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Case Study

CHOLESTEROL EFFUSION: A STUDY OF 2 CASES

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Abstract:

Background: Cholesterol crystals in the third space fluid are due to a high concentration of cholesterol in the body cavity fluid. The aetiology of such an entity is wide-ranging.

Objectives: a) To analyze the morphologic characteristics of two separate cases; in pleural and pericardial effusions due to long-standing tuberculosis and rheumatoid disease respectively.

b) To study the aetiopathogenesis of these crystals and review the available literature in brief.

Results: Both had an abundance of inflammatory cells and foamy macrophages along with birefringent cholesterol crystals.

Conclusion: The body fluids with a cholesterol effusion have peculiar features. This should necessitate a thorough investigation into the underlying pathology

Key words: cholesterol crystals, pleural effusion, pericardial effusion, tuberculosis, rheumatoid disease.

Introduction:

Body cavity effusion is defined as the excessive accumulation of fluid in the third space. The pleural fluid, the pericardial fluid and peritoneal fluid are the most commonly involved of the lot. These body cavities are anatomically covered by the parietal and visceral layers, on the outer and inner aspects, respectively, with a 10–24 mm separation normally between the two surfaces.[1] This space is usually filled with a very small amount of fluid; serving the purpose of lubrication, avoiding friction between the two layers. However, large amounts of fluid can potentially accumulate in these cavities under pathological conditions due to an imbalance between the forces regulating the fluid formation and its subsequent removal. The presence of significant amount of fluid is a vital finding because it may be a primary manifestation or a secondary complication of many disorders. Moreover, the analyses of body fluids are just as vital since its cellular and

acellular constituents provide useful insights into the nature of the underlying disease.

Cholesterol crystals in the body cavity effusions are associated with systemic diseases, such as tuberculosis, rheumatoid arthritis, hypothyroidism and long-standing hemorrhage. Many have been typed as idiopathic cases. [2]We herein describe two separate cases where a cholesterol crystal-rich effusion was noted in the pleural and pericardial space.

Case 1:

A 53 year old male patient presented to the hospital with a history of progressive exertion and dyspnea since 2 months. He also had a non-productive cough. There were no other associated symptoms. His past medical history was significant for a chronic smoking history and rheumatoid arthritis diagnosed 4 years back. He was treated previously for his rheumatoid arthritis but the treatment had been discontinued due to poor compliance. On examination, the patient was pale with bilateral pitting edema of both feet. The liver was mildly enlarged. A chest radiogram depicted an enlarged cardiac silhouette with the ensuing electrocardiogram showing a low-voltage QRS complex. An echocardiogram revealed a significant pericardial effusion with no or minimal signs of restriction. We received the drained pericardial fluid measuring 200 milliliters in volume with a hemorrhagic appearance on gross examination. The microscopic analysis showed the following parameters: neutrophils 49%, lymphocytes 48% and eosinophils 3% with the background showing abundant foamy histiocytes and erythrocytes. The smear also revealed numerous cholesterol crystals, seen as colorless, polyhedral to rectangular plates with notched edges (figure1).An occasional histiocyte with ingested crystal was also seen. The biochemical profile of the pericardial fluid showed the following: protein 3.3g/dL, glucose 0.2 mg/dL and lactate dehydrogenase (LDH) 2556 IU/L and pH 7.35. The tests for autoimmune serology including rheumatoid factor were negative.

Case 2:

A 72 year old male patient presented with a 7 day history of acute onset of respiratory distress and productive cough with streaky hemoptysis. He had a significant history of long-standing tuberculosis, diagnosed by a lung biopsy 6 years ago and had defaulted on treatment. On physical examination, the patient was tachypneic even at rest. The pulmonary examination revealed diffusely decreased breathing sounds, inspiratory crackles and dullness to percussion with decreased vocal fremitus on the left side. There accessory muscles of respiration were actively used to compensate for the dyspnea. The level of oxygen saturation (SPO2) was low (64%). The chest radiograph showed a left- sided pleural effusion. There was blunting of the left costo- phrenic angle. A diagnostic and therapeutic thoracocentesis was performed which yielded approximately 650ml of hemorrhagic fluid. The respiratory symptoms receded to a marginal extent and the fluid was sent to the laboratory for hematological and biochemical analysis. The thoracocentesis showed the following features: neutrophils 76%, lymphocytes 23% and eosinophils 1% with the background showing abundant foamy histiocytes and hemorrhage. The smear also revealed numerous cholesterol crystals. The biochemical tests confirmed the exudative nature of the effusion. The stain for acid fast bacilli was negative.

Discussion:

The body cavity fluid containing the presence of a high concentration of cholesterol, with low levels of triglycerides and absence of lymph, is also referred to in literature as pseudochylous effusion, chyliform or simply as a cholesterol effusion.[3,4] This results from a chronic, long-standing effusion, seen in a wide range

of systemic diseases, most notably in rheumatoid arthritis and tuberculosis.[5,6] Both of our cases were due to these aetiologies. In a large study of cholesterol-rich effusions conducted by Coe and Aikawa yielding a total of 101 cases; the average reported time for evolution of effusion into a cholesterol effusion was 5 years, although intervals of 11 to 15 years were not uncommon.[5] This was fairly consistent with the present cases as well with 4 and 6 years for the pericardial and pleural effusion respectively.

Although the pathogenesis of cholesterol effusions is still speculated, there are several theories about the mechanism involved in the accumulation of cholesterol. Coe and Aikawa divided these speculations into two classes[3]: the general metabolic theory and the local process theory. The general metabolic theory proposes that cholesterol effusions are merely a manifestation of systemic hypercholesterolemia. This hypothesis however, has been challenged [7]

The most accepted local process theory suggests that the cholesterol is a direct derivative of the cell membranes of degenerating red blood corpuscles (RBCs) and leucocytes in the fluid. The ensuing or co-existing inflammation and fibrosis of the pericardial or pleural layers impair lymphatic egress causing this cholesterol and other molecules to collect within the third space.[8]Tuberculosis in its active, chronic or even 'healed' form; can cause a delay in the resorption of such molecules. This added with the fact that tuberculosis is responsible for recurrent pleural effusions provides a perfect milieu for such a theory to unfold.

Pericardial effusions are also referred to as cholesterol pericarditis. This termis used in cases of chronic pericardial effusion with the presence of cholesterol crystals or an elevated concentration of cholesterol, or both.[9] This effusion is rich in low density lipoprotein (LDL) cholesterol, and can potentially form masses along with debris and fibrin, crystallizing over time and depositing in the pericardium, leading to pericarditis.[2]Cholesterol pericarditis is secondary to recurring outbreaks of acute pericarditis, resulting in inflammation and change in the absorption capacity of the pericardium. This causes precipitation of the crystals, which, located in the pericardial membrane, trigger a granulomatous response of the foreign body type. The result is exudation of the pericardial fluid, which leads to effusion.[9,10] In the present case, the long-standing rheumatoid disease and its pathophysiology are consistent with hypothesized tissue changes. However, the history was more or less acute and cholesterol levels were not measured.

The other important aspect of cholesterol effusion is the necessity to differentiate it from a chylous effusion. A true chylous effusion results from leakage of chyle from the thoracic duct following trauma or malignancy. The features typifying a chylous effusion are a sudden onset, a milky white appearance or yellow-bloody appearance on gross examination, a differential count of the fluid showing lymphocytosis and a high triglyceride levels (>110 mg dL). The cholesterol effusions on the other hand have a gradual onset, a milky or green metallic sheen on gross examination, a mixed cellular reaction on differential count with background cholesterol crystals and a low triglyceride level (<50 mg dL).[3]

Recently, Shen and Blair have reported cases of marked interference in the automated cell count by the presence of cholesterol crystals in the pleural fluid and have discussed the implications of this interference.[11] We had done the total count of the fluid on a manual haemocytometer in these 2 cases.

Conclusions:

Cholesterol effusions are not an uncommon occurrence in diagnostic parlance. Besides recognizing them morphologically, their presence should necessitate a thorough investigation into the underlying pathology, since the treatment is imperative.

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FIGURE AND LEGEND:

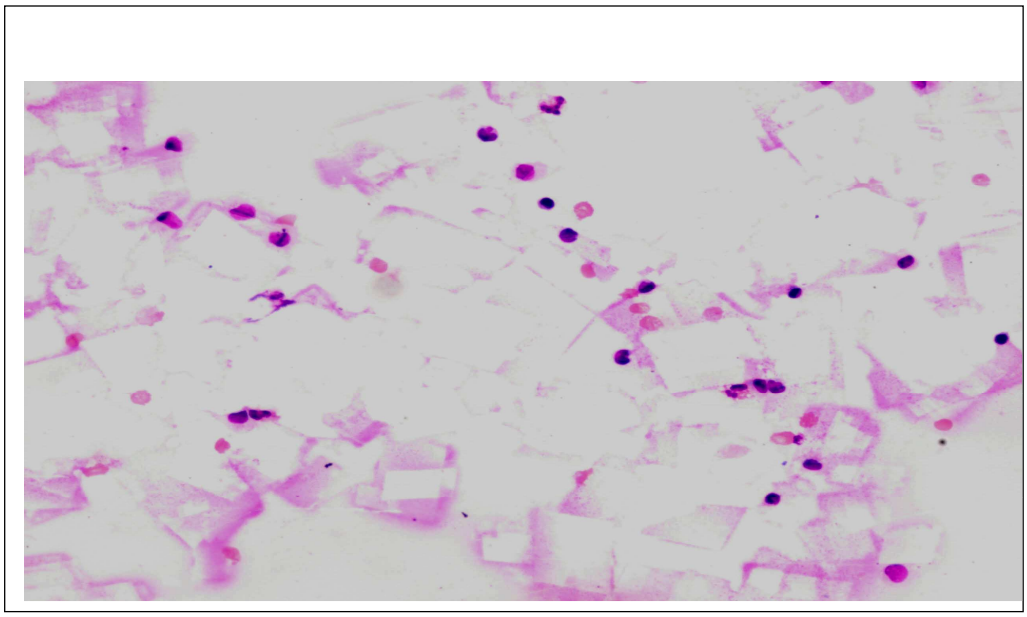

Figure 1: The pericardial fluid showing neutrophils, lymphocytes and numerous rectangular cholesterol crystals with notched edges in the background. (Leishman; x 200)