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Chylothorax and pseudochylothorax

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ABSTRACT: Chylothorax is the occurrence of chylus (lymph) in the pleura due to damage to the thoracic duct. There is a high content of triglycerides, and chylomicrons can be seen. It is usually right-sided, since most of the duct is within the right hemithorax. With damage at the level of the aorta, the chyle will appear on the left.

Traumatic rupture occurs after accidents or surgery. Of nontraumatic causes, the most common is a malignant lymphoma. Computed tomography (CT) scan of the thorax and upper abdomen should be performed. Lymphography can show where the leakage or blockage is situated. With repeated drains, large amounts of fat, proteins, and lymphocytes are lost. Treatment is with low-fat diet or parenteral nutrition to decrease the amount of chyle, but chemical pleurodesis or ligation of the thoracic duct, usually *via* thoracoscopy, is often necessary.

Pseudochylothorax (cholesterol pleurisy) occurs with long-standing fluid in a fibrotic pleura. The fluid has a high content of cholesterol but no triglycerides or chylomicrons. In both conditions, the pleural fluid is thick, opalescent, whitish or the colour of café-au-lait.

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Definitions

"Chylothorax" is the occurrence of chylus in the pleural space, and is due to damage or blockage of the thoracic duct. The diagnosis is made by analysis of the pleural fluid, which contains high levels of triglycerides, and is confirmed by the finding of chylomicrons. "Chylus", or chyle, is lymph, mainly from the gastrointestinal tract, which explains its composition.

"Pseudochylothorax" or "cholesterol pleurisy" or "chyliform effusion" is a fluid which has a very high content of cholesterol. Triglycerides or chylomicrons are, however, not present and the entity has nothing to do with lymphatic vessels or chyle. It can occur when a fluid has been present for a long time in the pleural space and, more especially, in a fibrotic pleura.

Both conditions have a common characteristic: the pleural fluid is usually thick, opalescent, whitish or the colour of café-au-lait or chocolate milk, due to its very high fat content. Apart from that, they have nothing in common.

Chylothorax

Diagnosis

Diagnosis is made by analysis of the pleural fluid. Triglyceride levels greater than 110 mg·dL⁻¹ are highly

suggestive of a chylous effusion. In equivocal cases, with triglyceride levels of 50–110 mg·dL⁻¹, a lipid electrophoresis will clarify the diagnosis [1]. Triglycerides below 50 mg·dL⁻¹ virtually exclude the diagnosis of chylothorax. Cholesterol values should be measured simultaneously, since high triglyceride levels can occur in pseudochylothorax [2], but the cholesterol level is always very high (>200 mg·dL⁻¹), and at microscopy, cholesterol crystals can be seen, which are thought to be diagnostic.

The gross appearance of the fluid can be misleading, and in any pleural effusion of undetermined cause, a lipoprotein analysis can be helpful [1]. The differential diagnosis of a turbid or milky fluid is an empyema; in case of an empyema, centrifugation of the fluid will show a clear supernatant.

Anatomy and physiology

The lymph vessels from the peritoneal cavity and the lower parts of the body come together behind the aorta, below the diaphragm, and form the thoracic duct. Usually, there is a widening of the duct at its origin, which has been termed the cisterna chyli. The duct passes through the diaphragm behind the aorta, and runs upwards on the right side of the vertebral column between the azygos vein and the aorta. At the height of the third or fourth vertebra, it turns to the left, crosses

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the mid-line, and continues upwards behind the oesophagus, medially of and behind the subclavian artery. It then turns laterally, often after making a small loop up into the neck region, and finally empties into the vena subclavia between the jugular and the vertebral veins.

This anatomy explains why a chylothorax is usually right-sided, since the largest part of the duct is within the right hemithorax, and this is also where it is most easily damaged due to stretching. When the leakage from the duct occurs where it passes over the mid-line, a bilateral chylothorax can occur [3, 4]. At the level of the aorta, the chyle tends to appear on the left side [5–7]. It has to be realized, however, that the anatomy of the duct can vary considerably. Two or more branches of the duct can be seen, and the duct can even empty into the right subclavian artery.

When the duct starts to leak, a collection of chyle below the pleura, a "chyloma", is at first formed but is only rarely seen clinically, for instance as a swelling of the supraclavicular fossa [3]. The formation of a "chyloma" can be a very dramatic clinical event, with acute chest pain causing dyspnoea and tachycardia suggesting myocardial infarction or pulmonary embolism. Such episodes seem to occur particularly after traumatic rupture of the thoracic duct. Soon the pleura ruptures and the chylus collects in the pleural space. There are some rare variations, for instance chylomediastinum, where the chylus collects in the mediastinum without breaking through the pleura [8], or chylopericardium, where it empties into the pericardial sac [9–11].

The thoracic duct contains many valves forcing the chylus in one direction only. Movement of the thorax propels the chyle forwards. There are numerous small connections with veins, making it possible to ligate the ductus without any resulting problems.

Apart from its protein and fat content, the chyle also contains a large number of lymphocytes and is bacteriostatic. The normal daily flow in an adult is around 2 L [12, 13]. The flow of chylus increases substantially with intake of food and drink, and decreases to a small trickle with starvation. With repeated thoracocenteses or continuous drainage of a chylothorax, large amounts of fat, proteins and lymphocytes are lost, quickly resulting in negative effects on the patient's nutritional and immunological status.

Aetiology of chylothorax

Chylothorax is due to leakage of chyle from the thoracic duct. This in turn is due to trauma, weakening of the wall, or blockage of the duct (table 1). The thoracic duct is a fairly weak structure, and, in fact, even an intense sudden stretching of it can cause rupture, as has been described after forceful cough, emesis, or the strains of childbirth, more usually in the infant but also encountered in the mother [14]. It should be stressed that the causes in table 1 are not mutually exclusive; on the contrary, one must always suspect some underlying cause when a fairly trivial incident, such as a cough, causes a chylothorax.

Traumatic rupture of the duct can be an early or late complication after traffic accidents, but is now seen increasingly often after various types of surgery involv-

Table 1. - Causes of chylothorax

Traumatic

Noniatrogenic

Any accident with damage or stretching of the chest wall or thoracic spine

Forceful cough or emesis

Childbirth [14]

Iatrogenic

Surgery of chest

Head-and-neck surgery

Radiation (often late sequelae)

Sclerotherapy of the oesophagus [15]

Diseases

Malignant

Lymphomas [16]

Other malignancies

Benign tumours

Retrosternal goitre [7]

Sarcoidosis [17, 18]

Diseases affecting the lymph vessels

Yellow nail syndrome [19]

Lymphangioleiomyomatosis

Haemangiomatosis (Gorham's syndrome) [20]

Congenital

Filiariasis [21]

Tuberculosis [22]

Amyloidosis

Thrombosis of the superior vena cava or other central veins Heart failure with increased venous pressure [23, 24] Transdiaphragmatic movement of chylous ascites [25–27]

Idiopathic

ing heart, lung or the head-and-neck region. It can occur even after thoracoscopic surgery. The incidence of chylothorax after chest surgery of various kinds is around 0.5% [28–30].

Of the nontraumatic causes, the most common is a malignant lymphoma. Whenever a chylothorax of unknown aetiology occurs, the first suspicion should be of an underlying malignant lymphoma. Other malignancies can cause blockage of the ductus by metastatic spread, but this is actually a fairly rare occurrence.

Apart from those diseases which directly affect the lymph vessels and where chylothorax is common, it is usually an extremely rare complication of most of the other diseases listed in table 1. For example, case reports in the world literature of chylothorax as a complication of sarcoidosis, goitre, or tuberculosis are easily counted on one hand.

Congenital chylothorax is more often due to malformation of the thoracic duct than trauma at birth [31].

Investigations

Once the diagnosis of chylothorax is clear and there is no obvious cause, investigations as to the cause should be performed. Since the most common cause of non-traumatic chylothorax is malignancy, and in particular lymphomas, a computed tomography (CT) scan of the thorax and upper abdomen should be performed, to visualize any enlarged lymph nodes or other signs of tumour, and to enable scrutiny of the lungs. Lymphography will usually show where the leakage or blockage is situated [32]. This can be of importance for the clinical decisions of where to take biopsies.

If no cause has been found, the next step is most often thoracic surgery, which is today usually performed by thoracoscopic methods. Biopsies of any suspect area should be taken, and before the operation it should also be decided whether ligation of the ductus should be performed at the same time. Biopsy of the lung, especially any suspicious part seen at CT, should be performed, since this is the best way to diagnose, for instance, a lymphangioleiomyomatosis. It should be remembered that chylothorax can be the first sign of a malignant lymphoma, and that even thoracic surgery might not give a definite diagnosis. In all unclear cases, treatment of the chylothorax should be performed, and the patient then followed-up.

Treatment

The large effusion causes respiratory distress, which is relieved by thoracocentesis. However, the chyle usually soon reaccumulates, and repeated thoracocenteses can be necessary. Apart from the diminished quality of life, the patient will lose protein and other nutrients, so that some alternative therapy will become necessary in these cases. A number of different treatments have been suggested (table 2).

Treatment of the underlying disease is important and will, in some cases, cause the chylothorax to disappear. Examples are corticosteroids in sarcoidosis [17] or treatment of heart failure. In many instances, notably malignant lymphomas [16], specific treatment will have good effect on the underlying disease, but the chylothorax can remain, and therefore further measures will be necessary.

A low-fat diet with medium-chain triglycerides, which to the largest extent are absorbed directly into the blood, will cause the chyle to decrease in amount, but there will still be a flow [34]. The next step is total parenteral nutrition, which will diminish flow even further. In around 50% of patients with traumatic chylothorax, spontaneous healing will occur with conservative treatment [30, 35]. Thus, a trial of such treatment is recommended by many surgeons [28, 36, 37]. However, with thoracoscopic, minimally invasive procedures, earlier intervention is now favoured by many, especially if the patient's nutritional status is already poor [29].

Chemical pleurodesis for pleural effusions, mainly

Table 2. - Treatment modalities of chylothorax

Treatment of the underlying disease
Conservative measures
Repeated thoracocenteses
Continuous drainage
Dietary modifications
Low-fat diet, medium-chain triglyceride diet
Total parenteral nutrition
Pleurodesis
Surgical measures
Pleuroperitoneal pump
Fibrin glue to close the leak in the duct [33]
Ligation of the thoracic duct
By thoracoscopy
By thoracotomy
Pleurectomy

malignant, has been in practice for decades. There are many different drugs that have been used, the choice of which depends less on scientific reports than on local customs. All of them have also been used for chylothorax. Examples are tetracycline, bleomycin [38], and talc [39]. The general impression is that it is more difficult to achieve a chemical pleurodesis in chylothorax than in malignant pleurisy, probably due to the normal pleura and perhaps a neutralizing effect of the chyle [21].

An alternative to pleurodesis, where for some reason this is not feasible, is the pleuroperitoneal shunt, which in principle is a one-way subcutaneous connection between the pleura and the peritoneum, with a pump which can be activated by light pressure. It requires daily pumping and, thus, a co-operative patient. It has been used in some cases of chylothorax [21, 35]. With time, the rupture in the duct often heals, making it possible to remove the shunt, and it is therefore recommended especially for infants and children [40]. However, in children, conservative measures are often also very effective [31]. After some time, almost all pleuroperitoneal shunts will close and have to be replaced.

Ligation of the thoracic duct is an almost invariably successful procedure, which can be done by thoracoscopy [41, 42]. Due to the rich network of collaterals, there are never any problems with lymph stasis afterwards. The ductus is ligated slightly above the diaphragm. If the patient has drunk full cream before the operation, the leakage is often visible at surgery [41]. Where the leakage occurs is, however, unimportant for the ligation procedure, making this procedure hardly worthwhile.

Some diseases with special aspects of chylothorax

Lymphomas. Most commonly, a non-Hodgkin lymphoma causes the chylothorax. As already mentioned, even if the malignant disease can be treated, it is often necessary to treat the chylothorax separately [16, 38]. Chemical pleurodesis is one option, ligation of the thoracic duct is another, and sometimes they are combined.

The aetiology behind the chylothorax is probably invasion of the wall by lymphoma, causing it to be more brittle. However, lymphoma cells are usually not seen in biopsies of the pleura or the duct [16]. Chylothorax can be the first symptom of the lymphoma, and definite diagnosis is sometimes not made until months or years later. Thus, treatment of the chylothorax even without knowledge of the underlying diagnosis is mandatory in these cases.

Lymphangioleiomyomatosis. This disease occurs only in females and mainly in the reproductive years. Cells resembling smooth muscle cells proliferate in the lymphatic vessels and in the lung, causing progressive reticulonodular infiltrates. Chylothorax occurs in a large proportion, 28% in one series [43]. Pneumothorax and haemoptysis are other symptoms. The prognosis is poor. Pleurodesis or thoracic duct ligation can control the chylothorax, but the lung disease is progressive. Some effects are probably seen by oophorectomy and/or progesterone treatment [43].

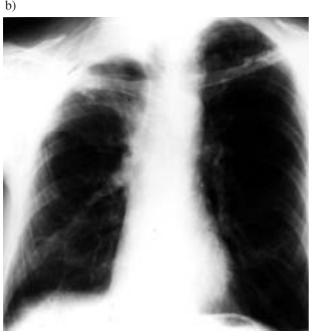
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Pseudochylothorax

Pathogenesis

Some exudates which remain for a long time (months or years) in the pleural space have a tendency to become enriched with cholesterol. Typically, this "cholesterol pleurisy" is seen in fluid, which is encapsulated in a fibrotic area of a grossly thickened pleura. The fibrotic scar tissue, which forms the walls of the chamber, is poorly vascularized and there are few cells, so there is little absorption of any substances in the fluid. Earlier theories suggested that blood cells, both red and white, which reached the fluid became necrotic and disintegrated. Cholesterol from the cell walls is poorly absorbed in these circumstances, and thus, with time,

a)



the levels of it would increase. However, analysis has shown that there is a predominant binding of the cholesterol to high density lipoprotein (HDL), which implies that it is derived from serum lipoproteins rather than from cellular debris [2].

Probably due to osmotic effects, the cholesterol effusion has a tendency to enlarge slowly. Over some years, an original small space can increase to a litre or more (fig. 1). Since the pleural fibrosis is very often associated with changes in the lungs as well, often causing a lowered lung function, this thickened pleura can cause considerable dyspnoea and a poor quality of life [44].

Aetiology

The kind of thick peel covering the whole lung can be seen after tuberculous pleurisy, therapeutic pneumothorax, or in chronic rheumatoid pleurisy, which are the three most common causes [44, 45]. The two first mentioned causes are increasingly rare in a modern industrialized society. However, the increasing problem with multiresistant forms of tuberculosis might cause a revival of pneumothorax treatment, so it might also be of interest in the future. Other causes are traumatic, *i.e.* profuse bleeding in the pleura which becomes organized, remnants of poorly treated empyemas, and other diseases which can cause extensive fibrosis of the pleura.

I have seen no report on cholesterol pleurisy in persons with asbestos-related diffuse pleural thickening. Possibly, in this type of pleural fibrosis, the fibrotic tissue contained is too dense, and there is no central pool of fluid, so that conditions for cholesterol pleurisy do not exist.

Fig. 1. – A case of pseudochylothorax in a man, born in 1922. In 1950, active tuberculosis was diagnosed. a) 1950: right-sided therapeutic pneumothorax. b) 1968: thickened pleura, especially apically, with some shrinking of the upper lobe on the right side. c) 1982: considerably increased thickening on the right side, causing respiratory distress.

Table 3. - Complications of cholesterol pleurisy

Respiratory insufficiency Infections

Reactivation of tuberculosis

Nonspecific infection

Fungal infection, particularly aspergillus [46]

Fistulae: bronchopleural, pleurocutaneous

Clinical course and treatment

Pseudochylothorax of small or moderate size is fairly common in patients with large pleural peels. In most cases, there is a benign course, and it is only if the patient has symptoms or if there has been a substantial increase in size that any intervention is needed. However, any thick peel around part or the whole of a lung should be carefully noted by the radiologist. Such peels practically always contain an area with fluid, and thus there is a risk of complications. An attempt should always be made to obtain earlier chest radiographs, and it is not sufficient to look at one that is only 1 or 2 yrs older. It is preferable to obtain one taken ≥10 yrs ago.

If the thickening has increased considerably in size, or if no earlier films can be recovered, there is a large pleural thickening and the patient has some symptoms, thoracocentesis should be performed. This is important not only to relieve dyspnoea but also to prevent complications, which can occur in untreated cholesterol pleurisy (table 3). A CT scan is very helpful to illustrate the anatomy. Great care should be taken before a pleural peel is declared to be "inactive".

Two points should be stressed regarding thoracocentesis in these patients: firstly, the peel is often of considerable thickness and in addition calcified, which makes puncture difficult (long needles can be needed!); and, secondly, the walls around the fluid are stiff, and, thus, may not adapt easily when the fluid is withdrawn so that a negative pressure can develop if forceful suction is applied. This is immediately felt by the patient and further fluid removal is painful and meaningless, unless air is allowed to enter to equalize the pressures. This can be helpful in delineating the cavity later.

Cultures for tuberculosis should always be made on the fluid, since a reactivation of this infection is always possible [47]. Even if the cultures are negative, it can be a good idea to give a patient who has never been treated properly for tuberculosis a course of chemotherapy.

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