Case for diagnosis

Acute respiratory failure with bilateral chylous thorax

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Case history

A 56-year-old man was admitted to Pneumology with a severe respiratory failure with bilateral pleural effusions and parenchymal opacities (Figure 1). The clinical documentation of the patient revealed a chylous ascites about 4 years old. At the time, the patient made several gastro-enterologic check-ups: an abdomen TC, which revealed peritoneal and mesenteric thickenings; a hepatic biopsy, which revealed a “portal lympho-histiocitic hepatitis with ductal proliferation” in a metabolic contest of moderate hepatocellular distress, and an epiploon biopsy, which revealed “note of aspecific inflammation, septum fibrosis and atipic mesothelial hyperplasia”. No definitive diagnosis was made.

Figure 1 - Chest radiograph A-P at the admission to hospital.

One year later the patient was admitted to the Massachusetts General Hospital of Boston for a gastro-enterologic revaluation. During hospitalization, endoscopic tests revealed jejunum and ileum lymphangectasis. Ascites effusion was treated with pharmacologic therapy and periodical paracentesis. No pathology was found at thoracic level.

After clinical stabilization, the patient made a thorax TC which revealed a bilateral chylous thorax and parenchymal opacities, without focal lesions or relevant mediastinic alterations. At abdominal level there was a remarkable chylous ascites (Figure 2). Pleural and abdominal effusions were treated with thoracentesis and paracentesis respectively.

Blood tests revealed only a moderate alteration of hepatic functional indices; no alterations of tumoral markers and auto-antibody pattern were found. No relevant alterations at the bronchoscopy with BAL, nor positiveness for BK or aspecific germs at culture test were found. The cytological tests revealed a normal cellularity (for number, formula and morphology) with aspecific note of acute phlogosis. The echocardiographic report was normal.

Figure 2 - Thorax and abdomen TC scan showing bilateral pleural effusion, parenchymal opacities and peritoneal effusion.

BEFORE TURNING THE PAGE, INTERPRET THE PATIENT HISTORY, CHEST RADIOGRAPHS, THORAX AND ABDOMEN CT SCANS.
Interpretation

The patient had a history of respiratory failure, chylous thorax, chylous ascites, parenchymal opacities, a moderate alteration of liver enzymes, aspecific note of acute phlogosis at BAL. Before the thorax CT, two clinical hypothesis were put forward: abdominal Tb or filariasis (patient has lived for a period in endemic zone), but neither was ever confirmed. In fact, nor positivity for BK or filariasis were found. A clinical hypothesis of systemic lymphangiomatosis was put forward on the basis of thorax CT, chylous thorax at thoracentesis and because of the clinical history of the patient (1). Being skeleton frequently involve (5), a series of bony radiographies were made, but clinical suspect wasn’t confirmed. For a definitive diagnosis a pleural biopsy in video-thorachoscopy was planned, but before the operation there was an inexorable decline of the patient’s general conditions and, eventually, the patient died.

Diagnosis: acute respiratory failure in presence of an advanced systemic lymphangiomatosis, confirmed at autopsy

Autopsy revealed that most of the peritoneal and omento-mesenteric districts presented zones with increased consistence and reddish nodularity which measured by few millimetres to about one centimetre (Figure 3A, arrows), also with big reddish lymphatic formations (Figure 3B, arrow) and dyschromical intramural areas. There was a moderate chylousperitoneum (about 2 liter). Lungs were congested, edematous, of increased consistence, with bilateral pleural adhesions, pleural fibrinous reaction at the base of the lungs (Figures 3C and 3D) and a relevant bilateral pleural effusion. Right arterial pulmonary circle was heavily embolized. Histologically, omental and mesenteric districts and intestine presented a diffused dilatation of lymphatic vessels (Figures 4A and 4B); mesenteric lymphonodes resulted hyperplastic and characterized by large lymphangectasia. Lungs presented a massive bronchopneumonic process and lymphatic channels with thin walls, very dilated (Figures 5A e 5B) and increased for size and numerosness. The border of most of lymphatic channels proliferated in abdomen and lungs revealed multifocus positivity at immunoenzimatic tests (technique of Biotina-ExtrAvidina (Sigma) with antibody anti CD31 (endothelial markers) [1:10, Ventana] and D2-40 [1:100, Dako]) with anti-D2-40 and CD31 (Figures 6A, 6B, 7A, 7B); in particular endothelial cells surrounding the irregular anastomosis lymphatic channels in the lungs were heavily pos-
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Figure 6 - Immunohistochemistry staining 40x, CD31+ cells 6A, D2-40+ cells 6B.

Figure 7 - Immunohistochemistry staining 40x, CD31+ cells 7A, CD2-40+ cells 7B.

Discussion

The present case showed respiratory complications in a 56-year-old patient with systemic lymphangiomatosis. Systemic lymphangiomatosis is a rare, misdiagnosed, disorder characterized by a diffuse proliferation of lymphatic channels which frequently affects people under 20 (7,9), although some isolated cases have been reported in people as old as 80 (5-8). Disseminate form is the most common because bones are interested in 75% of cases (5).

Disorders of lymphatic vessels must be associated with a lot of pathological conditions, such as trauma or neoplasia, or must be primitively correlated to congenital anomalous formations or idiopathic degenerations of lymphatic vessels (2-4), such as systemic lymphangiomatosis (which is different from the pulmonary lymphangiomiomatosis or LAM). Vessels proliferation could indicate a tumoral origin and the presence of destruction found in some forms testifies to an amartomatosa origin (9). Anatomopathologically, lymphangiomatosis can be assimilable to lymphangioma (11-13); in some cases venous malformations are also given (for example vena cava left-placed) (14). At pulmonary level pathological aspects include a proliferation of lymphatic anastomotic complexes with relevant expansion of lymphatic ways into the lungs and mediastinum (6). Surrounding parenchyma is not spared (d.d. with lymphangioleiomyomatosis) but can include agglomerates of macrophages with emosiderina inside (15, 16).

Clinically, lymphangiomatosis can involve several organs containing lymphatic channels, with a particular predilection for the lungs (10, 17). A lot of patients with systemic lymphangiomatosis have asymptomatic cystic masses full of fluid and not adherent to underlying tissues. Other clinical presentations can be dyspnea, easy tiredness, chylous pericardium, chylous thorax, electrolytic and proteinous deficit, loss of weight, intermittent chest pain and dysphagia. Moreover, chylolysis (19), hemoptysis (20), chylous ascites (4, 21), protein losing enteropathy (22), peripheral lymphedema (23), lymphopenia (24) and disseminated intravascular coagulation (25) are also described. Many patients can also experiment the onset of “wheezing” and so they can be erroneously labelled as asthmatic people before the correct diagnosis of lymphopaty is made (6).

An essential point for the diagnosis of disseminated forms is the coexistence of bone lithic lesions and chylous thorax. Diagnosis can be made with bond biopsy which reveal how these lithic lesions are lymphangioma with lymphatic fluid inside (6, 26). Lymphangiografia reveals multiple lesions of the thoracic duct, dilated lymphatic channels and lymphangioma into the bone and lung (27). Bilateral interstitial infiltrations and pericardial or pleural effusion are evident at chest radiography (18). Spirometry can reveal an obstructive-restrictive setting (6); instead HRTC reveals diffused and regular thickenings of the inter-lobular septum and of the bronco-vessel walls with a larger involving of mediastinum fat and perihilum regions (28). Hystologically, the antigens correlate to factor VIII and CD31 are useful endothelial markers for the immunohistochemical definition of these channels (29).

The natural history of this disease is characterized by a progressive growth of lymphatic complexes with compression of the near structures (6, 30). Therapy could be focussed on obtaining a reduction of the symptoms due to compression and a reduction of chylous effusion (30). Success of the surgical treatment is heavily limited by the difficulty of dissociating lymphatic complexes by the normal structure with a high rate of relapses (31, 32). For patients with disseminated and advanced disease therapy is palliative, like percutaneous sclerotherapy by doxyciclin which have done good outcomes (30). Diet at elevate proteic content and medium chain triglycerides can be useful (21). Recently good results for the control of chylous effusion and disease progression (33) have been reported in a case employing talidomide, a drug with immunomodulatory, antiphlogistic and antiangiogenic actions (34). Unfortunately the case reported is only an isolated one and other investigations and con...
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trolled studies will be required, which are made difficult by the fact that this pathology is quite rare, diagnosed quite late and its management is often very difficult (5). For our case report, analyzed at the end stage, after 5 years from the onset of the symptoms, no therapy was possible because of the quick and irreversible course of the events leading to the patient’s death.

References