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RECURRENT CHYLOTHORAX IN A PATIENT WITH NON-HODGKINS LYMPHOMA: CASE REPORT
B. J. Asuquo, MBBCH, FMCP, MRCP, Specialist Registrar and G. A. Gould, FRCP., MD., Consultant Physician, Department of Medicine, Weston General Hospital, Weston-Super-Mare, United Kingdom

Request for reprints to: Dr. B. J. Asuquo, Department of Medicine, Ashford Hospital, London Road, Ashford Middx, TW15 3AA, United Kingdom

RECURRENT CHYLOTHORAX IN A PATIENT WITH NON-HODGKINS LYMPHOMA: CASE REPORT

B. J. ASUQUO and G. A. GOULD

SUMMARY

Spontaneous chylothorax could arise as a complication of Iymphoma. There are no reports on the frequency of it's occurrence. It is associated with a high mortality rate. This is mainly due to severe nutritional deficiencies and wasting. This case describes a patient with non-hodgkins Iymphoma who developed recurrent bilateral chylothorax requiring repeated pleural aspirations and eventually talc pleurodesis which failed.

CASE REPORT

A sixty three year old woman was referred to the surgical out-patient clinic in December 1999 with a six month history of weight loss of 20Kg, night sweats, abdominal discomfort and distension. She denied a history of nausea, vomiting, change in bowel habit, shortness of breath or cough. On examination she had generalised Iymphadenopathy with a 6 x 2cm left cervical node fixed to underlying tissues, a 10 x 16cm right inguinal node and a 14 x 7 x 7cm firm irregular epigastric mass. The spleen was enlarged to 15cm. There were signs of bilateral pleural effusions.

Chest X-ray revealed bilateral pleural effusions (Figure 1). Ultrasound of neck revealed Iymph node enlargement surrounding the left carotid and jugular vessels. Ultrasound of abdomen revealed a left epigastric mass, possibly a primary gastric Iymphoma and the spleen was enlarged with probable metastases. Pleural aspiration revealed chylous fluid with the following constituents: - LDH 544 u/L, cholesterol 1.6 mmol/L, triglycerides 45.6 mmol/L, protein 9g/dL, and glucose 8.3 mmol/L. Haematological indices were: Hb 11.8 g/dl, WBC 7.6 x 10^9/L, platelets 431 x 10^9/L, INR 1.4. Lymph node biopsy revealed low-grade follicular type non-hodgkin's Iymphoma (Figure 2).

In view of the severe systemic symptoms, large tumour mass and large bilateral pleural effusions it was decided to treat her with an aggressive chemotherapy regimen. She received twelve cycles of cyclosphamide, etoposide, vincristine, bleomycin, mitoxantrone, and dexamethasone. Treatment was completed on 3rd April 2000.

She also had recurrent large bilateral pleural effusions requiring aspiration on several occasions, averaging 3.5L on the right and 2.5L on the left. The patient was reluctant to be admitted to hospital and declined further more invasive procedures for some months. Eventually she agreed to a video-assisted thorocoscopy and pleurodesis with talc. This was complicated by an upper gastro-intestinal haemorrhage and acute renal failure, which reversed with conservative management.

Figure 1

CD 79a: Strong staining of neoplastic follicle with pan B-cell marker (X50)

Figure 2

CD 10(B-cell marker): Strong expression in neoplastic follicle (X100)

Table 1

Constituents of chyle

	Normal range
Total fat	0.4 - 5g/dl
Total cholesterol	1.94 mmol/L
Total protein	2.8 - 3.6 g/dL
Albumin	1.6 - 2.4 g/dl
Globulin	1.1 - 36 g/dl
Fibrinogen	0.2g/dl
Glucose	7.5 mmol/L
Sodium	104 - 108 mmol/L
Potassium	3.8 - 5 mmol/L
Chloride	85 -130 mmol/L
Calcium	3.4 - 6.0 mmol/L
Lymphocytes	400 - 6800/mm^3
Erythrocytes	50 - 600/mm^3
AST	22 - 40 u/ml
ALT	5 - 21 u/ml
Amylase	50 - 83 u/ml

Table 2

Causes of chylothorax

Traumatic	Blunt injury Penetrating injury (5%) Cardiothoracic surgery (25%)
Neoplastic (45%)	Lymphoma, metastasis from cancer of the stomach, pancreas, ovary and lungs,
Inflammatory	Kaposi's sarcoma, sarcoidosis pancreatitis, pericarditis
Obstruction	Lymphatic stenosis Thrombosis of central veins, Extrinsic compression
Congenital	Lymphatic hypoplasia Primary Iymphangiectasia Congenital atresia of thoracic duct
Miscellaneous	Lymphangioleiomyomatosis, Lymphangiomatosis, Protein losing enteropathy, Crohn's disease, reticular hyperplasia, pleuritis, hepatic, cirrhosis, thoracic aortic aneurysm, yellow-nail syndrome, Gorshams syndrome

Figure 3

BCI2: Negative staining of neoplastic follicle (X50)

Figure 4

H and E: Neoplastic follicle (X50)

She responded extremely well to treatment and was in remission for one year, though her progress was complicated by a left proximal femoral deep venous thrombosis confirmed on Doppler ultrasound, treated with warfarin. Eight months later, she developed a recurrent chylothorax requiring further pleural aspiration. In March 2001 CT scan of thorax and abdomen showed relapse with progressive Iymphadenopathy and she received further chemotherapy, with five cycles of fludarabine. This produced only partial response so in November 2001 she received six cycles of cyclophosphamide, doxorubicin, vincristine and prednisolone, completed in March 2002. At the present time she remains well and in partial remission for over a year.

DISCUSSION

Chylothorax is an accumulation of fluid rich in triglycerides and characterised by the presence of chylomicrons in the pleural space. It is commoner on the left side and is due to leakage from the thoracic duct following trauma or obstruction(1-3). Chylothorax was associated with a 50% mortality rate, but currently mortality is estimated to be 10%, except in cases of malignancy(3-5). Death is related to severe nutritional deficiencies and wasting, impaired immune function and in some cases respiratory insufficiency(3). Chyle is produced by the ingestion of fats. Long chain triglycerides are converted into chylomicrons and low density lipoproteins by the digestive tract and then secreted into the intestinal lacteals and Iymphatic vessels and transported to the cisterna chyli at the level of the first or second lumbar vertebra. This structure gives rise to the thoracic duct that crosses the diaphragm at the aortic hiatus and ascends into the posterior mediastinum. The initial part of the thoracic duct lies to the right of the mid-line, and then at the sixth thoracic vertebrae it crosses to the left of the mid-line and passes behind the aortic arch, emptying into the left subclavian vein. The thoracic duct empties into

comparable veins on the right side of the neck in 10% of cases. The primary function of the thoracic duct is to transport skeletal and intestinal lymph but it is also the main pathway for the transport of proteins to the circulation. Lymphocytes constitute 95% of the cellular component of chyle and the majority of Iymphocytes are T cells. The exact composition of chyle is shown in Table 1. Any injury to the thoracic duct along its course from the cisterna chyli to the internal jugular vein may lead to a chylothorax. The causes of chylothorax are listed in Table 2(4-6).

Thoracocentesis will confirm the diagnosis of chylothorax. CT and MRI may be used to define mediastinal anatomy and Iymphangiography can sometimes define the exact site of obstruction or leakage from the thoracic duct.

Conservative management involves continuous suction drainage of the effusion allowing re-expansion of the lung. Nutritional losses are replaced by using a medium chain triglycerides (MCT) diet, which is high in protein and carbohydrates but low in fat. This helps to reduce chyle production(7). Parenteral alimentation should be used if there is a large effusion persisting irrespective of an MCT Diet. Treatment with somatostatin has been advocated by Ullibarn *et al*(8). It is a potent inhibitor of gastric pancreatic and intestinal motility and this may be useful in reducing chyle production. It is given as an intravenous infusion for a week in conjunction with parenteral nutrition.

Surgical options include ligation of the thoracic duct, usually between T5 and T8, although thoracoscopic clipping of the thoracic duct is a new technique that appears to reduce trauma, shortens drainage period and hospital stay(9). Pleuro-peritoneal shunting is another safe and simple procedure. This transfers the effusion to the peritoneum where it is absorbed by the Iymphatics overlying the liver and diaphragm, which drain into the right Iymphatic duct. Pleurodesis with tetracycline or talc may be particularly useful in patients with malignant disease as can the use of fibrin glue to seal a traumatic fistula using a thoracoscopic technique.

This patients biopsy showed follicular type non-hodgkins Iymphoma, but did not express the bcl-2 oncogene. This is rare but could occur in about 15% of patients with follicular Iymphoma(10). However she did express CD10 and CD79a which could be present in follicular Iymphoma(l1).

Our patient was deemed unsuitable for surgical procedures as she had stage 4B Iymphoma and she was treated with thoracoscopic talc pleurodesis. This lasted for a short period, after which she developed recurrence of the chylothorax requiring further drainage. In view of advanced disease with systemic symptoms in an elderly patient she received repeated courses of aggressive chemotherapy, which included cyclophosphamide, etoposide, vincristine, bleomycin, mitoxantrone, and dexamethasone(l2). This regimen is said to produce a remission rate in 58% of cases and is less toxic in the elderly(l2). She had a relapse of her symptoms, requiring further salvage chemotherapy, which included cyclophosphamide, doxorubicin, vincristine, and prednisolone(13,14). This is said to achieve 40-60% response and 20% complete remission(l3). She is currently well and has been in prolonged partial remission. This case highlights some of the difficulties in management of this condition, which tends to follow a relapsing and remitting course and does respond to chemotherapy. This has provided palliation of her symptoms and improved her quality of life which are the primary aims of therapy in advanced malignancy.

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