rupture the peritoneum overlying the retroperitoneal tissues and dissect its way into the mediastinum[13] and thus into the pleural cavity.[14]

Studies by Johnston and Loo[9] injecting Indian ink into the peritoneal cavity, and recovering macrophages laden with carbon particles in the pleural cavity, confirm facets of the above postulate. They also injected air into the peritoneal space and took serial X-rays of the chest, but failed to show any pneumothorax. By using intraperitoneal injections of radio-iodinated albumin, Johnston and Loo demonstrated radioactivity appearing in the pleural fluid and plasma at the same time, and in the same concentrations, suggesting indirect entry into the pleural space from the peritoneal cavity. In 2 of their cases, the chemistry of the pleural and ascitic fluid differed, eliminating the possibility of a direct communication between the 2 spaces.

Johnston and Loo favour transdiaphragmatic transport of the ascitic fluid into the pleural cavity as the most important cause of the hydrothorax. Evidence has been presented in the literature suggesting that particulate matter and protein are removed from the peritoneal cavity almost exclusively by the subdiaphragmatic lymphatics. After the fluid has passed into the lymphatic plexus on the peritoneal surface of the diaphragm, it is carried through the diaphragm into a similar plexus on the pleural surface. The lymph then passes from the diaphragmatic nodes into the collecting ducts, which run with the internal mammary vessels on both sides of the sternum, until they reach the anterior mediastinum. From nodes in the anterior mediastinum, these efferent vessels pass most commonly to the right side where they eventually enter the right subclavian or jugular vein. Lemon and Higgins[15] demonstrated that graphite injected into the peritoneal space of the dog appeared on the pleural surface of the diaphragm within 4 minutes.

If it is correct that hepatic hydrothorax is secondary to transdiaphragmatic transport of ascitic fluid in lymphatics, the question must be answered why hydrothorax does not occur in all patients with ascites. The explanation is not clear. Pleural effusion will only manifest itself when the rate of formation of pleural fluid exceeds the rate of absorption from the pleural space. Even in normal man,

pleural fluid is constantly formed but the rate of absorption prevents its accumulation. In the presence of ascites pleural fluid formation will be greater; hypoalbuminaemia will in addition decrease the reabsorption of this fluid. Local factors such as azygos hypertension impede the absorption of the pleural fluid. Thus it would appear that no single factor is applicable to all cases of hepatic hydrothorax.

No other cause of the hydrothorax was detectable in this patient, and there seems little doubt that the basic cause was her cirrhosis of the liver. It is noteworthy that her ascites had disappeared at the time when strikingly large quantities of fluid were being drained from her right pleural space. One could speculate that the development of a hydrothorax had decreased the tendency to the collection of fluid within the peritoneal cavity.

The therapy of hepatic hydrothorax should be directed to the underlying cirrhosis and hypoalbuminaemia with thoracocentesis only indicated for the relief of dyspnoea. Treatment must include salt restriction, diuretics and a high-protein diet, if this can be tolerated by the patient.

SUMMARY

A case of massive pleural effusion due to cirrhosis of the liver is reported. The patient had previously presented with ascites which appeared to remit completely with the advent of pleural effusion.

The aetiology, pathogenesis and treatment of hepatic hydrothorax are reviewed.

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