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Diagnostic challenges and the role of medical imaging in postpartum miliary tuberculosis

Dilemme diagnostic et rôle de l'imagerie dans la tuberculose pulmonaire miliaire en postpartum

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RÉSUMÉ

L'atteinte pulmonaire de la tuberculose est plus fréquemment rencontrée durant la grossesse et la période de post-partum chez la femme en âge de procréer. La forme miliaire est beaucoup moins courante, mais plus létale, vu son caractère disséminé, affectant plusieurs organes simultanément. La présentation clinique de la tuberculose pulmonaire miliaire pendant la grossesse est souvent masquée, voire confondue, avec les symptômes constitutionnels de la grossesse. La confirmation au laboratoire est souvent négative, en raison de l'obtention difficile des prélèvements biologiques, avec pour conséquent des retards significatif de diagnostic et de traitement. Ce délai de temps peut être raccourci, grâce au recours à l'imagerie médicale dans l'investigation des symptômes constitutionnels non spécifiques de la maladie. Ce qui permettra d'orienter vers une étiologie, et d'identifier l'aspect lésionnel micronodulaire disséminé, quasi-pathognomonique de la tuberculose pulmonaire miliaire. Afin d'alerter les cliniciens devant des difficultés diagnostiques, avec pour but de leur donner des outils diagnostics, nous rapportons un cas de tuberculose pulmonaire miliaire en post-partum chez une patiente négative à l'infection due au virus d'immunodéficience humaine, gravement malade, et sans diagnostic clinique certain.

ABSTRACT

Most tuberculosis (TB) infections in women of reproductive age occur around pregnancy and the postpartum period. Miliary TB is a disseminated form of the disease which is rare during pregnancy and postpartum but potentially fatal. The clinical presentation of miliary pulmonary TB is not specific and body specimens may be difficult to obtain or give a negative finding, leading to delayed diagnosis and treatment. The decision to investigate patients' symptoms with imaging can be rewarding as the miliary pattern can be easily recognized. We report a case of postpartum miliary pulmonary TB in a client negative for human immunodeficiency virus infection that was diagnosed with chest computed tomography after prolonged illness and no certain clinical diagnosis.

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1. Introduction

Tuberculosis (TB) infections in women is most frequent between the ages of 15 to 49 years old, and occurs especially around pregnancy and the postpartum period [1,2]. Hormonal changes, human immunodeficiency virus (HIV) infection and reduced access to care have been reported to impact TB morbidity and mortality in women [3,4]. The symptoms of TB can be masked during pregnancy due to the suppression of the T-helper 1 pro-inflammatory response [2]. The reversal of this suppression after delivery may lead to the exacerbation of symptoms, hence a higher TB morbidity during the postpartum period [5,6].

Miliary tuberculosis is a disseminated form of the disease and is due to lymphohematogeneous spread from a focus containing *Mycobacterium tuberculosis*. Miliary TB is rare during pregnancy and the postpartum period and the clinical presentation is not specific, resulting to it being overlooked by unsuspecting clinicians [7–9]. The atypical clinical presentation of miliary TB is further confounded by the difficulties in obtaining body specimens for laboratory diagnosis. These samples can also produce genuinely negative findings especially if they are extrapulmonary, given that extrapulmonary TB is paucibacillary [10]. Chest x-ray and computed tomography (CT) are important diagnostic assets in miliary TB, but their use may not be considered by some clinicians during this period as a precautionary measure for the rational utilization of ionizing radiation. The diagnostic dilemma of miliary TB during pregnancy and postpartum often leads to significant delays in the diagnosis and treatment, with a high likelihood of fatality [10,11].

TB remains endemic in sub-Saharan Africa and this is partly due to HIV endemicity, though there has been a steady decline in TB incidence in Cameroon over the past two decades [12]. During the search of the literature no empirical study was retrieved on postpartum miliary TB in Cameroon. To improve awareness and draw the attention of clinicians to the diagnostic difficulties we hereby report a case of postpartum miliary TB in a chronically ill patient negative for HIV infection that was diagnosed with chest CT.

2. Case presentation

A 28-year-old woman G2P1001 was followed up for a twin pregnancy at the outpatient Antenatal Clinic of Regional Hospital Limbe. Booking visits were regular and clinical, laboratory and sonographic assessments were unremarkable during the first two trimesters. Prophylaxis for malaria and anemia were prescribed as recommended by national guidelines and the client admitted to taking all medications as prescribed. The third trimester was marked by an episode of illness at 32 weeks of gestation with fever, dry cough and dyspnea on effort followed by an exacerbation of the constitutional symptoms of fatigue and anorexia. The client was admitted to hospital and laboratory investigations revealed a hypochromic normocytic anemia and leucopenia. Erythrocyte sedimentation rate (ESR) was slightly raised and direct urine microscopy analysis was normal. Abdominal sonographic assessment revealed homogeneous hepatosplenomegaly. Both fetuses were normal. Antibiotics, antipyretics and hematinics were prescribed and administered. The fever subsided but the client was persistently tired and anorexic. She was counseled for an elective Caesarean section as from 37 weeks of gestation which was successfully performed and both live babies were delivered. The rest of the admission was uneventful and she was discharged from hospital and returned home with both babies.

She later returned to hospital three weeks after discharge and complained of intense fatigue, anorexia, intermittent abdominal pain and shortness of breath during routine activities. There was no fever, cough, or neurological deficit. She reported exclusively breastfeeding her babies. The pulse, respiratory rate and blood pressure were normal. The patient was emaciated. Laboratory findings revealed hypochromic microcytic anemia and leucopenia. ESR was raised and HIV, hepatitis B and C serological assays were negative. Liver transaminases were slightly raised and blood urea nitrogen was normal. A urine microscopy test was normal. Abdominal sonography revealed a homogeneous hepatosplenomegaly, a thin layer of hypoechoic pericardial and left pleural effusions. These findings prompted recommendation for further investigation with a chest CT scan by the radiologist. The chest CT scan was performed with a 16-slice CT scanner (HITACHI SUPRIA©) in one breath-hold from the thoracic inlet to the umbilicus. Data acquisition was volumetric with a pitch of 1.3 and a 1.25x16mm collimation, without intravenous iodinated contrast material. Post-processing image analysis techniques such as windowing and multiplanar reformatting were used. CT revealed tiny

micronodules disseminated randomly in both lungs with a typical miliary pattern (**Figure 1**).

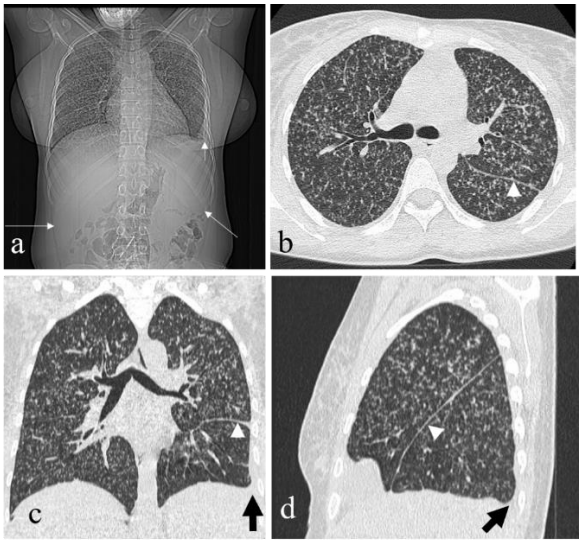

Figure 1. Chest CT (lung window). Scannogram (a) showing disseminated lung micronodules, left costophrenic angle blunting (short arrow) and an enlarged silhouette of the liver and spleen (long arrows). On reformatted axial (b), coronal (c) and sagittal (d) sections there are multiple lung micronodules disseminated in a random pattern. There is thickening of the left lung major fissure (white arrowheads) and blunting of the left lateral and posterior costophrenic angles (thick black arrows).

The thin layers of pericardial and left pleural effusions previously depicted with ultrasonography were confirmed (**Figure 2**). There were no other significant findings.

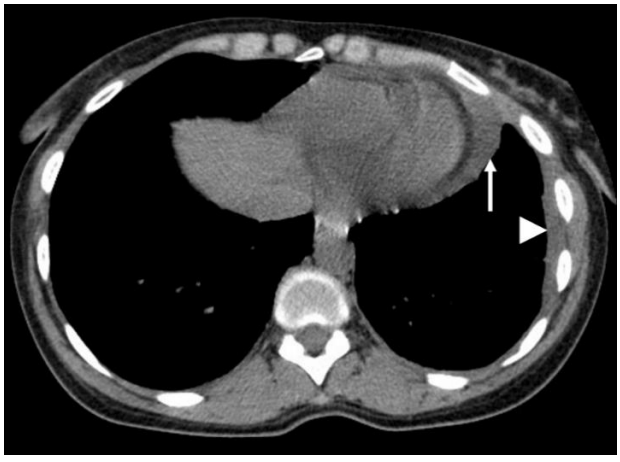

Figure 2: Axial unenhanced chest CT (mediastinum window). There is a thin layer of pericardial and left lateral pleural hypodense fluid (effusions)

A provisional diagnosis of pulmonary miliary TB was immediately advanced. Upon re-interview of the client there was no reported known previous exposure to anyone with TB or chronic cough. Sputum smear microscopy for acid-fast bacilli and molecular testing with GeneXpert were negative. She was nevertheless immediately placed on anti-TB treatment (Rifampicin, Isoniazid, Ethambutol and Pyrazinamide) following the national TB protocol for an expected duration of six to nine months after counselling by the clinical experts in charge of the TB program within the health facility. The patient was not admitted. Symptomatic treatment for anorexia was also prescribed and the client was counseled on the importance of proper nutrition for the treatment to be effective, given that she also reported exclusive breastfeeding of her twin babies. She was advised to continue breastfeeding during the anti-TB treatment and to consult with the hospital pediatrician with her babies for a comprehensive assessment.

A review of the client after three months of treatment showed significant clinical improvement with defervescence of symptoms and weight gain. She was encouraged to continue with the anti-TB treatment, feed well and report to the hospital should the need arise, and to breastfeed her child (upon review she revealed the recent sudden death of one of her babies briefly after arriving the hospital following a brief illness).

3. Discussion

The risk of TB out of pregnancy is higher during the postpartum period [13,14]. There has also been a reported increased risk of active TB during pregnancy and postpartum period in countries with high incidence of TB [15]. The case we have presented depicts a clinical diagnostic challenge of TB in pregnancy and the postpartum period. Not once was a diagnosis of TB suspected for this client given the non-specificity of the symptoms. It is obvious miliary TB was responsible for the illness during the third trimester of pregnancy, but went undiagnosed till the postpartum period. The decision to further investigate with chest CT scan was a reasoned choice from a hint finding following the innocuous ultrasound scan, and not because of constitutional symptoms. This however proved to be rewarding much to the relief of the physicians and the client.

Medical imaging significantly contributes to the diagnosis and management of miliary pulmonary TB [16,17]. Whilst chest radiography may only show disseminated tiny nodules later in the disease, chest CT due to its superior sensitivity typically reveals multiple small nodules of 1-3 mm in diameter disseminated

throughout both lungs in a random pattern [18,19]. The miliary pattern observed on chest radiographs/CT is however not specific to tuberculosis; other causes include histoplasmosis, mycoplasma, blastomycosis, sarcoidosis, tropical pulmonary eosinophilia, hypersensitivity pneumonitis, silicosis, and lymphangitic carcinomatosis, just to cite these [19]. However besides revealing the miliary pattern of lung involvement chest CT scan can reveal other associated anomalies, or provide an alternate diagnosis. In the case we have presented there was associated pericardial and pleural effusions, which can be of prognostic importance.

Besides the reluctance of treating physicians to use imaging, the diagnostic challenges in collecting appropriate samples which are sometimes negative for acid-fast bacilli, and limited access to care further compromise a timely diagnosis of miliary TB. To continually keep a hindsight of miliary TB it should be considered as a credible differential diagnosis in the wake of worsening constitutional symptoms despite treatment with routine antibiotics in a context where an infection is most likely.

4. Conclusion

The diagnosis of miliary tuberculosis during pregnancy and the postpartum period is challenging due to an atypical clinical presentation, difficulties in obtaining body specimens and often false negative findings. The role of medical imaging in unravelling clinical diagnostic uncertainties should be discussed with radiologists as this has proven to be useful many a time.

Conflict of interest

The authors declare no conflict of interest

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