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REVIEW

Tuberculous dactylitis—an easily missed diagnosis

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Abstract The prevalence of tuberculosis (TB) continues to rise worldwide. Current migration patterns and increased travel to high-prevalence TB countries will result in more frequent presentations of less common forms of TB. Tuberculous dactylitis, a form of tuberculous osteomyelitis, is well recognised in countries with a high prevalence of TB. We provide a systematic review of all published cases of tuberculous dactylitis in children and adolescents and describe a case to illustrate the typical features of the disease. Our review revealed 37 cases of tuberculous dactylitis in children and adolescents, all reported in the last 17 years. Children less than 10 years of age are most frequently affected and the hand is the most commonly affected site. Concurrent pulmonary TB is present in a fifth of cases and systemic symptoms are usually absent. Positive TST and IGRA support the presumptive diagnosis, but cannot be used as rule-out tests. The definitive diagnosis relies on the detection *M. tuberculosis* by PCR or culture. Treatment should comprise of a standard three to four drug anti-tuberculous regimen. The optimal treatment duration remains unknown. Surgery has a limited role in the treatment in general but may play a supportive role, and curettage of the cavity has been recommended for avascular lesions.

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Introduction

The prevalence of tuberculosis (TB) continues to rise worldwide [1]. With increasing migration from regions with a high prevalence of TB and increasing numbers of travellers to high-prevalence TB countries [2], less common forms of TB will be seen more frequently in industrialised countries. Extrapulmonary TB is more common in children and adolescents than adults, accounting for approximately one quarter of paediatric cases [3]. Less common forms of TB, such as tuberculous dactylitis, are well recognised in countries with a high prevalence of TB but may prove a diagnostic challenge to clinicians in industrialised countries who may be unfamiliar with the clinical features. This review summarises the epidemiology, clinical features and management of tuberculous dactylitis. It includes an illustrative case that highlights the important features as well as a summary of all previously published cases in children and adolescents.

Illustrative case

A 15-year-old Australian-born girl of Cambodian descent presented with a 6-month history of a swollen right middle finger associated with mild pain (Fig. 1, panel A). She did not recall any trauma and was otherwise well. She had not experienced similar symptoms in the past and there was no

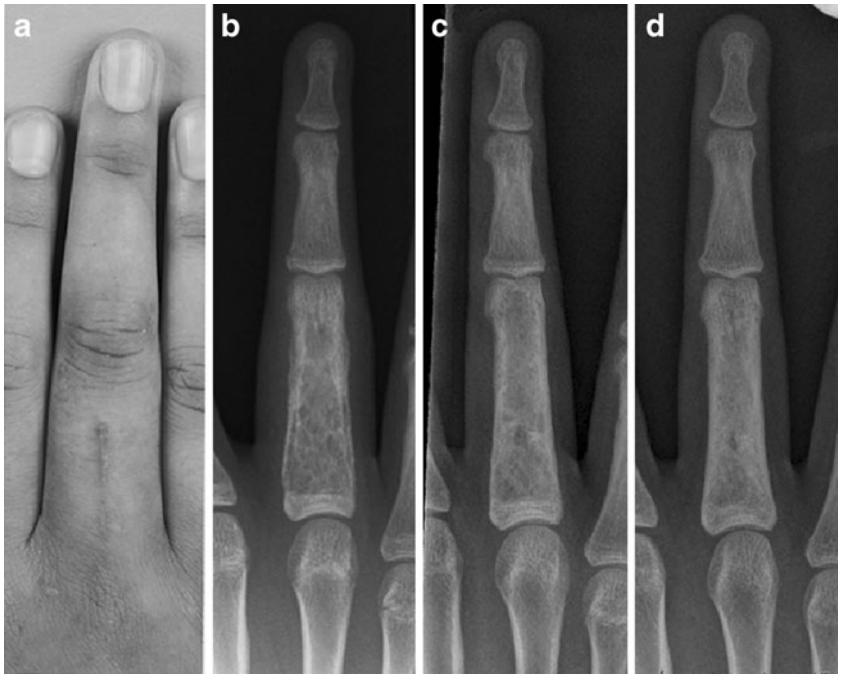

Fig. 1 **a** Swelling of the right middle finger with residual scar following bone biopsy four weeks prior. **b**–**d** Radiograph of the right middle finger showing diffuse lytic lesions in the proximal phalanx (**b**) before treatment and progressive resolution of the lesions with accompanying sclerosis after 4 months (**c**) and 9 months (**d**) of treatment

family history of rheumatological diseases. Her immunisations were up-to-date according to Australian guidelines, which do not routinely include Bacille Calmette-Guérin (BCG) vaccine. She had lived in Cambodia for one year at the age of 18 months. She had also visited Cambodia for a five-week period when she was 10 years old. At presentation, the only abnormal physical finding was swelling of the proximal phalanx of the right middle finger without associated erythema or tenderness. Inflammatory markers including white blood cell count, C-reactive protein and erythrocyte sedimentation rate were within the normal range. Serology for human immunodeficiency virus was negative. Radiography showed a diffuse abnormality in the proximal phalanx of the right middle finger with a mottled appearance (Fig. 1, panel b). A tuberculin skin test (TST) showed 22 mm induration after 72 hours. An interferon gamma release assay (IGRA) (QuantiFERON-TB Gold In Tube, Cellestis, Australia) was negative. Her chest radiograph was normal and a radionuclide bone scan did not reveal involvement of further sites elsewhere.

The medullary cavity of the affected bone was surgically curetted and lavaged. Histopathology examination of the bone showed granulomatous inflammation (Fig. 2). *Mycobacterium tuberculosis* was detected in the biopsy specimen by polymerase chain reaction (PCR) and subsequently by culture. Treatment was started with isoniazid 300 mg daily, rifampicin 600 mg daily and pyrazinamide 1000 mg daily in divided doses. Susceptibility testing of the isolate revealed a fully sensitive strain and pyrazinamide was stopped after the initial two months of treatment. Radiography after four months of treatment showed improvement of the honeycomb lesions. Following a total treatment duration of 9 months, the patient remained well and the swelling had almost totally resolved. Radiography at the end of treatment showed resolution of the honeycomb lesions with healing accompanied by sclerosis (Fig. 1, Panels c and d).

Search strategy

Publications were identified by a systematic search of Medline (1950–2010), EMBASE (1950–2010) and Web of Science (1898–2010) using the following search strategy: ("dactylitis" OR "ventosa") AND ("tuberc*" or "TB"). Reference lists from relevant publications and Google scholar identified an additional two articles. Publications in English, French, Italian and German were reviewed. Of the 114 publications identified, 49 were excluded (46 were not relevant, three were in other languages [Czech, Bulgarian and Mandarin]) leaving a total of 65 articles that were reviewed in detail. Of these, 28 included reports of tuberculous dactylitis in children and adolescents.

Epidemiology and clinical characteristics

TB osteomyelitis accounts for 1–2% of all TB cases but up to 10–20% percent of cases of extrapulmonary TB disease [4, 5]. Spinal TB (Pott's disease) is the most common form of tuberculous osteomyelitis. Extraspinal tuberculous osteomyelitis may manifest in any location but most commonly

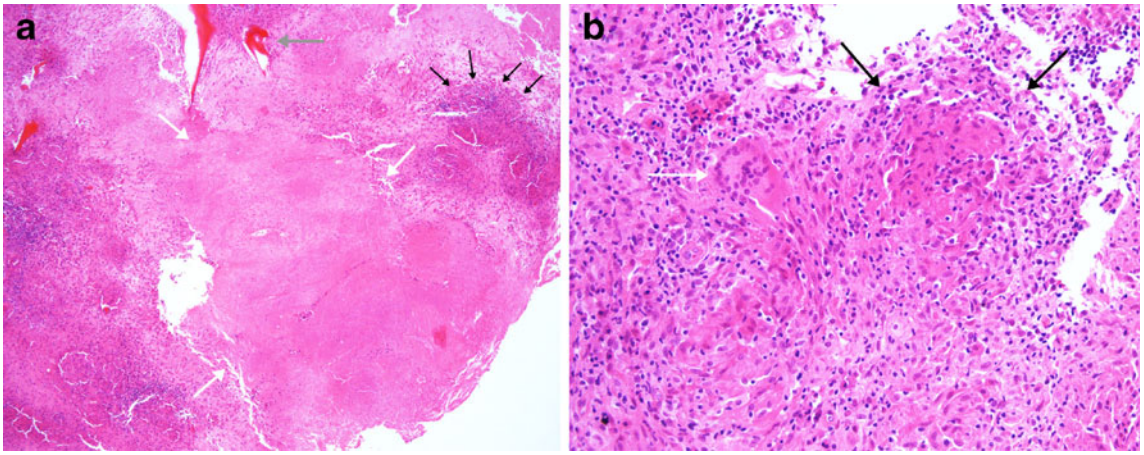

Fig. 2 Haematoxylin and eosin stained sections of the bone biopsy showing granulomatous osteomyelitis typically seen in tuberculous osteomyelitis. **a** The 5-fold magnification shows central caseating necrosis (*white arrows*) surrounded by granulomatous inflammation (*black arrows*); bone fragments are also seen (*grey arrow*). **b** The 20-fold magnification shows a granuloma (*black arrows*) composed of lymphocytes and epithelioid histiocytes with an adjacent multinucleate giant cell (*white arrow*)

involves the hands, feet, ribs and the skull [4, 6]. Tuberculous dactylitis is a less common but important form of tuberculous osteomyelitis. Our literature search identified a total of 37 cases of paediatric tuberculous dactylitis in 28 publications (Table 1). Tuberculous dactytlitis has most commonly been reported in children less than 10 years of age (Figs. 2 and 3). The hand is most frequently affected and only five (14%) out of 37 cases reported in the literature described tuberculous dactylitis in the foot [7–10]. Osteomyelitis caused by *M. tuberculosis* is thought to result from hematogenous spread during primary infection. The interval between primary infection and onset of symptoms is difficult to establish as the timing of primary infection is usually unknown. The index case has only rarely been identified and our case illustrates also the potential risk of this form of TB being acquired during travel to high TB prevalence countries [11]. Concurrent pulmonary TB is present in about a fifth of reported cases and systemic symptoms such as fever, night sweats and weight loss are frequently absent (Table 1). Concomitant involvement of other sites is present in about a quarter of published cases. The swelling is usually painless or only mildly painful, which can be an important feature to distinguish tuberculous from other causes of dactylitis [12, 13]. It typically affects the proximal phalanges or the metacarpal bones, most commonly involving a single bone (Table 1).

Diagnosis

A TST result was reported in 24 (66%) of the 37 cases and was positive in 21 (88%) and negative in three (12%) [10, 14, 15]. A positive TST therefore may be helpful in supporting the presumptive diagnosis of tuberculous dactylitis. An IGRA was not reported in any of the 37 cases previously reported. Notably, in our illustrative case the IGRA was negative. Only a few studies have assessed the performance of IGRAs for the diagnosis of extrapulmonary TB and in particular for tuberculous osteomyelitis. Two studies in adults with tuberculous osteomyelitis suggest a sensitivity of 41–67% [16, 17]. In addition, the sensitivity of IGRAs in children, particularly those under 5 years of age has been questioned [18, 19]. Based on this and the result in our case, an IGRA should not be used to exclude the diagnosis of tuberculous dactylitis. Radiographs typically show enlargement of the bone with periosteal thickening and destruction of the spongiosa resulting in a cystic appearance called ‘spina ventosa’. A diffuse infiltration with a lytic honeycomb appearance, as seen in our case, is less frequent. However, radiological features are not pathognomonic and confirmation of the diagnosis requires detection of *M. tuberculosis* from a bone biopsy by PCR or culture. Culture from a fine needle aspiration or from fluid collected from a sinus has also been shown to be helpful for diagnosis [20–24]. Differential diagnoses of tuberculous dactylitis include syphilis, acute bacterial or fungal osteomyelitis, sarcoidosis, gout, sickle cell dactylitis, bone tumours and rheumatoid arthritis.

Treatment and follow-up

Standard empiric treatment for tuberculous dactylitis is similar to that for pulmonary TB, comprising a three to four drug regimen including isoniazid, rifampicin, pyrazinamide and ethambutol. In cases of culture-proven tuberculous dactylitis with a resistant *M. tuberculosis* strain, change of anti-tuberculous drugs guided by resistance testing is required. Traditionally, a treatment duration of 12–

Table 1 Summary of all case reports of tuberculous dactylitis in children and adolescents

Age (years)/ Sex	Country of birth and country of presentation	Site of dactylitis (unless specified in the hand)	Method of diagnosis	Other affected sites	BCG	TST result (mm)	Anti-TB drugs (months)	Remarks	Reference
0.5/M	South Africa South Africa	Proximal phalanx IV	Bone biopsy (histology)	Forehead	–	0	Not specified (6)	–	[15]
0.5/F	'Asian' USA	Os metatarsale I	–	–	–	–	–	–	[8]
1/F	South Africa South Africa	Os metacarpale III	–	Tibia, lung	Immunised	30	INH (12) PZA (12) ETH (12)	Two adult pulmonary TB cases in household	[33]
1/–	– Bulgaria	Middle phalanx IV, os metacarpale V	Bone biopsy (unspecified)	None	–	'Positive'	–	–	[34]
1/–	Tunisia Tunisia	Os metacarpale I, middle phalanx IV	Culture of fluid from fistule	Face, lung	Non-immunised	'Positive'	INH (18) ETA (18) STRP (18)	Mother treated for pulmonary TB	[20]
1/F	– Turkey	Middle and distal phalanges II-V	–	Skin (Lupus vulgaris)	–	14	INH (12) RIF (12) PZA (2) ETH (2)	–	[35]
1/F	– Italy	Proximal phalanx I and V, ossa metacarpalia I and V	–	None	–	'Positive'	INH (−) STRP (−)	–	[36]
2/F	Portugal Switzerland	Os metacarpale I	Bone biopsy (histology) AFBs in gastric aspirate	None	–	'Negative'	INH (−) RIF (−)	–	[14]
2/M	– USA	Os metatarsale I	–	Skin (Lupus vulgaris)	–	14	–	–	[7]
2/–	– USA	Proximal phalanges II and IV, middle phalanges IV and V	–	None	–	–	No treatment	–	[27]
2/–	– USA	Proximal phalanx IV	–	None	–	–	No treatment	–	[27]
3/F	India India	Middle phalanx III	–	Lung, foot	–	'Positive'	Not specified (12)	–	[37]
3/F	India India	Middle phalanx III (foot)	–	–	–	'Positive'	Not specified (9–12)	–	[10]
3/F	India Belgium	Middle phalanges III and V	–	Lung. Os metatarsale I	–	'Positive'	INH (9–12) RIF (9–12)	Adopted child	[38]
3/–	Turkey Turkey	Os metacarpale IV	Bone biopsy (histology and culture)	None	–	–	Not specified (12)	–	[39]
3/M	China United Kingdom	Proximal phalanx III, ossa metacarpalia II and IV	–	–	–	17	–	Grandfather treated for pulmonary TB	[40]
4/M	India India	Proximal phalanges I and III, ossa metacarpalia I and V	Bone biopsy (histology)	None	–	20	INH (−) RIF (−) PZA (−) ETH (−)	–	[41]

4/M	– USA	Middle phalanges II, III, IV	Bone biopsy (histology and culture) Gastric aspirates (culture)	Lung, skin	–	15	INH (12) RIF (12)	–	[42]
4/M	India India	Ossa metacarpalia I and III	Bone biopsy (culture)	Lung, elbow	_	'Positive'	Not specified (9–12)	_	[10]
4/F	– Morocco	Ossa metacarpalia II and III, os metatarsale IV	Bone biopsy (unspecified)			20	INH (10) RIF (10) PZA (2)	Fever, loss of appetite and ascites	[43]
5/F	Somalia United Kingdom	Proximal phalanx II	Bone biopsy (histology and culture)	None	Non-immunised	25	INH (−) RIF (−) PZA (−)	Mother and three siblings negative on TB screening	[44]
5/F	India India	Os metacarpale II	Bone biopsy (histology)	Toe, canthus	Immunised	'Positive'	INH (6) RIF (6) PZA (2) ETH (2)	–	[45]
5/F	Malaysia Singapore	Os metacarpale I	Cervical lymph node biopsy	Lung, cervical lymph nodes	–	–	–	–	[46]
5/F	France France	Os metacarpale IV, proximal phalanx IV	Synovial biopsy (histology)	None	–	20	INH (12) RIF (6) ETH (12)	TB index case not found	[47]
6/F	India India	Ossa metacarpalia I and II	Fine needle aspiration (culture)	Calcaneus, spine	_	'Positive'	Not specified (9–12)	_	[10]
6/M	Philippines Denmark	Proximal phalanx V	Bone biopsy (histology and culture)	None	Unknown	Not done	INH (−) RIF (−) ETH (−)	Initial diagnosis enchondroma	[48]
7/F	Turkey Turkey	Proximal phalanx	Bone biopsy (histology and culture)	None	–	–	Not specified (12)	–	[39]
7/M	India India	Middle phalanx IV	Culture from fluid from sinus	Lung	_	_	–	_	[23]
8/F	Turkey Turkey	Proximal phalanx	Bone biopsy (histology and culture)	None	–	–	Not specified (12)	–	[39]
8/M	Madagascar Madagascar	Distal phalanx I	Bone biopsy (culture)	None	–	'Strongly positive'	INH (8) RIF (8) PZA (2) ETH (2)	Weight loss and fever	[49]
9/M	South Africa South Africa	Proximal phalanx IV	–	Lung	–	–	–	–	[12]
11/M	Pakistan Belgium	Os metacarpale I	Bone biopsy (histology and culture)	None	–	'Positive'	INH (10) RIF (10) ETH (4)	–	[50]
11/M	India India	Os metatarsale I	Culture from fine needle aspiration	_	_	_	–	_	[24]
11/F	India India	Middle phalanx IV	_	_	_	'Negative'	Not specified (9–12)	_	[10]
12/F	India India	Os metatarsale I Os metacarpale II	Culture from fine needle aspiration	_	_	_	–	_	[24]

Table 1 (continued)

Age (years)/ Sex	Country of birth and country of presentation	Site of dactylitis (unless specified in the hand)	Method of diagnosis	Other affected sites	BCG	TST result (mm)	Anti-TB drugs (months)	Remarks	Reference
15/M	Somalia Netherlands	Os metacarpale II	Bone biopsy (histology and culture)	Lung	–	–	INH (6) RIF (6) ETH (6)	Brother with pulmonary TB	[51]
15/F	Australia Australia	Proximal phalanx III	Bone biopsy (histology, culture and PCR)	None	Non-immunised	22	INH (9) RIF (9) PZA (2) ETH (2)	See text	[a]
15/F	– India	Middle phalanx III (foot)	Culture from fluid from sinus	–	–	14	INH (6) RIF (6) PZA (2) ETH (2)	–	[9]

M male, *F* female, *INH* isoniazid, *ETH* ethambutol, *ETA* ethionamide, *PZA* pyrazinamide, *RIF* rifampicin, *STRP* streptomycin

[a] Case described in this report

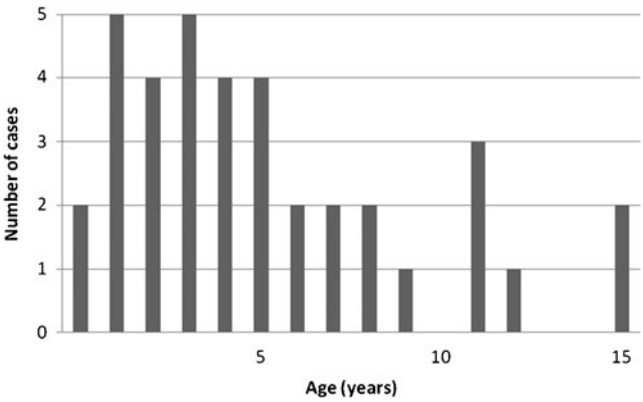

Fig. 3 Age distribution of published cases of tuberculous dactylitis in children and adolescents

18 months has been recommended for tuberculous osteomyelitis based on concerns about poor bone penetration and the difficulty of confirming cure [25]. The World Health Organization recommends a treatment duration of 9 months for TB osteomyelitis because of the difficulty in assessing treatment response [26]. A third of the case reports of tuberculous dactylitis did not detail the choice of anti-tuberculous drugs or the duration of treatment. Of those that specified the treatment duration, this was most commonly 9–12 months. The longest treatment duration reported was 18 months and one study did not treat with anti-tuberculous drugs and suggested "spontaneous complete healing is the rule" [27]. Prospective studies investigating treatment for tuberculous osteomyelitis in the spine suggest that a treatment regimen including isoniazid and rifampicin for a duration of 6–9 months is effective [28, 29]. It has also been suggested that 6 months of antituberculous treatment is sufficient as bacillary load is considered low in tuberculous dactylitis [9]. However, one recent retrospective study showed over 60% relapse rate in patients with spinal tuberculous osteomyelitis treated for six months compared to 0% relapse rate in those treated for nine months [30]. It is unclear whether data from spinal tuberculous osteomyelitis can be extrapolated to the treatment of tuberculous dactylitis. As evidence for the optimal treatment duration is not conclusive, we elected to treat our patient for 9 months. Surgery has a limited role in the treatment of tuberculous osteomyelitis in general but does have an important role in complicated spinal tuberculous osteomyelitis [28, 31]. For tuberculous dactylitis, surgery may play a supportive role and curettage of the cavity has been recommended for avascular lesions, for which anti-tuberculous therapy alone is unlikely to be successful [10, 25]. Monitoring clinical response for tuberculous dactylitis is difficult. C-reactive protein and erythrocyte sedimentation rate are frequently not elevated and repeat culture of the affected area is not practical. Clinical improve-

ment together with repeat imaging is therefore most commonly advocated for monitoring treatment success [10, 25].

Prevention

It is likely that the BCG immunisation that infants in high-risk TB countries receive routinely at birth plays an important role in preventing all forms of TB including dactylitis [32]. However, no study has investigated the protective efficacy of BCG specifically for tuberculous dactylitis. It is notable that the patient described in our illustrative case was not BCG immunised.

Conclusion

Tuberculous dactylitis is a readily-treatable disease that is easily missed. It needs to be considered even in the absence of pulmonary and constitutional symptoms or when potential exposure to *M. tuberculosis* has occurred many years earlier. Positive TST and IGRA may support the presumptive diagnosis, but cannot be used as rule-out tests. The definitive diagnosis relies on the detection of *M. tuberculosis* by PCR or culture from a bone biopsy, or fluid from a fine needle aspiration or draining sinus. Unless susceptibility testing reveals resistance, treatment should comprise a standard three to four drug anti-tuberculous regimen for 2 months followed by treatment with isoniazid and rifampicin for the remaining treatment duration. The optimal treatment duration remains unknown but current data does not support treatment longer than 12 months and most reported cases suggest 9 months of treatment is sufficient.

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