Special Communication

Asymptomatic full term pregnant patient with a grossly abnormal chest radiograph

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ABSTRACT

An asymptomatic full term pregnant lady with a grossly abnormal chest radiograph is presented as a clinical quiz. The diagnosis is discussed and the topic reviewed in detail.

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Case Presentation

A 37-year-old Lebanese housewife who was 8 months pregnant was admitted to the Gynecology Department, Riyadh Medical Complex, Riyadh, Kingdom of Saudi Arabia (KSA). She was para 2+0 and had uneventful previous and current pregnancies until the day of admission when she reported significant bleeding per vagina. She had no other symptoms referable to other systems and in particular had no respiratory symptoms. Past medical history was unremarkable except for laparoscopic cholecystectomy 2 years earlier that was uneventful. She attended the antenatal clinic in another facility and did not report any major event during the current pregnancy.

Examination revealed normal vital signs, and mild pallor. There was no clubbing or cyanosis. Examination of the chest was initially documented as being normal but later revealed minimal fine basal late inspiratory crepitations. Examination of the abdomen revealed a near full term gravid uterus. The other systems were normal on examination.

Initial investigations showed hemoglobin of 10.0 g/dL, normal urea, creatinine, electrolytes and liver function tests. Ultrasound scan of the abdomen demonstrated placenta previa as the cause of ante partum hemorrhage. Patient was scheduled for lower segment cesarean section. At this stage she gave the history of a "long standing chest problem" which led to the request of a chest x-ray (**Figure 1**) and arterial blood gases (ABGs) prior to surgery. Arterial blood gases revealed PO_2 of 88.5 mm Hg, PCO_2 30 mm Hg, pH 7.45, HCO_3- 27mmol/L and oxygen saturation of 98%. After delivery, pulmonary function tests (PFT) showed: forced expiratory volume in one second (FEV1) 3.6 L (90% predicted), forced vital capacity (FVC) 3.8 L, FEV1/FVC 94.7% and diffusion capacity for carbon monoxide (DLCO) was 82% predicted. She gave a family history, which lead to the diagnosis without further investigations.

Questions

1. What is the diagnosis?
2. What family history might she have given?

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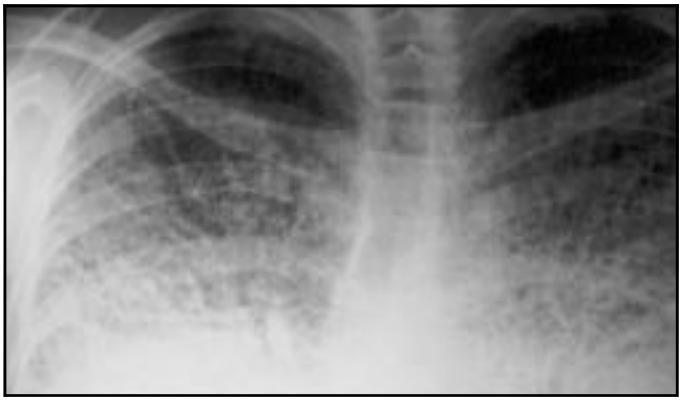

Figure 1 - Chest radiograph of patient.

Answers

1. The diagnosis is pulmonary alveolar microlithiasis (PAM). The chest radiograph (**Figure 1**) shows the classical widespread "sandstorm" micronodulation, which is predominant in the lower zones obscuring the heart borders and diaphragmatic outline. The patient, at full term pregnancy and inspite of the grossly abnormal chest radiograph, was asymptomatic. This is unique to PAM.

2. Patient gave a history of similar chest problem in 2 of her 3 brothers aged 39 and 41 years. One of the brothers had a lung biopsy for confirmation of the diagnosis. A positive family history is another clue to the diagnosis of PAM.

Discussion. Pulmonary alveolar microlithiasis is a rare condition of unknown etiology first described by Friedrich in 1856.[1] It is characterized by the deposition of calcispherytes in the alveoli. Over 300 cases have been reported in the international literature, a third of these from Turkey.[2] At least 8 cases have been reported from KSA.[3-5] There are 2 recognized patterns of the disease: (i) a familial form accounting for 50% of cases in which there is female predominance. The mode of inheritance is believed to be autosomal recessive and (ii) a sporadic form in which there is equal sex distribution. Although this condition commonly presents between the third and fifth decades of life, it has been described in infants and an 80-year-old.[6,7] The etiology is unknown and may be an inborn error of metabolism or inflammatory response to irritants or infections. A recent study by Castellana et al[8] however confirms the autosomal recessive nature of the inheritance but does not support the role of other non-genetic factors in the pathogenesis of this condition.

The characteristic feature of this condition is the dissociation between clinical and radiological features, which are pathognomonic. Most patients remain asymptomatic until late in the disease. Mariotta et al[9] described the largest case series of 48 patients in whom 35.4% were asymptomatic. Where there were symptoms, they include various grades of dyspnea (67.7%), cough (32.2%), chest pain (12.9%), fever (9.6%) and sputum with microliths (6.4%). Chronic cough may be the sole presentation.[10] Examination may reveal minimal crackles (19%). In the advanced stage of the disease there may be cyanosis and signs of cor pulmonale. Patients may present with spontaneous pneumothorax. Diagnostic investigations include a chest radiograph, which shows widespread 'sandstorm' micro nodulation with basal predominance as in our case. There are reticular lines, which tend to obliterate the bronchovascular bundle, heart and diaphragm. Computerized tomography (CT) scan of the chest shows a calcified reticular pattern with thickening of the interlobular fissure and septa, sub pleural air cysts and paraseptal emphysema. These changes are usually basal and peripheral in distribution. Although said to be pathognomonic,[11] similar CT findings were described in pulmonary sarcoidosis.[12] Technetium-99m scan often shows diffuse uptake in both lungs. This type of diffuse uptake is also seen in patients in whom there are no radiological calcification but with hypercalcemia, and in patients on chronic hemodialysis. The mechanism in all cases being chemisorption on hydroxyapatite crystals.[13] The presence or absence of diffuse uptake may depend on the stage and severity of the disease.[14]

Pulmonary function tests remain normal in most patients until late in the natural history of the disease as in our case in which the ABG was normal and the pulmonary function tests (PFTs) after delivery was normal. In Mariotta et al[9] series, 64.2% of cases had normal PFTs, 28.7% restrictive and 7.1% obstructive patterns. Although the standard chest radiograph is characteristic, diagnosis is confirmed by the identification of microliths in the sputum or bronchoalveolar lavage (BAL) or on lung biopsy. The microliths are formed of calcium and phosphorous salts in the ratio of 2:1. Numerous other substances were found to be increased in the BAL fluid including ionizable iron and total protein.[15] Microliths were not detected in the sputum of our patient and she declined further invasive procedures. Nevertheless, the confirmation of the diagnosis in her brother and the classical chest radiograph makes further invasive investigations unwarranted.

The lung is one of the internal organs most predisposed to soft tissue calcification. This can be either metastatic calcification, in which calcium is deposited in normal lung tissue or dystrophic wherein calcification is superimposed on previously injured lung. The former can further be sub-classified into benign or malignant causes. The most commonly causes of benign metastatic are chronic renal insufficiency on hemodialysis, orthotopic liver transplantation, primary hyperparathyroidism, milk-alkali syndrome and hypervitaminosis D. Common causes of malignant metastatic include parathyroid carcinoma, multiple

myeloma, breast carcinoma and choriocarcinoma. Dystrophic calcification is most common secondary to infections. These include tuberculosis, histoplasmosis, coccidioidomycosis, post varicella pneumonia, and paragonomiasis among others. Dystrophic calcification can also result from sarcoidosis, amyloidosis, and pulmonary vascular calcifications for example hemosidorosis; and inhalation of inorganic dusts such as silicosis and coal worker's pneumoconiosis. Pulmonary alveolar microlithiasis, however, is distinct from all these conditions. Apart from the classical radiological appearance as in **Figure 1**, it has a distinct histologic appearance. Unlike metastatic or dystrophic calcifications in which the calcification is in the interstitium or vascular compartments, in PAM lung biopsy reveals multiple concentric laminated calcispherytes within alveolar spaces measuring 250-750 µm and variable degrees of fibrosis. Although in most patients the calcification is localized to the lungs, similar radiologic and pathologic findings were documented in the lumbar sympathetic chains and testes,[16] kidneys[17, 18] and seminal vesicles.[19] These findings suggest PAM is a systemic disorder. When patients are symptomatic, treatment is usually supportive. Steroids have been tried but have not been found useful. Whole lung lavage, a highly successful means of treatment in pulmonary alveolar proteinosis, has not been found useful in PAM.[20] Anecdoctal reports of the use of disodium etidronate, an agent that inhibits the microcyrstal growth of hydroxyapatite, have given mixed results.[20,21] Nasal continuous positive airway pressure, by decreasing the physiologic intrapulmonary shunt may help alleviate symptoms in advanced cases.[22] Bilateral sequential lung transplant is a viable option for advanced cases.[23] The natural history of the disease is a very slow progression to cor pulmonale and death. This may range from as short as 5 years to as long as 41 years.[24]

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