

Encounters with an old foe: Childhood tuberculosis in Canada

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A previously well two-year-old child presented to the emergency department with a two-week history of fever and lethargy. Seven days before presentation, she was prescribed amoxicillin for otitis media. On examination, she appeared lethargic but conscious, responding to questions. There were no obvious focal neurological signs, although a possible neck stiffness was present. A lumbar puncture yielded clear cerebrospinal fluid (CSF) with a white blood cell count of 230 cells/ μ L (35% lymphocytes, 55% neutrophils and 20% monocytes), protein level of 1.4 g/L and glucose level of 2.1 mmol/L.

Ceftriaxone and vancomycin were initiated for presumed partially treated bacterial meningitis. On the following day, she appeared drowsier. A computed tomography scan of the head revealed enlargement of the lateral ventricles and basal meningeal enhancement, highly suspicious for tuberculosis (TB). A small amount of CSF was retrieved from the laboratory and sent for tuberculosis culture. Isoniazid (INH), rifampin, pyrazinamide and ethambutol were commenced, together with dexamethasone. A tuberculin skin test (TST) was negative (0 mm) at 48 h. The child's subsequent course included a ventriculoperitoneal shunt insertion for hydrocephalus. The original small CSF volume did not grow any organisms; however, the larger volume obtained at the time of shunt placement grew *Mycobacterium tuberculosis*, resistant to INH but sensitive to other first-line agents. INH was discontinued, and levofloxacin and cycloserine were added to the regimen. The child developed seizures on the 25th day of therapy, with magnetic resonance imaging evidence of a right-sided stroke with subsequent left hemiparesis and global delay.

On contact tracing by the public health department, a family member born in a TB-endemic country was identified with smear and culture-positive pulmonary TB. The patient's four-year-old asymptomatic brother was TST positive (11 mm induration) and found to have hilar lymphadenopathy on chest x-ray. His gastric aspirates did not grow *M. tuberculosis* and he underwent nine months of treatment with rifampin, ethambutol and pyrazinamide, with significant radiological improvement.

LEARNING POINTS

- In Canada, there was an average of 95 cases per year (range 75 to 114) of TB disease reported in children <15 years of age from 2005 to 2011 (1). The highest-risk groups are foreign-born individuals, children of foreign-born individuals and Aboriginals (2).

- The incidence of drug-resistant TB (ie, multidrug-resistant [MDR] and extensively drug-resistant [XDR] TB) is increasing in many parts of the world. Both are resistant to INH and rifampin, whereas the latter is also resistant to second-line drugs (3-6). While the majority of TB among Canadian children remains sensitive, 19 cases of paediatric TB resistant to one or more drugs and two cases of MDR TB were reported to the Public Health Agency of Canada between 2000 and 2011. These data, based on only 31 isolates, may underestimate the true burden of resistance in children.
- Childhood TB is often a sentinel event requiring a public health search for a source case. Many children with TB infection identified through contact tracing are asymptomatic but have abnormal chest x-rays (TB disease).
- Because rates of TB have declined in Canada, lack of diagnostic suspicion may contribute to delays in diagnosis (7).
- The diagnosis and management of TB in children, especially in those <5 years of age, are often complex. A team approach involving experienced clinicians is required.
- Young children have higher rates of extrapulmonary and/or paucibacillary (containing few mycobacteria) TB.
- TB meningitis is more common in younger children and may have devastating consequences. A positive TST may support the diagnosis of TB; however, it may be negative in up to 10% of children with TB disease. Due to a lack of specificity, a positive TST also does not imply that a disease process is due to TB.
- Treatment of resistant TB is complicated and often long. Online resources relevant to Canada have recently been published (8).
- Clinical or radiological deterioration during appropriate treatment occurs in up to 15% of children and is often difficult to distinguish from the development of drug resistance or another diagnosis (9,10).
- While cases of TB reported to public health departments are an important source of basic information, there are limitations to these data. A CPS study is underway to more fully understand and validate the epidemiology, clinical spectrum, diagnostic challenges, microbiology, Bacille Calmette-Guérin vaccination and treatment response to TB therapy in Canadian children <15 years of age (www.cpsc.ca/surveillance/study-etude/childhood-tuberculosis).

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