

Case Report

Acute miliary tuberculosis in a five-month-old boy

卡介苗引起之急性粟粒性結核病：五月大男嬰患上彌散性皮膚結核病

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A five-month-old boy presented with fever and multiple cutaneous papular eruptions. Skin biopsy revealed disseminated cutaneous tuberculosis (tuberculosis cutis disseminata). Tissue culture revealed *Mycobacteria bovis* (BCG). He was later diagnosed to have severe combined immunodeficiency. The clinical course, management and literature review of acute miliary tuberculosis will be briefly discussed.

五月大男嬰出現發燒和多處皮膚紅粒發疹，皮膚組織病理學檢查確診為彌散性皮膚結核病。皮膚組織細菌培植發現牛型結核菌。男嬰進一步診斷患上先天性嚴重綜合免疫力缺乏症。

Keywords: BCG, miliary tuberculosis, severe combined immunodeficiency, tuberculosis cutis disseminata

關鍵詞：卡介苗、粟粒性結核病、嚴重綜合免疫力缺乏症、彌散性皮膚結核病

Introduction

Acute miliary tuberculosis or tuberculosis cutis disseminata (TCD) is a rare presentation of miliary tuberculosis in adults and children. In recent years, with the increased use of immunosuppressive

therapy, the HIV epidemic, the emergence of multi-drug resistant *Mycobacterium tuberculosis* and globalisation, there has been a rise in tuberculosis infection¹ and hence resurgence of cutaneous tuberculosis. *M. tuberculosis* is the predominant agent, occasionally *M. bovis* and Bacille Calmette Guerin (BCG) can produce systemic and disseminated skin infection in immuno-compromised host.

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Case report

A five-month-old boy was admitted to Queen Elizabeth Hospital with persistent fever, cough and one month history of a skin rash on trunk and

lower legs in late January 2007. He was the first child of the family. There was no family history of inherited disease and no contact history of tuberculosis (TB). The antenatal history was unremarkable. He was born full term and delivered by Caesarean section because of breech presentation. The vaccination including BCG was up-to-date .

He presented with cough since November 2006. He developed a few non-pruritic papular rash on scalp, back and legs in December 2006. The skin rash remained static before admission. The boy began to develop on and off fever with increasing cough since mid-January 2007. He was treated as respiratory tract infection with courses of antibiotics but the fever and symptoms persisted. Swellings were also noted on the right index and middle finger since December 2006.

Physical examination revealed a few scattered erythematous papular lesions on trunk (Figure 1a) and left lower leg. There were two small papules on chin and one small papule on right parietal scalp. The papules were blanchable with no surface changes. There was no pustule

or ulceration. The BCG vaccination site over left deltoid muscle was markedly inflamed and indurated with scab formation (Figure 1b). There was no palpable lymph node. Mild hepatosplenomegaly was found. He was noted to have swellings in the proximal phalanges of the right middle and index finger.

Chest radiograph showed pneumonic changes in both lung fields. X-ray of the right hand showed radiolucency of the proximal phalanges of the right index and middle finger. Blood test upon admission showed increased white cell count 13.3×10^9 , low haemoglobin level 8.5 g/dL, ESR 71 mm/hr and C-reactive protein 128 mg/L. Blood culture was negative.

He was treated as pneumonia with courses of antibiotics including penicillin G, cefotaxime and clarithromycin. However the fever persisted and there was an increase in skin eruptions in trunk, limbs and face. Some of the skin eruptions began to ulcerate with scab formation. Differential diagnoses at this stage were infective exanthema, Langerhans and non-Langerhans cell histiocytosis, drug eruptions and eczema.



Figure 1. Erythematous papular rash was found scattered on trunk and left upper limb (a,b); induration and scab formation were noted over the BCG vaccination site on the left upper arm.

Gastric lavage, lumbar puncture and skin biopsy were performed. The skin biopsy showed suppurative granulomatous inflammation with numerous acid-fast bacilli seen (Figures 2-4). PCR for Mycobacterial tuberculosis gene was positive. Gastric lavage was positive for acid-fast bacilli while cerebrospinal fluid was negative.

The clinical diagnosis was acute miliary tuberculosis with cutaneous involvement (tuberculosis cutis disseminata). He was started on anti-tuberculous treatment with isoniazid, rifampicin, pyrazinamide and ethambutol. The fever subsided nine days after the start of anti-TB treatment. The skin rash gradually regressed. The culture of the skin biopsy specimen yielded *Mycobacterium bovis* (BCG).

Subsequent immunological studies showed that the boy was suffering from severe combined immunodeficiency (SCID). The HIV-1 and 2 antibodies were negative. He was referred to Queen Mary Hospital for consideration of bone marrow transplant.

Discussion

Miliary tuberculosis (TB) is a well known hazard to infants before the development of anti-TB chemotherapy and BCG vaccination. It is still a significant health problem in children in developing countries with malnutrition and poor hygiene. With the HIV and AIDS epidemic, miliary TB with cutaneous involvement is not uncommonly seen.²

A disseminated cutaneous lesion caused by miliary TB is known as tuberculosis cutis disseminata (TCD). It is caused by haematogenous spread of tubercle bacilli during the course of miliary TB with bacteraemia.^{3,4} Skin involvement is rare in miliary TB, the large case series in miliary TB mentioned little about cutaneous lesions. Miliary TB, TCD and cutaneous TB can be caused by *M. bovis* (BCG) after BCG vaccination. However, it is rare and usually due to underlying immunodeficiency

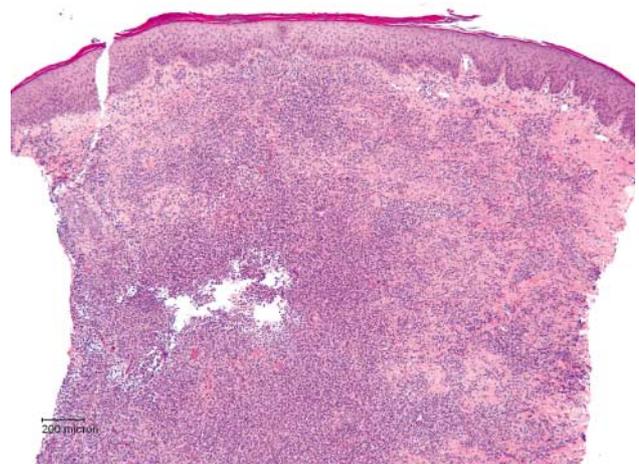


Figure 2. Low power view of skin biopsy from back lesion showing dense inflammatory infiltrate with a microabscess formation in the left side of the biopsy.

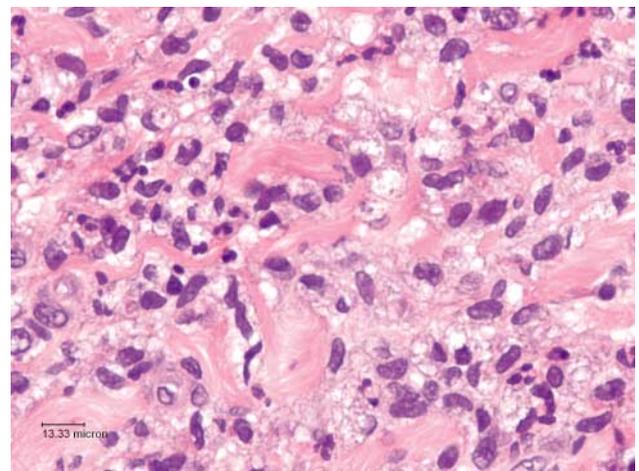


Figure 3. High power view showing suppurative inflammation with histiocyte containing bacillus organisms.

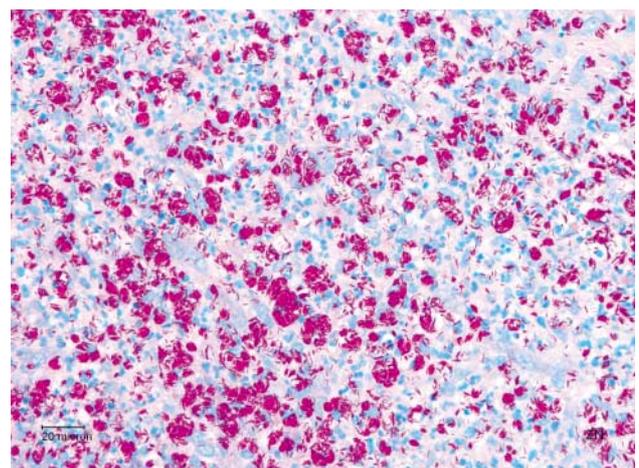


Figure 4. Ziehl-Neelsen stain demonstrates abundant acid-fast bacilli.

state.⁵⁻⁷ Associated immunodeficiency syndromes are severe combined immunodeficiency, cell mediated immune defect, chronic granulomatous disease, Di George syndrome and agammaglobulinaemia.^{5,7} BCG infection after intravesical BCG therapy for bladder cancer was also reported.^{8,9} Most of the reported cases of miliary TB and TCD were patients with AIDS infected by *M. tuberculosis*.²

In 2004, the notified cases of TB in Hong Kong were 6238, at a rate of 90.6/100,000.¹⁰ The notification rate of children under five years of age was 2.7/100,000 in 2004.¹⁰ Only 4% of the patients were in 0-19 age group in 2004.¹⁰ Extra-pulmonary involvement of TB occurred in 24% of cases, of which 12% had simultaneous pulmonary involvement. The most common extra-pulmonary involvement was pleura and lymph node. Other common sites included genitourinary tract, gastrointestinal tract, skeletal system, skin and meninges. About 4% were miliary TB. In the local study of cutaneous TB,¹¹ 11% were true cutaneous TB and 89% were tuberculids. Lupus vulgaris and tuberculosis verrucosa cutis were the most common type of cutaneous TB. There had been no documented cases of TCD in the study period.

Miliary TB usually presents with fever, cough, loss of appetite, weight loss and diarrhoea. Skin lesions initially are small red to violaceous vesiculopapular eruptions. The lesions may become necrotic with purulent discharge. The differential diagnoses of the skin lesion in mycobacterial infection are papulonecrotic tuberculid and lichen scrofulosorum. Most TCD patients have pulmonary involvement, hepatosplenomegaly and lymphadenopathy. Meningitis is another common presentation, other system involvement include gastrointestinal tract, eye, skeletal system and skin. The diagnosis is usually clinical with chest X-ray showing classic miliary pattern. Microbiological culture should be performed but the yield is usually low.

Histologically, TCD consists of dense infiltrate of mixed inflammatory cells composed of lymphocytes, plasma cells and neutrophils. There is focal area of necrosis and abscess formation in the superficial dermis. The most striking feature is abundant acid-fast bacilli with non-caseating granuloma. Occasionally, vasculitis may be seen.

The treatment of miliary TB and TCD stays with standard combination of anti-TB antibiotics. The prognosis described varies in different series,⁵ but generally is poor with underlying immunodeficiency syndromes.⁵ Meningitis is the commonest cause of mortality.

BCG vaccination is considered to be safe and offers protection to infants against the more serious form of tuberculosis such as meningitis and miliary TB. It is offered in Hong Kong to newborns and children under the age of 15 without prior BCG vaccination. The usual complications are grouped into specific and non-specific ones. Specific complications are those which mimic natural mycobacterial infection such as lupus vulgaris, local subcutaneous abscess with or without ulceration, regional lymphadenitis, scrofuloderma, localised or generalised tuberculids, osteitis, tuberculous foci in distant organs. Non-specific complications include keloid formation to various local eruptions. Fever, chills, arthralgia, malaise may occur in repeated vaccination.

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