SHORT REPORT

Pulmonary tuberculosis and extreme prematurity

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A mother, newly found to be positive for HIV, delivered her first baby at 25 weeks gestation. The infant initially did well in spite of a symptomatic patent duct and a severe intraventricular haemorrhage, but became severely unwell needing further respiratory support on day 18. Acid fast bacilli were found in endotracheal secretions. After the baby's death, the bacilli were confirmed to be *Mycobacterium tuberculosis*, and the same organism was grown from the mother's urine. The case raised challenging issues in relatively uncharted territory in terms of treatment of the infant, public health issues, ethical decision making, and media management.

The mother was from sub-Saharan Africa and in a stable marriage with the child's father. On a routine HIV screen, she was found to be positive with very high viral load at 23 weeks gestation. Before further investigations could be completed, and before starting antiretoviral therapy, she developed a fever at 24^{+4} weeks, without a cough or other symptoms. She was started on antiretroviral therapy and antibiotics. All bacterial and viral tests failed to identify an infection. She failed to respond to various combinations of antibiotic treatment including pentamidine and cotrimoxazole. A chest physician found no evidence of tuberculosis. At 25^{+4} weeks gestation she went into labour. The father was not aware of the mother's HIV status and she was not yet ready to tell him.

After vaginal delivery, the baby, weighing 870 g, was in good condition; she was intubated and given surfactant. Cranial ultrasound on the first day showed severe bilateral intraventricular haemorrhages with acute ventricular dilatation and a left haemorrhagic venous infarct. She was started on triple antiretroviral therapy (zidovudine, nevaripine, lamivudine) plus amoxycillin and gentamicin. We discussed the situation, other than the HIV status, with her parents; and we gently encouraged the mother to inform her husband about the HIV.

Although the baby managed nasal continuous positive airway pressure in air by 24 hours, she collapsed at day 6 and was reventilated because of a large patent arterial duct. She was therefore given indomethacin and soon successfully extubated back into air. At 18 days she was reventilated for major apnoeic episodes. *Aspergillus fumigatus* was isolated from a skin lesion and yeasts from the urine, so we gave ceftazidime, vancomycin, and liposomal amphotericin, but she worsened, with pyrexia and rising C reactive protein concentrations. Copious tracheal secretions were negative on culture for bacteria, *Aspergillus*, and *Pneumocystis carinii*. We sent off more secretions to test for mycobacteria. Echocardiography did not show vegetations in the heart. She developed post-haemorrhagic hydrocephalus.

The baby's secretions were positive for acid fast bacilli on staining, so we started her on rifampicin, pyrazinamide, and isoniazid. She was by now very unwell, with no respiratory effort during endotracheal tube changes and few spontaneous movements. After discussion with the parents and relatives, intensive care was discontinued and she died soon afterwards. The mother had been started empirically on antituberculous therapy without laboratory confirmation of infection. Several days after her baby had died, her urine grew *Mycobacterium tuberculosis*.

DISCUSSION

As the number of mothers found to be positive for HIV is rising, and some of these women may already have tuberculosis, this type of case may arise again. Although there are other case reports of congenital tuberculosis in term and preterm babies,[1–3] we present this case and the accompanying commentaries because it raises a set of important issues.

Congenital tuberculosis is very rare. Only about 300 cases had been reported in the English literature by1984[1 2] and only about another 77 thereafter to 2002.[3] Placental[4] and endometrial[5 6] biopsy could facilitate early diagnosis in suspected cases before cultures became positive in the infant.

We would like to highlight four particular issues. Firstly, the advice and information from various experts was often conflicting or impractical, and it was clear that no one group of people knew enough to deal with all the issues. This emphasises the importance of a multidisciplinary meeting at an early stage.

Secondly, two different ventilators and a nasal continuous positive airway pressure driver had been used for this infant. These were put out of commission pending advice on decontamination.

Thirdly, there are very limited data on the optimal dosage of antituberculous and antiretroviral drugs in preterm infants.

The final issue is management of neonatal contacts. The high risk contacts, defined as infants nursed at any period of their stay in the same ''hot room'' as this case, and medium risk contacts, defined as infants nursed at any time of their stay in the cubicles opening on to the hot room, were given prophylactic isoniazid for three months followed by Heaf testing. The low risk contacts (infants nursed in the separate ''cold room'') were monitored by their general practitioners.

We have learnt that we need to consider tuberculosis as a possible infection for any infant with a mother infected by HIV. We now know how to decontaminate the ventilators should we find ourselves in a similar situation; we can supply details of this. We have started using a filter routinely on the expiratory limb of all our ventilators and continuous positive airways pressure drivers to prevent dissemination of infection to the atmosphere. We should avoid overzealous treatment of possible contacts. We have learnt that it is important to hold a multidisciplinary meeting at an early stage to agree the overall management of the case. It is important to actively manage information to the media, while respecting confidentiality, rather than risk a leaked story causing sensationalist reporting. We have learnt that, although it is important to counsel the mother and maintain

confidentiality, it is also important to point out to her the responsibility and duty she owes to her relatives and the general population.

We were caught up in an unusual situation from which we have learnt much. Other units may feel that, in the light of our experience, it would be useful to have a written plan worked out in advance to deal with this contingency. The commentaries that follow pick up on some of the issues that we have raised.

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COMMENTARY

The number of pregnancies in HIV infected women is increasing. In 1998 there were just 185 confirmed cases, which increased to 758 in 2002.[1] This probably reflects an increase in incidence as well as an increase in ''identification'' by the introduction of routine antenatal screening. The success of routine antenatal screening is, however, variable, with the target of 90% of pregnancies being screened being achieved in very few areas. This highlights the need for far more training of both midwives and obstetricians, discussing openly the benefit and need for antenatal testing.

About three quarters of all women, globally, who are infected with HIV come from sub-Saharan Africa.

There has also been an increase in the incidence of tuberculosis, and this resurgence may, in some part, be due to the susceptibility of the HIV infected patient to this disease. Women from sub-Saharan Africa need to be screened thoroughly, and tuberculosis in particular should be considered when they have pyrexia of unknown origin and are known to be HIV positive. Significant pyrexia in pregnancy is known to trigger premature labour, and the cause needs to be identified urgently and effective treatment established as soon as possible.

In utero transmission of tuberculosis leading to congenital infection is rare. Even with vaginal delivery, in cases where the mother is known to have tuberculosis, transmission has been shown to be postnatal by nosocomial spread. However, there are no specific data on pregnancies complicated by both HIV and tuberculosis with regard to vertical transmission of tuberculosis, and in this situation the risk of in utero transmission may be different.

This case described by Katumba-Lunyenya *et al* highlights the need for a multidisciplinary approach to women with HIV in pregnancy, whether they are unwell or not. The multidisciplinary team should include:

- a consultant in adult infectious diseases or genitourinary medicine
- a consultant obstetrician
- a consultant in microbiology/virology
- a consultant in paediatric diseases
- a neonatal consultant
- an HIV support worker

It is particularly important to have a consultant microbiologist/virologist who can advise on the most appropriate specimens required and advise on sensitivities, etc.

The role of the HIV support worker/advisor is extremely important as they spend a great deal of time with these women, discussing all aspects of care and in particular confidentiality issues. Their role in being the patient advocate cannot be underestimated.

The obstetrician has an important role to play in explaining that a whole variety of carers will need to know the patient's HIV status in the best interests of both the mother and the baby. They need to encourage some documentation of the HIV status and plan for delivery in the hand held maternity notes. However, at all times the patient's wishes have to be respected, but the decision to withhold information must be informed, and consent sought for all relevant information to be held in a separate file and released on a ''need to know'' basis.

Many women with HIV deliver prematurely; the cause is not known. In this case the mother was clearly unwell, and whether the cause of the pyrexia was intrauterine had to be considered. Although the outcome is devastating for the parents, without an established diagnosis it would have been unwise to attempt to delay delivery by the use of tocolytic drugs.

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COMMENTARY

Katumba-Lunyenya *et al* present a fascinating but sad case.

ROUTE OF INFECTION AND INFECTIVITY

Neonatal tuberculosis is usually caused by someone, usually the mother, with open pulmonary tuberculosis coughing on