Atypical cause of fever in advanced pregnancy

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ABSTRACT

Although miliary tuberculosis (TB) is uncommon in pregnancy, it is difficult to diagnose when present and is often associated with a maternal history of intravenous drug abuse, malignancy, alcoholism, or human immunodeficiency virus (HIV) infection. TB in pregnancy can present with non-pulmonary symptoms, making the diagnosis and treatment challenging. We report a case of military TB in a lady with advanced pregnancy who presented with fever and cough without any history of exposure to TB patient. There was no history of alcoholism, intravenous drug abuse, or any other risk factors. Sputum for acid-fast bacilli stains and HIV screening were negative. The patient was started on anti-TB treatment after blood investigations ruled out other causes of fever and chest radiograph was suggestive of miliary TB. Confirming the diagnosis of miliary TB is an arduous process requiring a high index of suspicion. During pregnancy, histopathologic examination of tissue biopsy and GeneXpert may facilitate making an early diagnosis of extrapulmonary TB.

KEY WORDS: Pregnancy; Military Tuberculosis; Infection

INTRODUCTION

Tuberculosis (TB) is still a global public health problem in spite of worldwide control efforts.[1] TB is now the leading infectious killer, affecting nearly 10.4 million people each year and killing 1.7 million individuals, the precise number of pregnant women who have TB is unknown.[2] Miliary TB is a fatal form of disseminated TB that results from a massive lymphohematogenous dissemination from a mycobacterium TB-laden focus.[1] TB and pregnancy are two different types of stresses experienced by women. Their simultaneous presence affects them both physically and mentally. It is best described as a double-edged sword, one blade being the effect of TB on pregnancy and the pattern of growth of the newborn, while the other is the effect of pregnancy on the progression of TB.[3] The presence of TB disease during pregnancy, delivery, and post-partum is known to result in unfavorable outcomes for both pregnant women and infants. These outcomes include a roughly two-fold increased risk of premature birth, low birth weight, intrauterine growth retardation, and a six-fold increase in perinatal death, especially in women who are coinfected with human immunodeficiency virus (HIV).[4]

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Clinical diagnosis of TB in pregnant women can be difficult due to nonspecific symptoms related to the physiological response to pregnancy.[5] For pregnant women in most countries with a high TB burden, the current standard practice of care for TB screening and diagnosis is the same as that used to detect disease in the general population. Recommended diagnostic tests may include smear microscopy, culture, and molecular DNA detection methods such as GeneXpert TBPCR.[5] Shielded chest radiography, which poses minimal risk to the fetus, is also recommended in women with a recent TB contact.[6]

Management of such cases in the context of the Revised National Tuberculosis Control Programme (RNTCP) and

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Table 1: Blood and urine investigations

Test	Result
Hemoglobin	5.8 g/dl
Total leukocyte count	7800/cumm
Neutrophils	78%
Lymphocytes	15%
Eosinophils	5%
Monocytes	2%
Basophils	0%
Platelets	1.71 lacs
Random blood sugar	96 mg/dl
Card test for malaria	Negative
Peripheral blood smear for malarial parasite	Negative
Serum bilirubin total	1.2 mg/dl (D-0.7, I-0.5)
Aspartate aminotransferase	42 IU/L
Alanine aminotransferase	36 IU/L
Alkaline phosphatase	624 IU/L
Gamma-glutamyltransferase	49 IU/L
Total protein	5.8 g/dl
Albumin	1.9 g/dl
Globulin	3.9 g/dl
Serum iron	39.1 μg/dL
Ferritin	631.59 ng/ml
Folate	14.69 ng/ml
Vitamin B12	More than 1500 mg/dl
C-reactive protein	12.97
Erythrocyte sedimentation rate	72 at the end of 1st h
Serum creatinine	0.59 mg/dl
Estimated glomerular filtration rate	129 m/min/1.73 m^2
Serum electrolytes	Normal
Urine – pus cells	10–15 per high power field
Urine culture	No growth
Sputum for acid-fast bacilli	Negative
Thyroid-stimulating hormone	1.09 micro IU/Ml

the adoption of the directly observed treatment-short course need a strategy. Pregnant women have a higher proportion of non-pulmonary TB and diagnosis is often delayed due to the non-specific nature of clinical symptoms, the overlap with complaints commonly reported during pregnancy, and the delay in utilizing investigative modalities such as radiology.[7] Therefore, when dealing with at-risk groups, a high index of suspicion needs to be maintained. Pregnancy has no effect on the course of TB, including sputum conversion, stabilization of the disease, and relapse nor does it slow or hasten the progress of latent infection to active disease.[8]

CASE REPORT

A 24-year-old pregnant lady presented at 27 weeks of gestation with irregular fever and dry cough for 20 days. The patient was on regular antenatal checkup from local gynecologist. She was apparently asymptomatic 1 month back. She had no significant past history of TB nor any history of exposure to any patient with TB in past or in her family. Her previous menstrual cycles were regular. She was second gravida with previous full-term normal delivery.

On examination, the patient was conscious, oriented, febrile, toxic look, and thin built. Her pulse rate was 160/min, regular, and her blood pressure was 100/60 mm Hg. She was pale, jugular venous pulse was not raised, no pedal edema, thyroid swelling, or lymphadenopathy. Her heart sounds were normal and chest was clear. On abdominal examination, uterus was 26 weeks gestation.

Ultrasonography of abdomen revealed hepatomegaly. Gynecology examination and pelvic ultrasound revealed single, live fetus, biparietal diameter – 26W+6D, femur length – 28W+4D, arm circumference – 27W+6D, effective fetal weight – 1.16 kg, and amniotic fluid index – 10 cm, placenta was anterior and upper. Blood and urine investigation reports are given in Table 1.

Chest X-ray with abdominal lead shield was suggestive of military TB [Figure 1].

The patient was treated with injection cefepime, artesunate, intravenous fluids, and two units packed red blood cells. After chest X-ray, patient was started on four-drug anti-TB treatment (ATT) with isoniazid (H) 300 mg optical density (OD), rifampicin (R) 450 mg OD, ethambutol (E) 800 mg OD, pyrazinamide (Z) 1200 mg OD, and Benadon 20 mg OD. As per EHO protocol, HRZE for 4 months advised. At discharge, the patient was afebrile and clinically stable on 8th day of hospitalization.

DISCUSSION

TB remains a global health problem. Over the past two decades, significant changes have occurred in its epidemiology with increased migration, rates of HIV infection, and incidence of disease in younger age groups. The clinical picture of TB in pregnancy is often nonspecific and difficult to diagnose; therefore, diagnostic delays are very common with important negative consequences on treatment outcomes that are further worsened by the increased risk of complications resulting from the impaired immunologic response related to pregnancy.[8] In the setting of incomplete treatment and advanced or extrapulmonary TB, the chances of perinatal complications such as preeclampsia, intrauterine growth retardation, antepartum hemorrhage, low birth weights, preterm delivery, and perinatal mortality rates for neonates are increased.[9] The diagnostic approach to evaluation of TB in pregnant and nonpregnant women is the same. This may include tuberculin skin testing (TST) with 0.1 mL intradermal injection of five tuberculin unit strength purified protein derivative, chest radiograph for TST-positive, or TST-negative

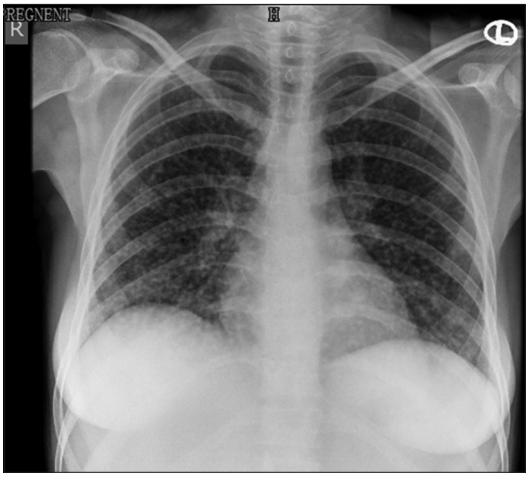

Figure 1: Chest X-ray

patients with recent contact with an active TB case, and acid-fast bacilli stain and culture of clinical material.[10] TST is considered safe in pregnancy and reactivity is not affected by pregnancy. Interferon-gamma releasing assays such as T-SPOT. TB assay and QuantiFERON®-TB Gold In-Tube are more specific than the TST because they tend to give fewer false-positive test results in patients with prior bacillus Calmette-Guerin (BCG) vaccination or during exposure to environmental mycobacteria.[11] Polymerase chain reaction testing of blood yields positive results in most cases of HIV-related disseminated TB. Mycobacterial blood culture is also found to be positive in 14–30% of cases with advanced HIV.[12]

TB and pregnancy are two different types of stresses. India accounts for 30% of the burden of all TB cases in the world. According to reports of WHO 2006 - 9.2 million incident cases and 1.7 million deaths with 80% in the age group of 15–54 years. Miliary TB accounts for 1.3% cases of TB with mortality rate around 20%. The diagnosis is often delayed. Weight gain and the height of uterus versus the period of gestation in tuberculous pregnant women are significantly less. Adverse pregnancy outcome is seen in 20% cases. If ATT is started early in pregnancy, the outcome is same as that in nonpregnant patients. Late diagnosis and care are associated with 4-fold increase in obstetric morbidity and 9-fold increase in pre-term labor.[13] It is associated with increased perinatal mortality (morbidity – 23%). TB lymphadenitis had no effect on pregnancy or perinatal outcome. Women with other-site extrapulmonary disease suffered more antenatal hospitalizations, babies with lower Apgar scores, low birth weight, and adverse neonatal outcomes.[14]

Raised diaphragm due to pregnancy helped collapse of pulmonary cavities situated mostly in the lower lung regions. There are chances of induced abortion, stress, and loss of protective antibodies in mother during lactation. Hematogenous spread of the bacilli through umbilical vein to fetal liver or there could be ingestion or aspiration of infected amniotic fluid. Poor fetal health can be due to late pre-natal diagnosis of disease, late institution of ATT, incomplete/irregular adherence to therapy, advanced lung lesions, poor maternal nutrition due to poverty, and ignorance.

The treatment regimens in pregnant and nonpregnant patient are same. Under RNTCP, breast-feeding of neonates is recommended regardless of the mother's TB status. Chemoprophylaxis with INH for 3 months or until the mother becomes non-infectious to the infants. BCG vaccination may be postponed or done with INH-resistant BCG vaccine.

CONCLUSION

Pregnant women have a higher proportion of non-pulmonary TB. It is one of the major causes of mortality and morbidity among pregnant women worldwide. Diagnosis of TB in pregnancy is frequently delayed due to nonspecific nature of symptoms and delays in utilizing investigative modalities such as radiology. Therefore, high index of suspicion needs to be maintained when dealing with at-risk group.

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