Case report

BCG lymphadenitis of a healthy infant

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Abstract:
This is a case of a 2-month-old infant who had suppurative lymphadenitis at left axilla after Bacille Calmette Guérin (BCG) vaccination. She presented with a non-healing BCG wound and left axillary swelling associated with one-week fever at 2 months of age. Aspiration under general anaesthesia was done and pus sent for mycobacterium culture grew Mycobacterium tuberculosis complex. The patient improved without anti-tuberculosis treatment.

Keywords: BCG; lymphadenitis; mycobacterium tuberculosis; abscess

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Introduction:

Tuberculosis (TB) is caused by *Mycobacterium tuberculosis,* one of the infectious diseases that affect a large number of human population and causing significant morbidity and mortality. The organism was estimated to infect about one third of world human population with about 2 million deaths annually.[1] Tuberculosis spread by airborne mode and primarily affects lungs. It is associated with overcrowding condition, poor hygiene and increasingly associated with Human Immunodeficiency Virus (HIV) pandemic. In 2008, there were an estimated 1.4 million new cases of TB among persons with HIV infection and TB accounted for 23% of AIDS-related deaths.[2] Diagnosis of TB can be difficult that lead to delayed diagnosis and treatment initiation that might cause further spread. Treatment is also not without complication..

TB preventive measures are BCG vaccination, treatment of patient with latent tuberculosis and other epidemiological measures like prevention of overcrowding, contact tracing and screening as well as chemoprophylaxis in certain age group. This is the case of lymphadenitis of a healthy developed after BCG vaccination.

Case report:

PNI is a 2-month-old baby girl who presented with 1 week history of fever associated with swelling over the left axilla which was increasing in size. She was initially treated with syrup cloxacillin as an outpatient. However, the swelling did not subside and her parents brought her again to the hospital after 5 days on antibiotic. PNI was born at full term via spontaneous vaginal delivery at Universiti Kebagnsaan Malaysia Medical Centre (UKMMC). She was discharged one day after delivery. BCG vaccination was given on the left shoulder before discharged.

On examination, there was no other source of infection but the swelling over the left axilla which was tender, erythematous and fluctuant measuring 5x5cm. BCG wound on the left shoulder has not healed and there was swelling over the area. However, no pus collection noted at the injection site.

She was admitted to the ward and diagnosis of lymph node abscess was made. Aspiration of abscess was performed under general anaesthesia. During the procedure, pus was aspirated and was sent for bacterial and mycobacterial culture. There was no bacterial growth from routine pus culture. Acid fast bacilli (AFB) stain was negative, however, culture

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in Lowenstein Jensen media grew *Mycobacterium tuberculosis* complex after 4 weeks of incubation. Investigations revealed high total white blood cell count of 21.2 $x10^9$/L with lymphocytes predominance and slightly high monocytes count. Blood electrolytes and liver function were normal. She was given intravenous cloxacillin while in the ward and was discharged well after 1 week. She was followed up in the clinic after 2 weeks. The abscess subsided and the BCG site healed well.

Discussion:

Tuberculosis remains one of the deadliest diseases in the world, in 2013 it was estimated 9 million new cases and 1.5 million associated with deaths.[3]Ninety five percent of cases occur in developing country where there were limited resources for treatment and common HIV infection. Tuberculosis is a social disease with medical implications. Poverty, overcrowding and migration of people from high endemic country contributed to the development and spread of the disease. This patient developed suppurative lymphadenitis based on the culture resulted the growth of *Mycobacterium tuberculosis* complex. Usually, tuberculous lymphadenitis presents as painless swelling of one or more lymph nodes. The nodes commonly involved are those of the posterior or anterior cervical chain or those in the supraclavicular fossa.[4] Initially the nodes are discrete and later become matted and the overlying skin inflamed and may eventually developed sinus tract which is slow to heal. In persons not infected with HIV, systemic symptoms are rare unless there is concomitant tuberculosis elsewhere. In the early part of the 20th century, Calmette and Guerin, working at the Institute Pasteur, attenuated a virulent strain of *M. bovis* originally isolated by Nocard from a cow with tuberculous mastitis. By repeated subculture over 13 years, they produced an attenuated strain which, by 1919 was shown to be avirulent in guinea pigs, cows and several other animals. In 1921, the successful vaccination of a newborn boy whose mother had died from severe TB within days of delivery was performed by Weil-Hallein who administered a culture of the BCG orally in three doses of 2mg soon after the birth of the child. The child was thriving after six months despite being in the care of his tuberculous grandmother and living with affected siblings. Following the success of the early vaccination studies, the BCG was distributed worldwide by the Institute Pasteur. The BCG vaccine is administered to 100 million children each year and global coverage rates exceed 80% in countries where TB is endemic. BCG vaccination is a highly cost-effective intervention against severe childhood TB.[5] While BCG generates good level of protection against childhood and disseminated TB, it is less effective against adult pulmonary TB and it does not prevent reactivation of latent pulmonary infection.[6] BCG also has been used as immunotherapeutic in bladder cancer where intravascular instillation is done and it also protective against leprosy. Adverse reaction toward BCG vaccine occurs around 4-30 cases per 1000 vaccinated infant. Regional reactions include lymphadenitis, keloid, suppurative lymphadenitis, whereas disseminated BCG infection which can be fatal is estimated to occur in 0.19-1.56 cases per million vaccines and occur in patient with severe cellular immunodeficiency. In Brazil, from 1974 to 1979 in a study reported the incident of adverse reactions was 0.4 per 1000 following intradermal vaccination using the Moreau strain.[7]In the United Kingdom, an increase in the incidence of BCG associated suppurative lymphadenitis was recorded following the change from the percutaneus administration of Glaxo-Evans 1077 BCG vaccine to intradermal administration of Danish-SSI 1331 BCG vaccine in August 2002.[8] Both the change in strain and route of administration contributed to the increase incidence of adverse reaction. Vaccination at $<$ 1 month old has been identified, as the main predictor of increased risk of lymphadenitis.[9]Such infants had twice the incidence of lymphadenitis as those vaccinated at $>$3 months of age.[10] Diagnosis of BCG lymphadenitis is usually made on clinical ground. Small lymph node enlargement occurs as a natural process after vaccination and not considered as complication. However, when axillary lymph node site become visibly enlarged after BCG vaccination and causes concern to the patient, this is considered adverse reaction. Usually there are lack of systemic symptoms like fever and tenderness over the swelling. However, presence of the symptoms does not exclude the diagnosis. As in this patient had only fever and skin erythema. Other investigations like Mantoux test, blood investigation and chest radiograph are not helpful to diagnose tuberculous lymphadenitis. Laboratory diagnosis for mycobacteria started with performing acid fast bacilli (AFB) staining either by ZiehlNeelsen, Kinyoun or auramine stain that has been using until now. Molecular diagnosis provides definitive differentiation between *M.bovis* BCG and other closely related virulent *Mycobacterium tuberculosis*

complex. In this particular patient, pus from lesion for AFB was negative but growth on Lowenstein Jensen media confirmed to be *Mycobacterium tuberculosis* complex by BD ProbeTec ET system. This system used molecular method to identify the isolate using strand displacement amplification method that uses fluorescence energy transfer for detection. Treatment of BCG lymphadenitis remains controversial. Prevention of suppuration should be the main aim. However, for this patient who already presented with suppurative lymphadenitis, accelerating resolution and prevention of sinus formation is the utmost important. This could be achieved by needle aspiration like in this case. There is no role of antibiotic like erythromycin, and starting antituberculous is not only uneffective but there are possible side effects of the drugs. Results from controlled trial indicate that antituberculosis neither prevent suppuration nor reduce time for resolution.[11]Surgical excision may be considered in patients with multiloculated abscess or failed aspiration. In fine, diagnosis of BCG lymphadenitis is made based on clinical history but culture and identification of the growth corroborate the diagnosis. Suppurative lymphadenitis can be treated with surgery and does not require administration of anti-tuberculosis agents.

Conflict of interest: None declared

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