Diagnosing tuberculosis in pregnancy: a case report

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SUMMARY

A case of miliary tuberculosis complicated by deciduitis and sub-chorionitis in a pregnant woman manifesting also influenza A/H1N1v infection and urinary tract infection is reported. Diagnosis of tuberculosis was obtained before delivery by examining amniotic fluid for *Mycobacterium tuberculosis*. Even though maternal symptoms did not suggest TB, diagnosis was early enough to start effective treatment in both the mother and the neonate and prevent in-hospital *M.tuberculosis* diffusion. A high index of suspicion by health professionals is required to detect and manage tuberculosis in pregnancy and newborns in both the developed and developing word.

KEY WORDS: Perinatal tuberculosis, Pregnancy, Prematurity

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CASE REPORT

Most tuberculosis (TB) cases in pregnant women and neonates are reported in non-industrialized countries were the majority occur in HIV co-infected women, but a growing number are being reported in Western countries (Adhikari *et al*., 1997; Pillay *et al*., 2004; Pillay, 2000; Whittaker *et al.*, 2008). Multi-drug resistant tuberculosis is also a rising concern (Whittaker *et al*., 2008; Khan *et al*., 2007).
Conditions at increased risk of congenital TB include: miliary TB, genital TB, untreated TB or positive sputum smears in the mother and HIV co-infection.

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The diagnosis of perinatal TB is difficult, symptoms may be non specific or mimic other conditions and many cases may be asymptomatic with disease manifesting after delivery both in mother and newborn (Adhikari *et al*., 1997; Pillay *et al*., 2004; Pillay, 2000; Whittaker *et al*., 2008; Khan *et al*., 2007; Chang *et al*., 2005; Manoga *et al*., 2008; Saitoh *et al*., 2001; Cantwell *et al*., 1994).
We describe a case of tuberculosis in a 24-year-old woman and her preterm neonate.
A 24-year-old African native woman arrived in Italy one week before hospitalization. She was in her 23rd week of pregnancy and presented to a local emergency room complaining of fever, low back pain, suprapubic heaviness and headache over the previous five days. Two days before she also had frequency, urgency, dysuria and macroscopic hematuria. Thus, a urinary infection (UTI) was diagnosed and an oral cephalosporin was prescribed. Four days later the fever still persisted and vaginal bleeding was also present. On admission to the local hospital symptoms associated with UTI had ceased while a mild non productive cough manifested. Physical examination

was normal except for minimal vaginal bleeding. Lab tests results included: Hb 9.4 g/dl, RBC 3.070X10^3/mmc, MCV 82.9 fl, WBC 13180/mmc with 84% neutrophyls, ESR 120 mm 1 h, CRP 10.5 mg/dl, LT48/IU/l, AST 77 IU/l, LDH 361 IU/l, pyuria and positive Rt-PCR for influenza A/H1N1v virus on naso-faringeal secretions. Right lower lobe infiltrate with pleural effusion were reported on chest radiograph. O_2 saturation was normal. Ceftriaxon, azitromycin, oseltamivir were prescribed and two mg of betamethasone were also administered before transfer to our hospital's Infectious Diseases Department (IDD). Temperature was 39.4°C. She had uterine contractions which increased in intensity and frequency despite tocolysis with atosiban. Vaginal blood loss worsened. Ceftriaxon was substituted for piperacillin/tazobactam and teicoplanin. HIV, syphilis, hepatitis, toxoplasmosis, leishmaniasis, and *Herpes 2* tests were negative. IgG for *Cytomegalovirus*, *Herpes1* and Rubella were positive while IgM negative. Blood, urine resulted negative for bacteria as well as cervical, urethral and vaginal secretions. Testing for malaria was negative. The patient's condition deteriorated. Hb dropped to 6.8 g/dl. Four days following admission to the IDD the amniotic liquid was obtained for microbiologic studies and it was found positive for acid-fast bacilli (AFB) and *M.tuberculosis* complex was identified by Probetec ET Mycobcaterium Tuberculosis Complex Direct Detection (DTB test, Becton Dickinson, USA). Mantoux and γ-interferon tests (Quantiferon-TB Gold Cellestis, Ausralia) resulted positive. Anti-TB therapy (isoniazid, rifampin and ethambutol) was started and labour induced. Multi-susceptible *M.tuberculosis* grew from the amniotic fluid while blood, respiratory and urine cultures were negative. Sputum and urine cultures were obtained a few days after treatment was started.

The day after delivery the mother was afebrile. Placenta histopathology showed deciduitis, subchorionitis and AFB (Figure 1). Two days after delivery pyrazinamide was added to the anti-TB therapy. A chest CT scan two weeks after delivery disclosed bilateral diffused nodular lesions and small areas of subpleural consolidation with pleural effusion on the right lung (Figure 2).

It was then discovered that the patient had been in contact with a case of pulmonary TB seven months before and she had never been tested before arriving in Italy. The patient is still on treatment and is responding well.

The neonate was born on the 23rd week and 3 days, weighing 651 gr with an Apgar score 4 at 1' and 7 at 5'. She was resuscitated, intubated and put under airborne precaution (Pillay *et al.*, 2004). There was no evidence of hepato-splenomegaly, enlarged lymph nodes or skin rash. Blood count, ALT, AST and ALP levels were normal and GGT was 75 IU/l (VN 49 IU/l). Chest X-ray suggested

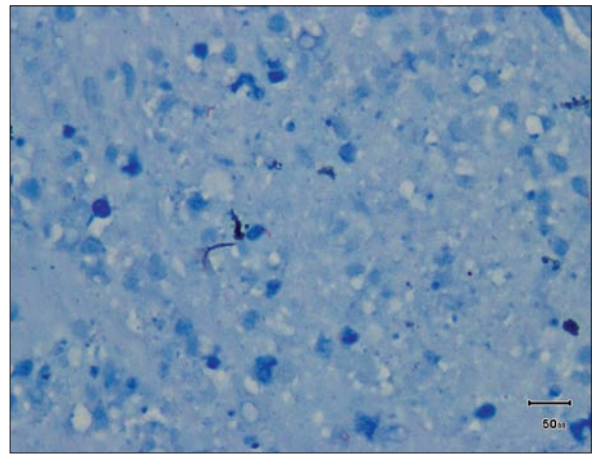

FIGURE 1 - *Histopathology section of the placenta, Ziehl-Neelsen stain: AFB (arrows).*

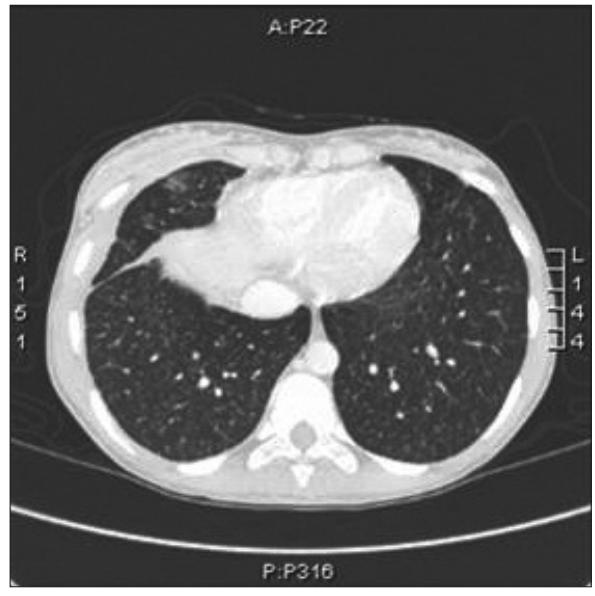

FIGURE 2 - *Diffuse nodular bilateral infiltrate, on the right areas of subpleural consolidation of small size with pleural effusion.*

respiratory distress (RDS). Gastric aspirate resulted repeatedly negative for AFB while non-bronchoscopic broncho-alveolar lavage at days 3 and 9 after birth showed AFB. MTD was positive for *M.tuberculosis* complex and multi-susceptible *M.tuberculosis* was isolated from both samples. Four subsequent respiratory secretions samples were negative.

Isoniazid and rifampin I.V. were started soon after birth. Pyrazinamide was added after four weeks when total enteral feeding was possible (Whittaker *et al*., 2008; Chang *et al*., 2005). During hospitalization the neonate had several complications: 3rd degree bilateral intraventricular hemorrhage, bacterial pneumonia, *Candida albicans* sepsis with *Candida* central line (CVC) infection, premature retinopathy (ROP) complicated with retinal detachment despite laser therapy and vitrectomy, chronic lung disease (CLD), cholestatic hepatitis with jaundice (total bilirubin level 20 mg/dl with direct bilirubin 15.5 mg/dl). Two months after birth ventilator support was shifted to nasal O_2 and two months later the neonate was able to be fed by mouth and was discharged with a weight of 2665 gr on oral therapy. At the seventh month of anti-TB treatment, pyrazinamide was stopped. The neonate is still on isoniazid and rifampin.

CONCLUSIONS

This was a case of acute miliary tuberculosis complicated by deciduitis, sub-chorionitis causing preterm delivery and neonatal tuberculosis (Cantwell *et al*., 1994). The patient was a pregnant African native woman arriving in Italy a few days before being admitted who also manifested urinary tract infection symptoms and A/H1N1v influenza.

Progressive *M.tuberculosis* infection and miliary TB can occur soon after primary infection in untreated children and young adults. Miliary TB can occur also as a late event in untreated patients, pregnant woman and patients with underlying diseases. Pleural effusion, peritonitis or meningitis can also be observed in as many as two thirds of these cases (Fitzgerald *et al*., 2005).

In our patient several factors such as pregnancy, young age and recent immigration concurred with acute miliary TB soon after primary *M.tuberculosis* infection and pleural effusion. Hematogenous dissemination also led to placenta and fetal infections (Cantwell *et al*., 1994). It is highly probable that the patient acquired TB in Africa were she had been for the last 24 years and moreover she had been in contact with a case of bacillary TB about seven months earlier but this information was supplied to us only after she was diagnosed with tuberculosis. In the end, concomitant A/H1N1v influenza and urinary tract infection were not particularly relevant to this morbidity. The clinical picture worsened despite oseltamivir therapy with a follow up Rt-PCR negative in naso-pharyngeal secretions and amniotic fluid after five days of treatment and chest radiology findings were due to TB rather then viral pneumonia (Hewagama *et al.,* 2010). Also, urine culture was rapidly negative after antibiotics were administered.

Even though maternal symptoms did not suggest TB, diagnosis was early enough to start effective treatment in both the mother and the neonate and prevent in-hospital *M.tuberculosis* diffusion (Saitoh *et al*., 2001).

The very premature neonate weighed 651g and had several premature birth associated complications plus tuberculosis (Cantwell *et al*., 1994). Anti-TB therapy was well tolerated and effective. Even in non-endemic countries the suspicion of TB must be elevated in every patient including pregnancy.

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