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Case report

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Untreated chronic tuberculous salpingitis followed by successful *in vitro* fertilization conception and congenital tuberculosis

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Learning Point for Clinicians

Female reproductive tract tuberculosis is rare in the developed world and its diagnosis is challenging. However, this case illustrates the importance of including female reproductive tract tuberculosis in the differential for any gynaecological complaint in healthcare workers, due to the high mortality associated with vertical transmission.

Case

A 4-month-old Caucasian girl presented with a cyanotic episode requiring immediate intubation, following 2 weeks history of cough and fever and failure-to-thrive since birth. She was born 2.9 kg at full term via uncomplicated vaginal delivery. She was up-to-date with the UK vaccination schedule. On physical examination, there were delayed developmental milestones, muscle wasting, generalized lymphadenopathy and hepatosplenomegaly. Peripheral chorioretinitis was evident on fundoscopy.

Chest radiograph showed widespread bilateral nodular infiltrates. Centrally necrotic cervical lymph nodes and massive hepatosplenomegaly were seen on ultrasound. Routine blood tests demonstrated elevated liver transaminases (AST 118IU/l and ALT 341IU/l) and acute phase reactants (CRP 55 mg/l, ESR 28 mm/h), but serological tests for HIV, CMV and toxoplasmosis were negative. CSF analysis was also normal. Initial QuantiFERON®-TB test was negative. Repeat sampling yielded an equivocal result.

Despite standard antibiotic therapy, she failed to improve clinically. Cervical lymph node scrapings were then obtained, showing caseating granulomas. Pansensitive *Mycobacterium tuberculosis* (Mtb) was confirmed by microscopy and culture of both lymph node biopsy specimens and bronchial washings obtained at bronchoscopy. She was commenced on isoniazid, rifampicin, pyrazinamide and ethambutol and, after 4-day therapy, successfully extubated.

Her mother, a 32-year-old healthcare worker, described a 3-year history of intermittent vaginal discharge. Past medical history was notable for bilateral salpingectomy for cyclical pain and a self-

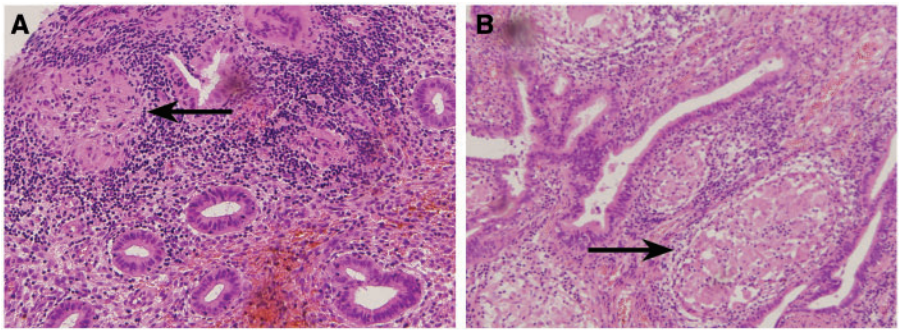

Figure 1. Histopathological sections from endometrial biopsy (**A**) taken from mother after infant's diagnosis and of fallopian tubes (**B**) resected from mother 3 years previously, both demonstrating non-caseating granulomas (arrows).

limited episode of optic neuritis 6 weeks prior to her daughter's presentation. She had known exposure to two patients with tuberculosis (TB) through her work and her maternal grandmother had been treated for TB previously; however, she reported having a negative tuberculin purified protein derivative skin test 4 years ago. Physical examination including pelvic examination was normal, chest radiograph clear and trans-vaginal ultrasound unremarkable.

A repeat tuberculin purified protein derivative skin test was strongly positive at 25 mm. She proceeded to endometrial biopsy, which revealed non-caseating granulomas (Figure 1A). ZN (Ziehl–Neelson) stain was negative, as was GeneXpert-MTB/RIF® PCR-based assay. However, pansensitive Mtb was cultured from biopsy specimens at 14 days and GenoType®-MTBDR assay was positive. She was commenced on isoniazid, rifampicin and pyrazinamide. (Ethambutol was omitted due to her history of optic neuritis.)

At this stage, clinical notes from her investigations for cyclical pain 3 years previously were reviewed. Hysterosalpinography and laparoscopy had demonstrated ''badly scarred'' fallopian tubes and she had undergone bilateral salpingectomy. Both salpingectomy and endometrial biopsy specimens had contained non-caseating granulomas and Langerhan's giant cells, felt possibly to be consistent with resolved tubercular infection (Figure 1B). ZN stain was negative, however, and as symptoms had resolved following surgery, no further investigations were pursued. TB culture and PCR-based assays were not performed.

Three years later her daughter, conceived following one cycle of *in vitro* fertilization, presented with potentially fatal congenital TB as described. Fortunately, though the pre-conception diagnostic opportunity had been missed in this case, both mother and child responded well to antimicrobial therapy and the child has experienced no long-term sequelae to date.

Discussion

Congenital TB presents a diagnostic challenge. Symptoms are generalized and non-specific, immune-based diagnostics (such as QuantiFERON®-TB) are frequently negative in the early weeks of life, and though by definition requiring vertical transmission (either by haematogenous spread or by inhalation of infected amniotic fluid *in utero*), detailed review of published cases by Cantwell *et al.*[1] found over half of mothers to be undiagnosed until after the diagnosis was made in their infant. However, delayed diagnosis is associated with a 5-fold higher mortality compared with cases where prompt and appropriate antimicrobial therapy is initiated.[1,2]

Pre-conception identification and treatment of female genital tract TB could prevent congenital TB. However, the wide variety in nature and severity of clinical presentation[3] and the lack of a gold standard diagnostic test (as well as the inconsistency of different diagnostic modalities, demonstrated in this case)[4,5] render this challenging. Though extremely rare in developed countries,[3] this case demonstrates that female genital tract TB must be included as a differential for healthcare workers presenting with any gynaecological complaint.[4] Furthermore, combined diagnostic modalities must be employed to enhance identification of cases and prevent vertical transmission.[4,6]

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