A case of tuberculosis in a pregnant woman and review of current literature

B C H Kwan MBBS FRACP, **Y Yu** MBBS and **H Goldberg** MBBS FRACP

Department of Respiratory Medicine, Prince of Wales Hospital, Randwick, NSW, Australia

Summary: Tuberculosis (TB) in pregnancy can present with non-pulmonary symptoms, making diagnosis and treatment challenging. We present a case of TB in a pregnant woman and review current management recommendations.

Keywords: pregnancy, tuberculosis, treatment

INTRODUCTION

Pregnant women have a higher proportion of non-pulmonary tuberculosis (TB) and diagnosis is often delayed because of 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.¹ 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 relapse² nor does it slow or hasten the progress of latent infection to active disease.³ We report herewith a case of TB in a pregnant woman with delayed presentation and non-specific symptoms.

CASE REPORT

Mrs HK, a 29-year-old woman presented at 31 weeks gestation with signs of premature labour. Upon presentation, she also reported 3–4 weeks history of occasional visual disturbances including zigzag lines and flashes. She had been assessed by an ophthalmologist who suspected an infective cause. Furthermore she also developed cough, weight loss, fever, night sweats and one episode of haemoptysis during this period.

She was previously well and denied taking regular medications. She reported allergy to penicillin and sweet potato. Mrs HK moved to Australia from Vietnam at the age of three. Her past travel history included Bali, Vietnam and Thailand. She denied any contact with TB and had not previously received bacillus Calmette-Guérin (BCG) vaccination. She was working in a financial institution as a clerk.

On examination, she was tachypnoeic and hypoxic. She was in labour after premature membrane rupture. Auscultation of her chest revealed diffuse fine crepitations throughout both lung fields. Her chest X-ray and computed tomography (Figure 1) showed a diffuse micronodular infiltrative pattern

with calcified nodules at both lung apices, suggestive of an acute infective cause with likely old granulomatous lung disease. A diagnosis of reactivated miliary TB was suspected. Blood and sputum culture was collected for analysis.

She had a normal vaginal delivery with an epidural anaesthetic, delivering a healthy baby girl, IK. Further cultures were taken from the placenta and cerebrospinal fluid. Antibiotic treatment was commenced postpartum with ceftriazone and azithromycin, with further addition of HREZ anti-TB therapy (isoniazid, rifampicin, ethambutol and pyrazinamide, respectively) and pyridoxine after a review by the respiratory team. Mrs HK developed respiratory distress on the next day and intravenous hydrocortisone was given, with subsequent change to oral corticosteroid with reducing dose over two weeks.

During this period, blood and sputum smear samples confirmed the presence of acid fast bacilli (AFBs). *Mycobacterium tuberculosis* (M.tb) polymerase chain reaction was also positive. Blood, sputum and placental cultures eventually confirmed the growth of M.tb, which was fully sensitive to HREZ. Repeat sputum smears and cultures collected two weeks after commencement of treatment were negative for AFBs. An HIV test was negative. Magnetic resonance imaging of her brain revealed a superior right cerebral subcortical tuberculoma measuring 5 mm and multiple other tiny miliary subcortical TB foci.

Mrs HK's clinical course was complicated by fever after cessation of corticosteroids. A septic screen was carried out but no infective foci were found. Possible paradoxical reaction or drug fever was suspected and prednisolone was recommenced at 7.5 mg daily with a slow weaning over two months. Mrs HK's TB treatment totalled 23 months, including six months of HREZ and 17 months of HR (isoniazid, rifampicin) therapy. At completion of her therapy, Mrs HK had no further reports of visual, skin, respiratory or joint abnormalities.

Baby IK spent four weeks in humidicrib but was otherwise healthy. Gastric aspirate was negative on the culture of M.tb. Baby IK was commenced on isoniazid, rifampicin and pyrazinamide with pyridoxine. She received a total of six months treatment and remained well throughout and subsequently.

Correspondence to: Benjamin Kwan
Email: ben.kwan@sesiahs.health.nsw.gov.au

Figure 1 Computed tomography of chest demonstrating widespread fine nodularity throughout both lung fields with calcified lesions within the right apex – consistent with military tuberculosis

TB IN PREGNANCY

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. A recent hospital-based TB case series from the UK demonstrated differences in pregnant and non-pregnant populations. Women in the former group tend to be of ethnic minority background, present with non-specific symptoms, often suffering a delay in diagnosis, and present with extrapulmonary disease as commonly as pulmonary disease.⁴ Pregnancy does not adversely affect the course of TB if appropriate therapy is instituted.² In the setting of incomplete treatment and advanced or extrapulmonary TB, the chances of perinatal complications such as preeclampsia, intrauterine growth retardation, antepartum haemorrhage, low birth weights, preterm delivery and perinatal mortality rates for neonates are increased.⁵

The diagnostic approach to evaluation of TB in pregnant and non-pregnant 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 patients with recent contact with an active TB case, and acid-fast bacilli stain and culture of clinical material.⁶ TST is considered safe in pregnancy and reactivity is not affected by pregnancy.⁷ Recent development of an interferon- γ -based whole-blood assay using M.tb antigens (QuantiFERON; Cellestis, Carnegie, Australia) for detecting latent TB infection lacks validation data in specific populations including pregnancy.⁸

TB TREATMENT

TB treatment can be categorized into first line or second line. The former include isoniazid, rifampin, ethambutol, pyrazinamide and streptomycin. Of these, the first four drugs are considered safe in pregnancy. However due to rifampin's induction of cytochrome P450 microsomal hepatic enzyme, it may render low-dose oral contraceptives ineffective and can decrease both maternal and infant vitamin K levels, so supplementation is recommended. The fifth medication, streptomycin, has a risk of auditory and vestibular damage and should not be used in pregnancy.⁹ Second-line treatment has had less extensive use in pregnant patients. The risks of treatment-related complications are less commonly reported than TB-associated complications. Pyridoxine (vitamin B₆) at 10–25 mg should be added to any isoniazid-containing regimen to prevent neurotoxicity.

Treatment of those TB patients with HIV co-infection or multidrug-resistant strains is more complicated with increased frequency of treatment-related side-effects. Overall direction of care should be referred to clinicians with expertise in the field.¹⁰

Treatment for active TB should be initiated as soon as possible. If pregnancy occurs, treatment should not be suspended. There is also no basis upon which to recommend therapeutic abortion given the overall safety of first-line TB medication.

LATENT TB INFECTION IN PREGNANCY

Over 90% of new TB cases arise from patients with latent tuberculosis infection (LTBI)^{11,12} but treatment of LTBI in pregnancy remains controversial.

Treatment with isoniazid in patients with LTBI has been reported to be safe and effective with no demonstrated teratogenic potential. The most common treatment-related complication is elevated liver enzymes with the risk of clinically significant isoniazid-induced hepatitis occurring in 0.15–2% of individuals treated, and a 0.001% risk of fatal hepatitis.¹³ Despite its apparent safety and effectiveness, a retrospective study of Hispanic women published by Franks *et al.*¹⁴ in 1989 reports increased hepatotoxicity risks from isoniazid in the setting of pregnancy. This association may be related to age. Current recommendation is not to delay treatment of LTBI in pregnancy, especially in those co-infected with HIV or who have other risk factors (e.g. immunosuppressed, HIV, diabetes, close contact with infected person, documented recent conversion) for progression.¹⁵ However, for those with LTBI but no risk factors, experts differ in their recommendations as to whether preventive treatment should begin antepartum or postpartum. In this setting, the authors would favour a postpartum approach.

CONGENITAL TB AND NEONATAL

Congenital TB is rare and often fatal. It is usually spread from the mother to the fetus haematogenously through the placenta and umbilical cord. Spread may also occur by the fetus ingesting infected amniotic fluid.¹⁶ Beitzke in 1935 detailed criteria for congenital TB as: (1) firm diagnosis of TB in newborn, (2) primary complex in newborn's liver, (3) not related to respiratory transmission by an infected mother or family member or (4) if no primary complex is identified in liver, TB lesions must be documented in the first few days of life to exclude extrauterine infection.¹⁷

Neonatal TB is far more common, and occurs when a newborn is infected after exposure to infected people. Most cases of neonatal are related to respiratory transmission by an infected mother or family member. In neonates born to mothers with active TB, isoniazid prophylaxis should be given (5 mg/kg) prior to clinical and TST reassessment between six weeks and three months. If the infant is TST positive and has signs of active disease, full anti-TB treatment should be given. If signs of active TB are absent, treatment for LTBI should be continued. If TST is negative, BCG vaccination should be discussed and chemoprophylaxis stopped.

BREASTFEEDING

Breastfeeding is not contraindicated while on TB treatment. Although anti-TB medications are found in breast milk, serum levels of isoniazid in breastfed infants are less than 20% of usual therapeutic level and less than 11% for other anti-TB medications.¹⁸ Pyridoxine should be given to both the infant and mother should an isoniazid-containing regimen be used. Therefore, babies who are being breastfed by mothers who are taking isoniazid (and pyridoxine) should be given pyridoxine 5 mg on the days that the mother receives her isoniazid dose.¹³

In women with active TB who are potentially infectious, direct mother–infant contact should be avoided. Women may express their milk to be fed to the infant. Breast milk does not contain tubercle bacilli, except in women with active tuberculous breast lesions. In such cases, the recommendation is to express the breast milk and discard it until the lesion is fully healed.¹⁹

CONCLUSION

Tuberculosis in pregnancy can present with non-pulmonary symptoms, hence making diagnosis and treatment challenging. It is then important for clinicians to remain vigilant when managing pregnant women from at-risk groups in the hope of minimizing harm to both the mother and the baby. To conclude, for active tuberculosis, treatment with first-line drugs is generally safe and improves maternal and neonatal outcome.

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