Abstract
This report describes the case of a pregnant woman with extrapulmonary tuberculosis which was not diagnosed during routine antenatal care despite a four-month history of intermittent fever, cough and weight loss. In the third trimester her condition deteriorated with progressive hepatic impairment, splenomegaly and ascites. Tuberculosis was diagnosed in the referral hospital. She was delivered by emergency Caesarean section of a low birth weight infant at 34 weeks’ gestation. Despite intensive care the mother died. The infant survived. This case highlights the importance of early diagnosis and the prevention of congenital tuberculosis.

CASE REPORT

Tuberculosis in pregnancy: the need to improve the rate of diagnosis

Introduction
Tuberculosis remains the leading infectious cause of mortality and morbidity worldwide. Although the lung remains the commonest site of infection, extrapulmonary disease is becoming more prevalent. In Saudi Arabia the rate of extrapulmonary tuberculosis increased to 4.7 cases per 100,000 population in 1974-6. Abdominal and gastrointestinal cases accounted for 16% of all extrapulmonary tuberculosis. The clinical presentations of such cases were often non-specific, leading to delay in diagnosis resulting in increasing morbidity and mortality. Although specific statistics on tuberculosis in pregnancy are not reported, the increase in the rate of tuberculosis among the young implies that tuberculosis in pregnancy may be a more prevalent problem. Here we report the case of a pregnant woman with peritoneal and abdominal tuberculosis which resulted in preterm delivery of a low birth weight infant. We highlight the importance of early diagnosis and the prevention of congenital tuberculosis.

Case report
A female preterm infant was born to a 24-year-old Saudi mother, gravida 2 para 1, by emergency Caesarean section at 34 weeks’ gestation. The Apgar score was 6, 8 and 9 at 1, 5 and 10 minutes respectively. The birth weight was 1380 gm. The infant was admitted to the neonatal intensive care unit (NICU) with mild respiratory distress. Other systemic examination revealed nothing remarkable. She required only two days of nasal CPAP with FiO2 0.35. She received a five-day course of antibiotic (ampicillin and gentamicin) for suspected culture-negative neonatal sepsis.

Maternal history
Early in her pregnancy the mother presented with a four-month history of intermittent fever, cough and weight loss. She received multiple courses of antibiotics from different medical local centres. However, her general condition deteriorated with progressive hepatic impairment, hepatosplenomegaly and ascites, and she was then referred to King Khalid University Hospital. On admission this pregnant lady looked severely ill, pale and icteric. The size of the uterus was of 32 weeks’ gestation, with massive ascites and huge hepatosplenomegaly. The respiratory and cardiovascular systems were normal and no lymphadenopathy was detected. Her initial investigation showed anaemia, elevated liver enzymes and an ESR of 67 mm/hour.

Emergency Caesarean section was performed for suspected pregnancy-induced hepatic failure. Laparotomy revealed an unhealthy looking omentum...
and peritoneum with multiple areas of necrosis. Biopsies from the omentum, liver and ascitic fluid were taken and sent for analysis and culture. The result of the omentum biopsy was positive for acid-fast bacilli (AFB) with granulomatous changes (Figures 1 and 2). Unfortunately the placenta was discarded without histopathological study. The mother subsequently died from intestinal perforation and miliary tuberculosis, in spite of maximum intensive care and antituberculosis chemotherapy.

Evaluation of the patient’s family members and hospital contacts for possible contagious pulmonary tuberculosis was negative. The infant continued to be asymptomatic with negative results for AFB from nasopharyngeal and gastric aspirates. Purified protein-derived (PPD) skin tests at 3 and 6 months of age were negative. Our patient was started on isoniazide (INH) chemoprophylaxis for 9 months, after which an INH-resistant BCG vaccine was given.

The WHO’s Expanded Programme on Immunization recommends that BCG vaccine be given as a single dose as soon as possible after birth in all populations at high risk. It is one of the most widely used vaccines in Saudi Arabia and is currently given at or soon after birth. Neonates born to mothers with infectious TB should be given chemoprophylaxis with INH for 3 months or until the mother becomes non-infectious. BCG vaccination may be postponed or given with INH-resistant BCG vaccine.

**Discussion**

Tuberculosis remains the leading infectious disease for mortalities throughout the world. The World Health Organization (WHO) estimated that during the 1990s 90 million individuals developed tuberculosis and 30 million people died from the disease worldwide. Active pulmonary tuberculosis during pregnancy has been associated with adverse pregnancy outcome, including intrauterine growth retardation (IUGR) and toxaemia. Extrapulmonary tuberculosis is also fairly common and has been observed in 20% of cases. Lymphadenitis is the most common form followed by intestinal, spinal, endometrial and meningeal tuberculosis, which had an increased rate of antenatal hospitalization, low birth weight and low Apgar scores. The causes of frequent hospitalization were delays in diagnosis and initiation of chemotherapy, in addition to a lack of any localizing symptoms or signs.

The diagnosis of tuberculosis requires a high level of clinical suspicion. To grow the causative organisms, a collection of surgical specimens should be sent for special stains and inoculation in special culture media. These measures may not be taken or be available in many health care facilities. Subsequently, a diagnosis of extrapulmonary tuberculosis may be delayed compared with the rate of diagnosis of pulmonary tuberculosis. As demonstrated in our patient, peritoneal tuberculosis was diagnosed only after laparotomy and tissue biopsy, which showed chronic granulomatous inflammation with caseous necrosis (Figure 2), and positive acid-fast staining (Figure 3). We suggest that in all pregnant women suspected of having tuberculosis, staff should go through the early prenatal history emphasizing previous positive tuberculin skin tests, previous treatment for tuberculosis and known exposure to adult tuberculosis. High-risk
groups (see Table) are candidates for tuberculin testing. Screening for HIV antibody is not performed during antenatal visits, but in this case HIV antibody testing in the mother after delivery and in the infant was negative.

Some experts believe that all pregnant women should receive a tuberculin skin test. The effect of pregnancy on tuberculin hypersensitivity as measured by skin test is controversial. Some studies have shown a decrease in in vitro lymphocyte reactivity to purified protein derivative during pregnancy. However, in vivo studies have demonstrated no effect of pregnancy on cutaneous delayed hypersensitivity to tuberculin.

The indications for treatment of active tuberculosis in a pregnant woman are the same as for a non-pregnant woman. Treatment should be initiated without delay. Review of published data reveals that INH is safe during pregnancy. Although it crosses the placental barrier, it is not teratogenic even when administered in the first trimester. In one study, the rate of congenital malformations in infants who received rifampicin was 3.35% and included limb reduction, CNS lesions and haemorrhagic complications. However, the incidence falls within the safety limits and rifampicin is generally considered to be safe. Ethambutol is the next commonly-used drug in pregnancy with an incidence of malformations reported at 2%. Although it was feared that ethambutol might interfere with ophthalmological development, this was not observed in doses of 15-25 mg/kg body weight/day. Pyrazinamide, the bactericidal drug used in most first-line regimens, does not have sufficient studies to ensure its safety during pregnancy.

Management of a neonate whose mother has active tuberculosis

If the mother has clinical and radiographical evidence of active tuberculosis, the local health department should be informed immediately about the mother so that a contact investigation can be performed and neonatal prevention can be planned. The neonate should be evaluated for congenital tuberculosis through a physical examination and high-quality postero-anterior and lateral chest radiography. The mother and infant should be separated until the infant receives chemotherapy or the mother is judged to be non-contagious. Prophylactic isoniazid (10 mg/kg/day) for newborn infants born to mothers with tuberculosis has been so efficacious that separation of the infant from the mother is no longer considered mandatory once therapy is started.

Chemoprophylaxis should be continued at least until the mother has been shown to be culture-negative for 3 months. At that time, the child has a Mantoux tuberculin skin test. If it is positive INH prophylaxis should be continued for a total of 9 months, after ruling out active tuberculosis by the appropriate investigations.

If the follow-up skin test is negative and the mother or contact has good adherence and response to treatment, INH may be discontinued in the infant. The infant needs close follow-up, and it is prudent to repeat the tuberculin skin test after 6-12 months.

The Centers for Disease Control and Prevention recommend that the infant should receive isomiazide-resistant BCG (bacillus Calmette-Guérin) vaccination. Vaccination with BCG appears to decrease the risk of tuberculosis in exposed infants.

Conclusion

It is important to make an early diagnosis of tuberculosis infection and disease in a pregnant woman. Tuberculosis in pregnancy is as common as in the non-pregnant women. Better results are obtained in women known to have tuberculosis before the onset of pregnancy and who have been treated, compared with untreated patients with active tuberculosis. The poorest results have been shown to occur in patients in whom tuberculosis is first discovered in the puerperium, since it has been unsuspected and untreated during pregnancy and the disease is generally well-advanced. If tuberculosis is diagnosed and treated appropriately, the prognosis for both mother and child is excellent.

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References