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-
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 pro-
ceeded to endometrial biopsy, which revealed
non-caseating granulomas (Figure 1A). ZN (Ziehl–
Neelsen) 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 pyra-
zinamide. (Ethambutol was omitted due to her his-
tory of optic neuritis.)

At this stage, clinical notes from her investigations
for cyclical pain 3 years previously were reviewed.
Hysterosalpingography and laparoscopy had demon-
strated “badly scarred” fallopian tubes and she had
undergone bilateral salpingectomy. Both salpingect-
yomy and endometrial biopsy specimens had con-
tained 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 follow-
ing one cycle of in vitro fertilization, presented with
potentially fatal congenital TB as described. Fortu-
nately, 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. Symptons 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 presentation3 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

References

1. Cantwell MF, Shehab ZM, Costello AM, Sands L, Green WF,
2. Flibotte JJ, Lee GE, Buser GL, Feja KN, Kreiswirth BN,
McSherry GD, et al. Infertility, in vitro fertilisation and con-

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).

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