Congenital tuberculosis in a premature infant

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Summary

Congenital tuberculosis was first suspected in a premature infant with patent ductus arteriosus (PDA), progressive respiratory distress and septic shock, when an enlarged mediastinal lymph node was noted intraoperatively at the time of PDA ligation. Culture revealed *Mycobacterium tuberculosis*. The asymptomatic mother was subsequently diagnosed with urogenital tuberculosis.

Key words: tuberculosis; congenital; patent ductus arteriosus; respiratory distress

Case report

A 36-year-old gravida 2 para 2 mother with pre-eclampsia and progressive hypertension was delivered of an 800-gramme girl by C-section at 28½ weeks’ gestation. The first pregnancy had been marked by secondary C-section in the 39th week of gestation due to pre-eclampsia. During the current pregnancy ultrasound performed two days before delivery showed intrauterine growth retardation with otherwise normal intrauterine morphology. The Apgar scores were 5/9/9 at 1, 5 and 10 minutes respectively. Mild respiratory distress was treated by continuous positive airway pressure for one day. Gentamicin and amoxicillin were administered intravenously for 5 days for suspected sepsis due to leucocytopenia. At 2 weeks of age a cardiac murmur and bounding pulses were noted; cardiac echo confirmed the presence of PDA, which was treated with fluid restriction. At 4 weeks of age chronic lung disease was evident from the persistence of increased oxygen requirement and typical findings on chest x-ray.

At 9 weeks of age increasing respiratory dis-

Figure 1
Chest x-ray showing enlarged heart, basal air-trapping and bilateral infiltrates.
tress and hepatomegaly developed. Chest x-ray showed prominent bilateral lung infiltrates, hyperinflation of the basilar segments and an enlarged cardiac silhouette (fig. 1). Late onset sepsis, worsening chronic lung disease and cardiac insufficiency due to the PDA were considered in the differential diagnosis. Intravenous antibiotic therapy was initiated with amoxicillin and gentamicin, then changed to vancomycin and imipenem-cilastin after three days due to lack of clinical improvement. In addition, therapy with immunoglobulin (0.4 g/kg) and hydrochlorothiazide/spironolactone was instituted. However, the respiratory insufficiency progressed. The patient was intubated at 9½ weeks of age and transferred to another hospital where PDA ligature could be performed. The patient was considered to have pneumonia, septic shock and heart failure due to PDA and sepsis. In spite of continued treatment with antibiotics (vancomycin and meropenem), C-reactive protein increased from 42 to 99 mg/l in 24 hours and pancytopenia as well as disseminated intravascular coagulopathy developed. Additional management consisted of inotropic support and transfusions with packed red blood cells, platelets and fresh frozen plasma. The patient’s condition nevertheless continued to deteriorate.

At 10 weeks of age PDA ligature was performed. Unexpectedly, an enlarged mediastinal lymph node was noted intraoperatively and biopsied, revealing numerous acid-fast bacilli on direct stain with auramine/fluorescence. Subsequent culture of tracheal secretions yielded *Mycobacterium tuberculosis* sensitive to the major tuberculostatic drugs. The Mantoux tuberculin skin test was negative. Examination of cerebrospinal fluid was negative for acid-fast bacilli on direct stain as well as *Mycobacterium tuberculosis* in culture. Therapy with isoniazid, rifampicin, pyrazinamide and intravenous amikacin was instituted.

The immediate postoperative course was characterised by lung oedema, ascites, massive he-
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patosplenomegaly, left-sided perforated otitis media (direct stain positive for acid-fast bacilli, culture negative for *Mycobacterium tuberculosis*), marked cervical lymphadenopathy and transient peripheral facial palsy. The patient's condition gradually improved over the following 6 months, although chronic lung disease persisted. After the initial two months of treatment amikacin was stopped.

At 12 months of age left-sided cervical lymphadenopathy recurred. Computerised tomography of the lung revealed scattered infiltrates, consolidation and calcifications (fig. 2). High resolution computerised tomography of the temporal bone showed complete opacification of the mastoid air cells with destruction of trabecular and cortical bone (fig. 3). The findings were indicative of persistent tuberculosis otomastoiditis with Bezold's abscess. Cortical mastoidectomy and neck dissection were performed at age 14 months. Direct stain of material obtained from the Bezold's abscess revealed acid-fast bacilli. Direct stain, polymerase chain reaction (PCR) and culture of mastoid tissue were negative for tuberculosis bacteria. Postoperatively, left-sided peripheral facial palsy was noted and interpreted as a complication of surgery. At age 15 months inflammation of the left parotid gland developed and required surgical drainage. PCR revealed *M. tuberculosis complex*. Culture and direct stain were negative for tuberculosis bacteria.

Within the first week after mastoidectomy/neck dissection the pulmonary condition improved dramatically. Over the following four weeks the patient was weaned from additional oxygen. Feeding and weight gain subsequently improved. With the exception of residual unilateral facial palsy and complete left-sided hearing deficit, neurological development was normal at 18 months of age. Tuberculostatic treatment with isoniazid, rifampicin and pyrazinamide was continued for a total of 18 months. At the end of therapy chest x-ray demonstrated residual scattered calcifications (fig. 4).

Family history

Evaluation of the patient’s family members and hospital contacts for possible contagious pulmonary tuberculosis was negative. The patient's mother was of Philippine origin but had lived with her Swiss husband in Switzerland for the past 10 years. She had been in good health and was asymptomatic. At C-section the peritoneum, uterus, and placenta were macroscopically normal. Histology of the placenta showed infarcts, increased intravillous fibrin and increased trophoblastic buds considered consistent with pre-eclampsia. The mother's Mantoux test, chest x-ray and human immunodeficiency virus test, performed after tuberculosis was diagnosed in the child, were negative. Laparoscopy performed 4 months postpartum revealed fibrinous, purulent exudates and extensive small mesenteric granulomas. Direct stains of material obtained from the endometrium via curet-
tage revealed granulomas and acid-fast bacilli. Culture of material obtained from the mesenteric granulomas and endometrium, as well as from a urine specimen, yielded *Mycobacterium tuberculosis* sensitive to standard tuberculostatic medication. Therapy with isoniazid, rifampicin and pyrazinamide was instituted. Two weeks after laparoscopy the mother was readmitted to hospital with subacute abdomen and fever. She improved under therapy with intravenous antibiotics for one week and continued tuberculostatic medication. Complete recovery occurred under continued treatment with isoniazid, rifampicin and pyrazinamide for a total of two months, followed by isoniazid and rifampicin for seven months.

Discussion

Active pulmonary tuberculosis during pregnancy has been associated with adverse pregnancy outcome, including toxaemia [1]. Although extrapulmonary tuberculosis is apparently less deleterious, it has been associated with an increased rate of antenatal hospitalisation, low birth weight and low Apgar scores. One team reported one case of severe pregnancy-induced hypertension in a patient with tuberculous lymphadenitis [2].

Congenital tuberculosis, a rare disease, should be distinguished from the more frequent acquired neonatal tuberculosis, in which the infant is infected after birth by an adult suffering from contagious pulmonary tuberculosis. Congenital tuberculosis may occur as a result of maternal tuberculosis when the illness involves the genital tract or the placenta. Tuberculosis bacilli are introduced into the foetus haematologically via the umbilical vein, or via infected amniotic fluid which is ingested or aspirated in utero or at birth [3]. Revised diagnostic criteria as proposed by Cantwell et al. [4] in 1994 are proven tuberculosis lesions in the infant plus one of the following: (1) lesions occurring in the first week of life, (2) a primary hepatic complex, (3) maternal genital tract or placental tuberculosis or (4) exclusion of postnatal transmission by thorough investigation of contacts.

As demonstrated in our patient, congenital tuberculosis is particularly difficult to diagnose. The mothers are often apparently healthy; in one review 24 of 32 mothers were asymptomatic [5]. The Mantoux test is frequently initially negative in neonates; for example in the classic study of Hageman et al. only 2 of the 14 infants with congenital tuberculosis who were tested had positive skin tests [6]. Because the signs and symptoms of tuberculosis in neonates – hepatosplenomegaly, respiratory distress, fever, lymphadenopathy, abdominal distension and lethargy – are non-specific [3–7], they are initially attributed to other causes such as prematurity, congenital viral infections or sepsis [3, 7]. In particular, common premature conditions such as chronic lung disease, PDA, pneumonia and sepsis are readily mimicked by tuberculosis [7]. The only somewhat specific sign, painless ear discharge, occurs in fewer than 20% of patients [3, 5, 6]. In our patient ear discharge did not occur until late in the course of disseminated tuberculosis and so did not expedite diagnosis.

Congenital tuberculosis is still a dangerous disease. In a review of 58 cases reported since isoniazid was introduced, 26 of the 58 patients died. Eighteen of the 26 patients died before receiving treatment, suggesting that delay in diagnosis may have been decisive [5]. Furthermore, high-risk newborns are disproportionately represented; 12 of 31 patients reported since 1980 were born prematurely [5]. Finally, the clinical course is often fulminant, characterised in many cases by dissemination or meningitis [3]. Our patient's course was marked by invasive focal complications which required surgical as well as medical therapy. As the patient was hospitalised throughout the first year of life, compliance was assured. Measurement of serum levels of isoniazid and rifampicin confirmed adequate drug absorption. Hence it is unlikely that secondary drug resistance was the cause of the persistent focal complications; rather, these sites served as anatomical sanctuaries which could not be eradicated by medication alone.

Because it is rare, because it mimics other neonatal illnesses and because it is nonetheless relentless, congenital tuberculosis, an eminently treatable disease, is often diagnosed too late. Awareness of this illness, with expeditious action to secure material for microbiological proof and prompt institution of empirical therapy, are mandatory if survival is to be improved.

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References

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