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Management of Bacillus Calmette-Guérin Lymphadenitis

WM ***Chan,*** YW ***Kwan,*** CW ***Leung***

Abstract Bacillus Calmette-Guérin (BCG) related regional lymphadenitis is not an uncommon complication following BCG vaccination. We present a case series of 11 infants with suppurative BCG lymphadenitis managed in Hospital Authority Infectious Disease Centre of Hong Kong over a 5-year period. All of them presented with isolated left axillary mass which suppurated at a mean of 3.5 months (range 2 to 5 months) after BCG vaccination. The diagnosis of the condition is basically clinical. Five infants who were initially managed with needle aspiration alone showed significant regression in the sizes of their enlarged lymph nodes and surgical excision was spared. Surgical incision and drainage was performed in 5 other infants prior to referral to our centre. They all developed significant irregular scarring and 2 eventually developed keloids over their scars upon healing. We recommend that suppurative BCG lymphadenitis should be managed initially by needle aspiration. Total excision should be considered if aspiration fails or suppuration recurs despite repeated needle aspiration. Incision and drainage is mentioned to be condemned.

Key words Bacillus Calmette-Guérin (BCG); Lymphadenitis; Management

Introduction

The live attenuated Bacillus Calmette-Guérin (BCG) vaccine is the oldest vaccine that continues to be widely used nowadays. It is derived by in vitro attenuation of an isolate of *Mycobacterium bovis* specially cultured in an artificial medium for years and named after its discoverers, the French bacteriologist Albert Calmette and veterinarian Camille Guérin. The product was subsequently distributed to many laboratories, which continue to propagate the vaccine strain under different conditions. The marketed strains of BCG from different pharmaceutical companies are now bacteriologically different.[1]

BCG was first used in humans to prevent tuberculosis (TB) since 1921. It is now used worldwide in childhood immunisation programmes. It helps to protect vaccinees, especially infants and children, against disseminated TB and tuberculous meningitis, with an estimated efficacy of 78% and 64%, respectively.[2] The efficacy for protection against pulmonary tuberculosis in adults and children remains unclear.[3] However, BCG still is one of the most cost-effective vaccines, which only costs about HK$1,600 per life-year gained.[4] In Hong Kong, the universal neonatal BCG immunisation programme was introduced since April 1952, which dovetailed a declining TB notification rate from 697.2 per 100,000 population in that year to 76.36 per 100,000 population (provisional figure) in the year 2009. Neonatal BCG vaccination coverage in Hong Kong has been persistently around 99% since 1980.[5]

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Complications from BCG Vaccination

BCG vaccine is considered to be safe and has a low incidence of serious adverse reactions.[6,7] The most common complications after receiving BCG are local reactions and regional lymphadenopathy.[8-10] The local reactions at the inoculation site can range from erythema and induration, to the formation of papule, discharging ulcer or abscess. Regional lymphadenopathy arises as a result of enlargement of ipsilateral lymph nodes, principally involving the axillary, and rarely, the lower cervical chain. The higher the BCG injection site above the insertion of the tendon of the deltoid muscle, the higher the likelihood of cervical lymphadenopathy, if regional complication does occur. Serious complications such as regional or distant soft tissue granulomas, osteomyelitis and disseminated disease (disseminated BCGosis) are rare, which mainly affect patients with impaired immunity, like those with acquired immunodeficiency syndrome (AIDS) or primary immunodeficiencies.[11-13] However, similar complications can rarely occur in previously healthy or immunocompetent individuals. Notwithstanding, further investigations for an underlying aetiology or immune defect is warranted whenever serious complications develop after BCG vaccination.

BCG Lymphadenitis

Regional lymph node enlargement after BCG vaccination generally undergoes spontaneous resolution but may occasionally progress slowly to become suppurative.[13,14] This is a continuous spectrum of lymph node reactions and there is no specific guideline or recommendation to clearly define and differentiate normal from abnormal. The term "BCG lymphadenitis" is usually coined when ipsilateral axillary, supraclavicular or lower cervical lymph node enlargement developing after BCG vaccination is severe enough to arouse significant concern from the child care provider to seek medical attention.[14]

Types of BCG Lymphadenitis

There are two forms of BCG lymphadenitis.[15,16] The non-suppurative form (simple form) is characterised by a benign clinical course and the lesion resolves spontaneously without any sequelae over a period of weeks[17] (Figures 1a & 1b). The suppurative form is marked by the progressive enlargement of regional lymph nodes leading to a collection of suppurative material, with recognisable fluctuation in the swelling. Overlying skin changes is universal, with

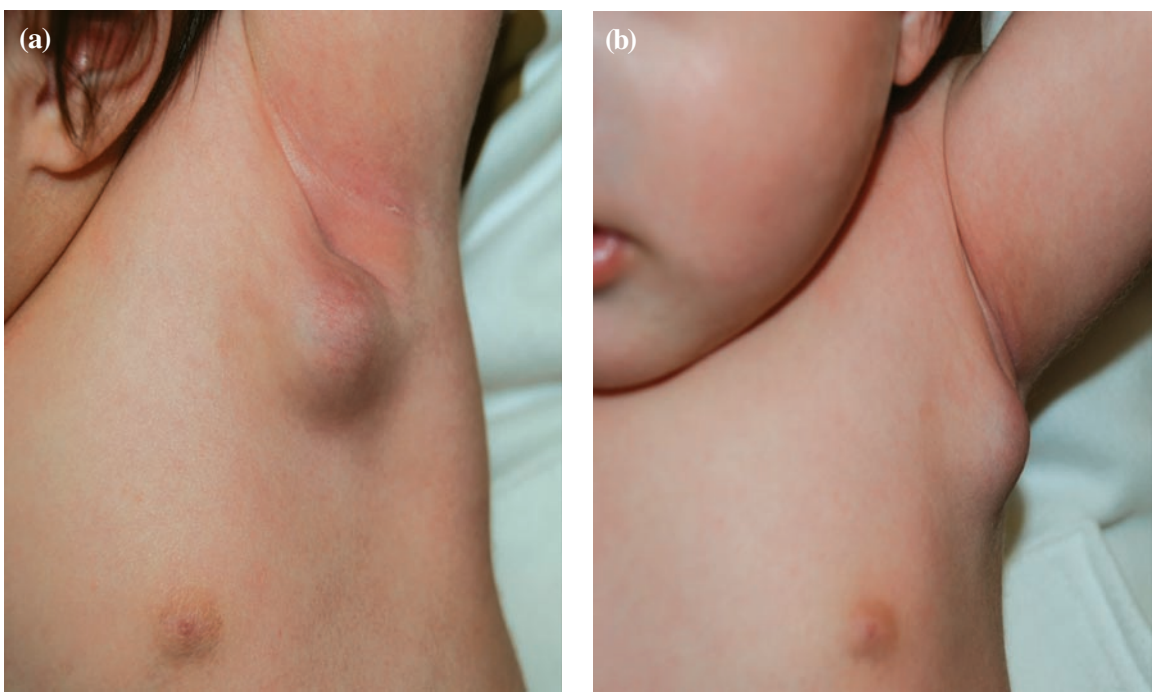

Figure 1 Two views of non-suppurative BCG lymphadenitis in an infant.

erythema, edema, increased pigmentation and pustule formation (Figures 2a & 2b). If left untreated, the suppuration will eventually rupture, leading to persistent caseous discharge and sinus formation (Figure 3). Wound healing inevitably takes several months, which is unpleasant to both patients and their care providers. Frequent and meticulous wound dressing is required, and secondary bacterial infection, unsightly scarring or keloid formation are not uncommon sequelae.[18]

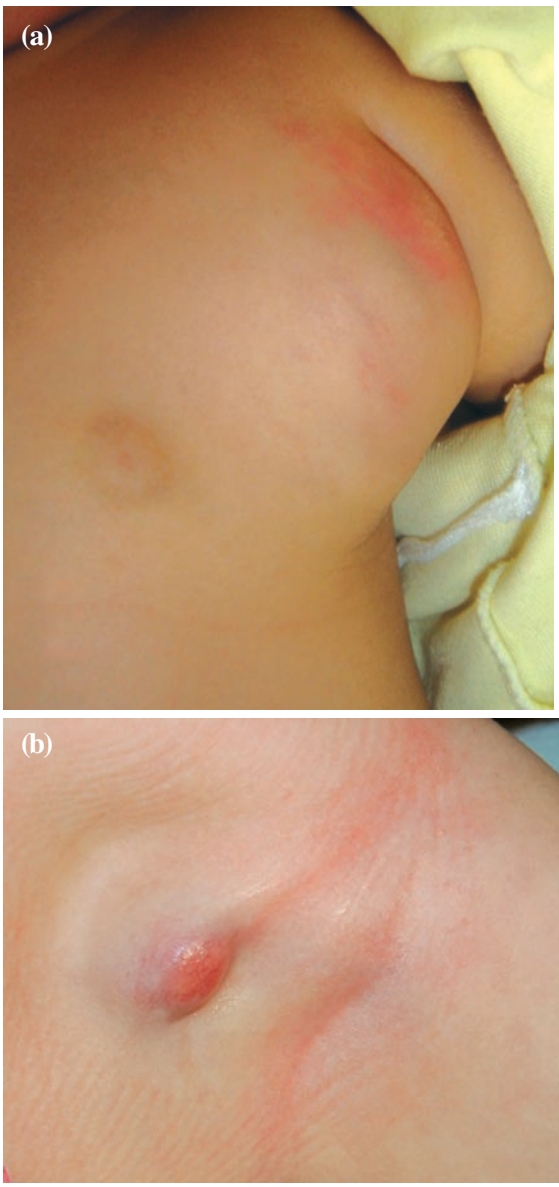

Figure 2 Suppurative BCG lymphadenitis before spontaneous rupture.

Case Series

Infants suffering from BCG lymphadenitis are commonly referred to the Hospital Authority Infectious Disease Centre of Hong Kong for further evaluation. We present an illustrative case series to describe the characteristics and outcome of infants affected by the condition who were managed in our centre over a 5-year period. This is followed by a review of the risk factors for development of the disease entity, clinical features and approach to its proper management.

Table 1 summarises our recent experience in the management of 11 infants who presented with suppurative BCG lymphadenitis from January 2006 to December 2010. Seven of them were male infants (male to female ratio of 1.75 to 1). All of them had received BCG vaccination (9 at birth, 1 at 2 months and 1 at 11 months of age) and presented with isolated left axillary mass which later suppurated as the only abnormal physical finding at a mean of 3.5 months (range 2 to 5 months) after vaccination. All were thriving well and none of them developed fever or constitutional symptoms. Tuberculin skin tests were performed in 7 of them using 2 units of tuberculin (PPD-RT23) administered by the Mantoux method. Six were positive (≥10 mm

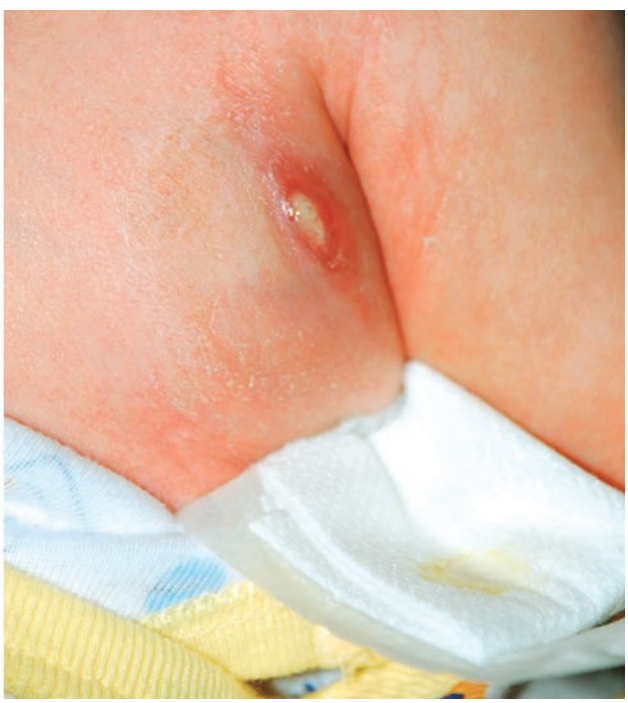

Figure 3 Persistent discharging sinus in suppurative BCG lymphadenitis after spontaneous rupture.

Table 1 Characteristics and outcome of 11 infants with suppurative BCG lymphadenitis

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10	Case 11
Sex	F	M	M	M	M	M	F	M	M	F	F
DOB	Nov 05	Dec 08	Nov 08	Aug 08	Jul 08	Aug 09	Sep 09	Dec 09	Feb 09	Apr 10	May 09
Age at presentation (months)	2	2	3	3	5	5	4	5	13	4	5
Duration after vaccination (months)	2	2	3	3	5	5	4	5	2	4	3
Size of left axillary LN at presentation (cm)	3	3 x 1.5	2.5	2.5 x 2.5	1.5	1.5 x 1.5	2 x 1	1 x 2	3 x 4	1.5	1.5 x 1.5
Max size of fluctuation (cm)	4 x 5	2 x 1.5	2 x 1	1	1	2 x 2	1	2.5 x 2.5	2 x 1.5	1.5	2.4 x 1.8
Appearance of BCG injection site at presentation	Normal scar	Normal scar	Normal scar	Normal scar	Normal scar	Normal scar	Normal scar	Scabbed	Normal scar	Normal scar	Normal scar
Mantoux test (2 units)	N/A	13 mm	21 mm	23 mm	19 mm	9 mm	30 mm	N/A	10 mm	N/A	N/A
CXR	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Bacteriologic investigation of LN content	*M. bovis* isolated from culture	*M. bovis* isolated from culture	Culture-negative	Not performed by referring doctor	*M. bovis* isolated from culture	*M. bovis* isolated from culture	*M. bovis* isolated from culture	*M. bovis* isolated from culture	*M. bovis* isolated from culture	*M. bovis* isolated from culture	N/A
Management	I&D prior to referral	I&D prior to referral	I&D prior to referral	I&D prior to referral	I&D performed twice for failed needle aspiration	Needle aspiration	Needle aspiration	Needle aspiration	Needle aspiration	Needle aspiration	Spontaneous rupture 1 month after presentation
Wound care	Daily wound toilet and dressing until complete wound healing					None	None	None	None	None	Dressing for 2 weeks
Outcome at latest follow-up by end of Dec 10	Wound healed with irregular scar and 1 cm keloid in 4 months	Wound healed with 1 cm irregular scar in 3 months I&D for isolated left supraclavicular lymphadenitis appearing shortly after resolution of axillary lymphadenitis, wound took 4 more months to heal.	Wound healed with 1 cm irregular scar in 6 months	Wound healed at 4 months 1 cm keloid requiring plastic surgical excision	Wound healed with 2 cm irregular scar in 3 months	Complete resolution in 1 month Spontaneous rupture of adjacent LN which resolved in 2 weeks	Complete resolution in 0.5 month Spontaneous rupture of adjacent LN which resolved in 4 weeks	LN almost completely resolved (0.2 cm at 5 months)	LN resolving (0.5 cm at 6 months)	LN resolving (0.4 cm at 3 months)	Wound healed in 2 weeks with 3 mm depressed scar, LN resolved in 4 months

CXR: chest radiograph; I&D: incision and drainage; LN: lymph node; N/A: not recorded or not available; PCR: polymerase chain reaction

induration at 48 to 72 hours after intradermal injection) and the remaining one had an induration of 9 mm. None had abnormal findings on chest radiographs. Bacteriologic investigations were performed in 9 infants. *Mycobacterium bovis* (BCG strain) was isolated from culture of the needle aspirates obtained from the enlarged suppurative axillary lymph nodes of 5 infants. Three of 5 infants who had incision and drainage performed (Cases 1-4 prior to referral to our care and Case 5 after failed needle aspiration) were also culture-positive for BCG. Of the remaining 2 patients, 1 was culture-negative (Case 3) and the other (Case 4) was not subjected to microbiologic investigations by the referring doctor. One infant (Case 11) had spontaneous rupture with minimal discharge of the axillary lymph node 1 month after presentation.

Needle aspirations were attempted in 6 infants (Cases 5-10). One of them (Case 5) failed the attempt (dry tap) and subsequently underwent incision and drainage twice despite our referral for surgical excision. Wound healing took 3 months in this infant and was not satisfactory as he developed a 2 cm irregular scar. All 5 infants who were initially managed with successful needle aspiration alone showed significant regression in the sizes of their axillary lymph nodes after the procedure. Two infants with the lymph node sizes of 1-2 cm resolved completely over 2 to 4 weeks (Cases 6-7). However, enlargement of adjacent solitary lymph nodes occurred about 1 month after needle aspiration and spontaneous rupture ensued before the infants returned for follow-up. Despite this apparent failure of hastening recovery with needle aspiration, the discharge from the subsequently enlarging adjacent lymph nodes was minimal, requiring only simple dressing, and stopped spontaneously, one after 2 weeks and the other 4 weeks. The other 3 patients (Cases 8-10) had regression of lymph node size from 2.5 to 0.2 cm (92% reduction), 2 to 0.5 cm (75% reduction), and 1.5 to 0.4 cm (73% reduction) at 5, 6 and 3 months after needle aspiration, respectively, with no further complication or need for surgical intervention up to the time of latest follow-up (Figures 4a & 4b). In summary, five of the 6 infants who were managed initially with needle aspiration were spared surgical excision (Cases 6-10). The remaining one (Case 5) unfortunately was managed with a surgical procedure which was not our intention, resulting in suboptimal wound healing (Figure 5).

Surgical incision and drainage had already been performed in 4 other infants (Cases 1-4) prior to referral to our centre for further management of their persistently discharging wounds, and was also performed in the one

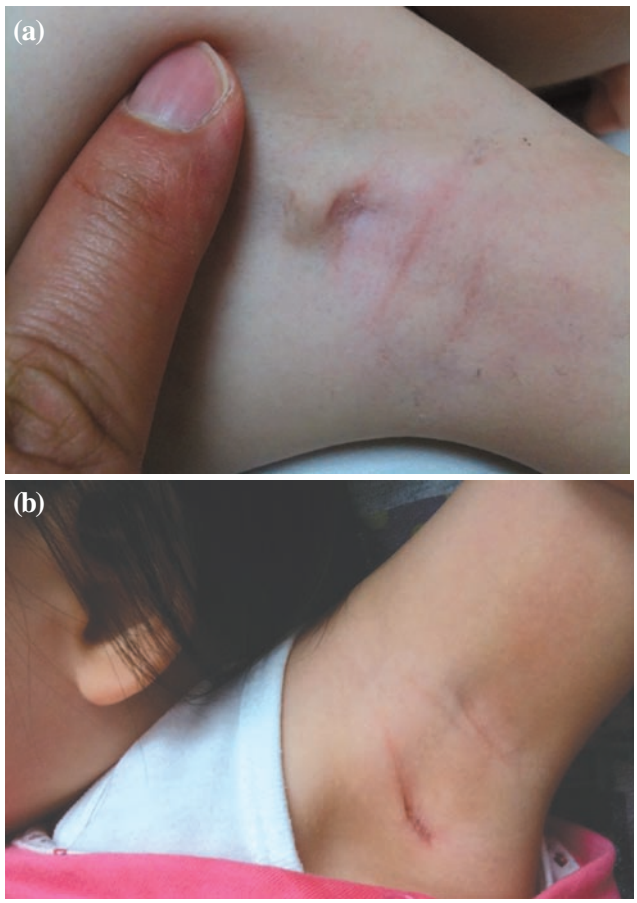

Figure 4 Wound healing after needle aspiration.

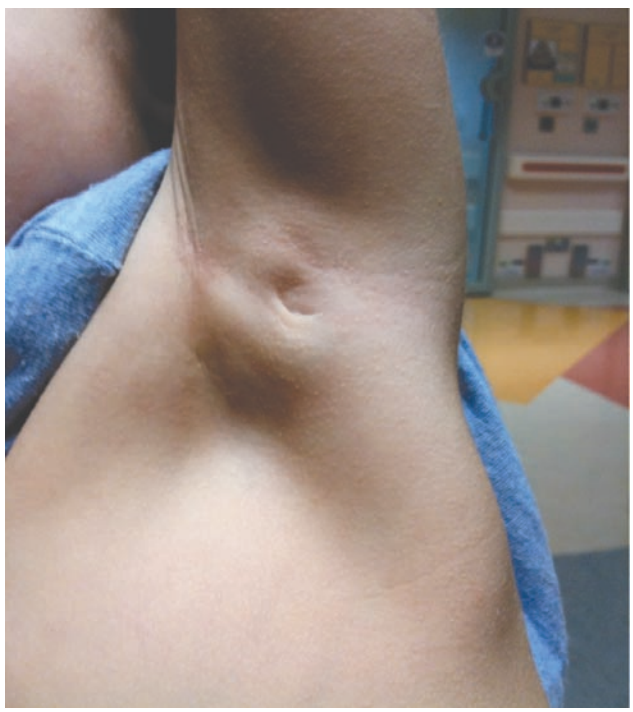

Figure 5 Wound healing after incision and drainage.

referred for surgical excision after failed needle aspiration in our centre (Case 5). Daily wound toilet and dressing for an extended period in hospital, and then clinic until complete resolution were required. Unfortunately, upon healing all 5 of them developed significant irregular scarring and 2 eventually developed keloids over their scars, with 1 necessitating plastic surgical excision. The mean duration from incision and drainage to complete wound healing and resolution of the lymph node enlargement in these 5 infants who were managed by incision and drainage was 4 months (range 3 to 6 months).

The infant (Case 11) who had spontaneous rupture of the axillary lymph node that suppurated 1 month after presentation only required daily simple dressing. The draining sinus healed after 2 weeks and resolution of the lymphadenitis took 4 months to complete, leaving behind a 3 mm depressed scar. The resolution in this infant was fortunately satisfactory because the discharging content of the suppuration was not copious.

Isolated left supraclavicular lymphadenitis occurred in 1 infant (Case 2) 4 months after BCG vaccination, shortly after resolution of the axillary lymphadenitis. Unfortunately, incision and drainage was performed by surgeon and the wound took 4 more months to heal. Immune function tests performed in this patient were normal.

Review of BCG Lymphadenitis

The risk factors associated with BCG lymphadenitis can be either host-related or vaccine-related.[14,19-21]

(A) Host-related factors:

1. Age. Vaccine given during the neonatal period is associated with a higher risk of regional lymphadenitis.
2. Immunocompetence. Immunocompromised patients such as those suffering from severe combined immunodeficiency or AIDS have increased complication rates of local as well as disseminated BCG infections.
3. Route of administration. Failure of intradermal injection may result in inadvertent subcutaneous administration, which contributes to increased complication rate.[10, 11]
4. Race. A wide variation in the incidence of BCG-related complications has been reported in different countries and ethnic groups.

(B) Vaccine-related factors:

1. Dosage of BCG vaccine. Overdosage may lead to more severe adverse reactions.
2. Residual virulence of the BCG strain. BCG strains from different pharmaceutical manufacturers are known to have different reactogenicity.[11]
3. Viability of final vaccine product (the relative proportions of living and dead bacilli). This is related to the quality of the administered vaccine and is affected by storage conditions such as the cold chain.

Clinical Features

A detailed and accurate documentation of the symptoms and signs is imperative for making the proper diagnosis.[15] Sometimes, it may be difficult to differentiate BCG-related reaction from lymphadenitis or abscess formation secondary to acute pyogenic bacterial infection, or rarely, chronic tuberculous or non-tuberculous mycobacterial infection, although in general the latter two conditions are more "cold" than "hot" in presentation i.e. the classical TB or non-tuberculous mycobacterial (caused by rapid growers such as *Mycobacterium chelonae*) lymph node or soft tissue abscess is a cold abscess. The following features should lead to the suspicion of BCG as the aetiology:

1. History of BCG vaccination on the ipsilateral arm.
2. Onset is usually 2 to 4 months after BCG vaccination, although it may range from 2 weeks to 6 months. Almost all cases occur within 24 months.
3. There is absence of fever or other constitutional symptoms.
4. Absent or minimal local tenderness over the lesion(s).
5. >95% of cases involve ipsilateral axillary lymph nodes, but supraclavicular or cervical glands may be involved in isolation or in association with axillary lymphadenopathy.
6. Only 1 to 2 discrete lymph nodes are enlarged (clinically palpable) in the majority of cases. Involved lymph nodes are rarely matted together.

Diagnosis

The diagnosis of BCG lymphadenitis is basically clinical. The patient must have a history of recent BCG vaccination that should normally be at birth in Hong Kong, so the commonest age of presentation is from 2 to 4 months of age, and almost all are diagnosed within the first two years of life. The recognition of characteristic clinical features ipsilateral to the site of BCG vaccination that is not associated with fever or constitutional symptoms, and in the absence of other attributable causes of lymphadenitis, can usually lead to a diagnosis.[15,16]

Further investigation is of limited value except to exclude disseminated BCG infection in the immunocompromised host, which should have other suggestive clinical signs and symptoms, and superinfection of the involved lymph

node(s) by pyogenic bacteria. Clinically, it can be difficult to differentiate BCG lymphadenitis from tuberculous lymphadenitis notwithstanding the temporal relationship of recent BCG vaccination and the common age of presentation, though isolated tuberculous axillary lymphadenitis is extremely rare.[22] A tuberculin skin test is not useful for making a diagnosis of BCG lymphadenitis with typical presentation. The test is expected to be positive after recent BCG vaccination in immunocompetent host so it cannot help to differentiate reaction caused by *M. bovis* or *M. tuberculosis*. A positive tuberculin skin test and, if available, supplemented by a negative interferon-gamma release assay (IGRA) for *M. tuberculosis*, together with a normal chest radiograph (CXR) might help in diagnosis by excluding TB in the rare situation of BCG lymphadenitis presenting atypically as an isolated left cervical mass without concomitant axillary involvement. However, information on the negative predictive value of IGRA and its utility in infants to exclude infection by *M. tuberculosis* remains controversial, and over-reliance on the test in this young age group is discouraged. The absence of any reaction to the tuberculin skin test in an infant presenting with axillary and/or cervical lymphadenopathy who has received BCG vaccination and is not thriving should prompt further investigation for the possibility of primary immunodeficiency. CXR examination is the bare minimum that one should perform in all cases. It should be normal in an infant with localised BCG lymphadenitis. Any abnormal pulmonary infiltrates or opacities suggestive of intrathoracic lymph node enlargement should prompt further investigation to exclude tuberculosis or disseminated BCG infection.

Acid fast bacilli (AFB) may be seen on microscopy of any discharge or aspirate from the suppurative lymph node.[23] A positive *M. bovis* culture can confirm the diagnosis of BCG lymphadenitis. However, a negative mycobacterial culture, or even a positive culture of pyogenic bacteria, cannot exclude BCG as the underlying cause because viable *M. bovis* may not be isolated, and secondary bacterial infection can superimpose on BCG lymphadenitis. The definitive identification of BCG isolated by appropriate culture requires phage typing or mycobacterial gene analysis.[24] The conventional polymerase chain reaction (PCR) test for *M. tuberculosis* complex is not specific enough to differentiate *M. bovis* from *M. tuberculosis*.

Treatment

Three treatment options have been described for BCG lymphadenitis.

(A) Antibiotic Therapy

Several antibiotics (e.g. erythromycin) and anti-tuberculous medications (e.g. isoniazid and rifampicin) have been used. There are case series suggesting their efficacy.[25, 26] Well controlled trials involving more subjects have shown that these drugs cannot prevent suppuration nor shorten the duration of healing.[27-32] It should also be noted that BCG is generally not susceptible to pyrazinamide, a first-line agent for treating TB. Antibiotic therapy is, however, often indicated for treatment of suppurative lymphadenitis proven to be caused by superinfection with pyogenic bacteria such as *Staphylococcus aureus* or *Streptococcus pyogenes*, as definitive therapy or an adjunct to surgical intervention.

(B) Needle Aspiration

For suppurative BCG lymphadenitis, given time there is almost universal development of spontaneous perforation and sinus formation if left untreated. Recent studies have shown that needle aspiration can help to prevent this complication and shorten the duration of healing, apart from offering valuable diagnostic information.[33-35] Sometimes repeated aspirations are required for optimal management, and wider-bored needles are preferred for ease of evacuation of thick inflammatory materials. Banani and Alborzi demonstrated in their randomised controlled trial that patients with suppurative BCG lymphadenitis treated with needle aspiration had a significantly higher chance of wound healing without surgical excision (95% vs 68%), and shorter duration of recovery (6.7 weeks vs 11.8 weeks) when compared with the control group.[34] It is considered to be a safer option when compared with total surgical excision, which likely will require general anaesthesia in young infants.[33,34] Others have advocated the use of local isoniazid instillation therapy during needle aspiration.[27] Whether this offers additional benefit remains to be confirmed.

(C) Surgical Excision

Surgical excision is a definitive way to remove the affected lymph node(s) and promote early cure and better wound recovery. However, the patient needs to bear the risks of general anaesthesia in addition to the risks of surgical manipulation, which are considerably higher in infants as compared to older individuals.[34] Surgical excision should be considered as the last resort in case of failed needle aspiration (dry tap or recollection despite repeated aspirations), and in those patients with matted and multiloculated lymph nodes.[34] Simple incision and drainage

is not recommended because it results in persistent discharges requiring cumbersome dressing, inadequate evacuation of inflammatory materials, suboptimal wound healing, scarring and delayed recovery.[33,36,37]

Discussion

Our case series suggested that needle aspiration in the management of suppurative BCG lymphadenitis is more likely to result in better cosmetic outcome as compared to incision and drainage in appropriately selected patients. Even if spontaneous rupture ensued in some of our patients who underwent needle aspiration, the duration of wound dressing required appeared to be shorter. No complication was encountered during and after needle aspiration and the procedure was simple and well tolerated. Wound healing following incision and drainage is expected to be unsatisfactory, and resolution is prolonged. Not all suppurative BCG lymphadenitis should be managed by excision, although the procedure itself appears to be an instant cure. Some infants can be spared invasive surgical procedures and an initial less traumatic approach with needle aspiration should be considered. Close monitoring of the infant is warranted after needle aspiration as recollection is not uncommon, necessitating repeated aspiration, and emergence of enlarging adjacent nodes with or without suppuration can occur, which may require early intervention. We suggest that surgeons should reconsider surgical excision as the last resort for definitive treatment of suppurative BCG lymphadenitis. It should preferably be reserved for infants who failed needle aspiration or failed to respond to repeated needle aspirations, after balancing the risks of general anaesthesia and potential surgical complications in very young infants. Incision and drainage should be avoided at all costs due to the risk of resultant persistent draining wound.[36] In addition, delayed wound healing and unsatisfactory scar formation can be problematic. A management algorithm is proposed as in Figure 6.

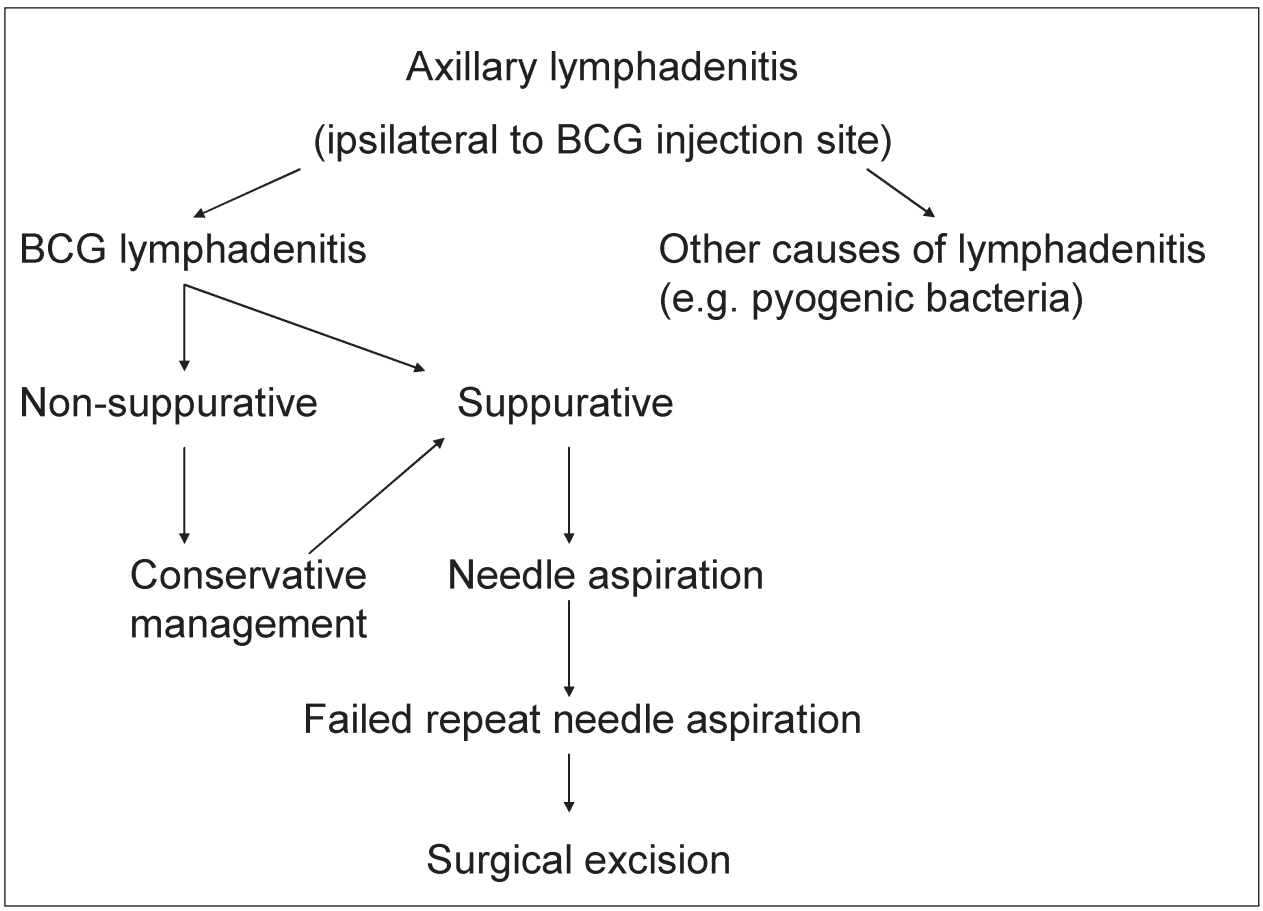

Figure 6 Management algorithm for BCG lymphadenitis.

Good immunisation technique, correct dosage and quality control of the BCG vaccine are presumed to be of paramount importance in avoiding untoward reactions following its administration. To prevent severe local BCG lymphadenitis and more extensive or disseminated BCG infection, avoidance of BCG vaccination in patients with known primary or acquired immunodeficiencies should be seriously considered. However, it is very difficult, if not impossible, to suspect or identify primary immunodeficiency at or soon after birth, unless there is a known family history or the patient presents with features of a known immunodeficiency syndrome (e.g. Di George syndrome). World Health Organization has made human immunodeficiency virus (HIV) infection in infants a contraindication to BCG vaccination in the revised consensus statement of 2008, though information on the risk-benefit ratio, especially in developing countries, is limited and the recommendation may be subject to further debate.[13,38,39] We in Hong Kong have adopted the revised WHO recommendation of withholding BCG vaccination in infants known to be HIV positive as well as those born of HIV-infected mothers, pending testing for HIV infection.[40]

Conclusion

In summary, non-suppurative BCG lymphadenitis is a relatively common benign condition that will regress spontaneously over a matter of weeks to months. Reassurance and masterly inactivity with regular follow-up are all that is required. If the enlarged lymph node progresses to suppuration, then needle aspiration (which can be repeated if necessary) should be performed first in an attempt to hasten resolution by emptying its content, and provide material for appropriate microbiological investigations. Complete surgical excision should be considered for failed needle aspiration or recurrence of suppuration despite repeated aspirations. The addition of antimicrobial therapy is of no proven benefit. Incision and drainage is mentioned to be condemned.

References

1. Fine PE. The BCG story: lessons from the past and implications for the future. Rev Infect Dis 1989;11(Suppl 2):S353-9.
2. Colditz GA, Brewer TF, Berkey CS, et al. Efficacy of BCG vaccine in the prevention of tuberculosis: meta-analysis of the published literature. JAMA 1994;271:698-702.
3. Wilson ME, Fineberg HV, Colditz GA. Geographic latitude and the efficacy of Bacillus Calmette-Guérin vaccine. Clin Infect Dis 1995;20:982-91.
4. Trunz BB, Fine P, Dye C. Effect of BCG vaccination on childhood tuberculous meningitis and miliary tuberculosis worldwide: a meta-analysis and assessment of cost-effectiveness. Lancet 2006; 367:1173-80.
5. Department of Health, HKSAR. Annual Report of Tuberculosis and Chest Service, 2000.
6. Lotte A, Wasz-Hockert, Poisson N, et al. Second IUATLD study on complications induced by intradermal BCG-vaccination. Bull Int Union Tuberc and Lung Dis 1988;63:47-59.
7. Milstien JB, Gibson JJ. Quality control of BCG vaccine by WHO: a review of factors that may influence vaccine effectiveness and safety. Bull World Health Organ 1990;68:93-108.
8. Romanus V, Fasth A, Tordai P, Wiholm BE. Adverse reactions in healthy and immunocompromised children under six years of age vaccinated with the Danish BCG vaccine, strain Copenhagen 1331: implications for the vaccination policy in Sweden. Acta Paediatr 1993;82:1043-52.
9. Szczuka I. Adverse events following immunization with BCG vaccine in Poland 1994-2000. Przegl Epidemiol 2002;56:205-16.
10. Daoud W. Control of an outbreak of BCG complications in Gaza. Respirology 2003;8:376-8.
11. Awad R. BCG vaccine and post-BCG complications among infants in Gaza Strip, 1999. East Mediterr Health J 2001;7:211-20.
12. O'Brien KL, Ruff AJ, Louis MA, et al. Bacillus Calmette-Guérin complications in children born to HIV-1-infected women with a review of the literature. Pediatrics 1995;95:414-8.
13. Hesseling AC, Cotton MF, Fordham von Reyn C, et al. Consensus statement on the revised World Health Organization recommendations for BCG vaccination in HIV-infected infants. Int J Tuberc Lung Dis 2008;12:1376-9.
14. Victoria MS, Shah BR. Bacillus Calmette-Guérin lymphadenitis: a case report and review of the literature. Pediatr Infect Dis J 1985;4:295-6.
15. Helmick CG, D'Souza AJ, Goddard RN. An outbreak of severe BCG axillary lymphadenitis in Saint Lucia, 1982-1983. West Indies Med J 1986;35:12-7.
16. Lotte A, Wasz-Hockert O, Poisson N, et al. Second IUATLD study on complications induced by intradermal BCG-vaccination. Bull Int Union Tuberc Lung Dis 1988;63:47-59.
17. Singla A, Singh S, Goraya JS, Radhika S, Sharma M. The natural course of nonsuppurative Calmette-Guérin bacillus lymphadenitis. Pediatr Infect Dis J 2002;21:446-8.
18. Sagić L. Adverse events following BCG vaccination. Med Pregl 2004;57(Suppl 1):41-7.
19. Hsing CT. Local complications of BCG vaccination in pre-school children and newborn babies. Bull World Health Organ 1954; 11:1023-9.
20. Gołębiowska M, Andrzejewska E, Stryjewska I, Baranowska H, Drazkiewicz A. Adverse events following BCG vaccination in infants and children up to 36 months of age. Przegl Epidemiol 2008;62:71-5.
21. Talbot EA, Perkins MD, Silva SF, Frothingham R. Disseminated Bacille Calmette-Guérin disease after vaccination: case report and review. Clin Infect Dis 1997;24:1139-46.
22. Ustvedt HJ. Local reactions in BCG vaccination. Bull World Health Organ 1950;2:441-68.

23. Gupta K, Singh N, Bhatia A, Arora VK, Singh UR, Singh B. Cytomorphologic patterns in Calmette Guérin Bacillus lymphadenitis. Acta Cytol 1997;41:348-50.
24. Yan JJ, Chen FF, Jin YT, et al. Differentiation of BCG-induced lymphadenitis from tuberculosis in lymph node biopsy specimen by molecular analysis of pcnA and oxyR. J Pathol 1998;184:96-102.
25. de Souza GR, Sant'Anna CC, Lapa e Silva JR, Mano DB, Bethlem NM. Intradermal BCG vaccination complications - analysis of 51 cases. Tubercle 1983;64:23-7.
26. Power JT, Stewart IC, Ross JD. Erythromycin in the management of troublesome BCG lesions. Br J Dis Chest 1984;78:192-4.
27. Noah PK, Pande D, Johnson B, Ashley D. Evaluation of oral erythromycin and local isoniazid instillation therapy in infants with Bacillus Calmette-Guérin lymphadenitis and abscesses. Pediatr Infect Dis J 1993;12:136-9.
28. Caglayan S, Yegin O, Kayran K, Timocin N, Kasirga E, Gun M. Is medical therapy effective for regional lymphadenitis following BCG vaccination? Am J Dis Child 1987;141:1213-4.
29. Kuyucu N, Kuyucu S, Ocal B, Teziç T. Comparison of oral erythromycin, local administration of streptomycin and placebo therapy for non-suppurative Bacillus Calmette-Guérin lymphadenitis. Pediatr Infect Dis J 1998;17:524-5.
30. Close GC, Nasiiro R. Management of BCG adenitis in infancy. J Trop Pediatr 1985;31:286.
31. Baki A, Oncü M, Usta S, Yildiz K, Karagüzel A. Therapy of regional lymphadenitis following BCG vaccination. Infection 1991;19:414-6.
32. Hengster P, Sölder B, Fille M, Menardi G. Surgical treatment of Bacillus Calmette Guérin lymphadenitis. World J Surg 1997;21:520-3.
33. Caglayan S, Arikan A, Yaprak I, Aksoz K, Kansoy S. Management of suppuration in regional lymph nodes secondary to BCG vaccination. Acta Paediatr Jpn 1991;33:699-702.
34. Banani SA, Alborzi A. Needle aspiration for suppurative post-BCG adenitis. Arch Dis Child 1994;71:446-7.
35. Sataynarayana S, Mathur AD, Verma Y, Pradhan S, Bhandari MK. Needle aspiration as a diagnostic tool and therapeutic modality in suppurative lymphadenitis following Bacillus Calmette Guérin vaccination. J Assoc Physicians India 2002;50:788-91.
36. Tam PK, Stroebel AB, Saing H, Lau JT, Ong GB. Caseating regional lymphadenitis complicating BCG vaccination: a report of 6 cases. Arch Dis Child 1982;57:952-4.
37. Oğuz F, Müjgan S, Alper G, Alev F, Neyzi O. Treatment of Bacillus Calmette-Guérin associated lymphadenitis. Pediatr Infect Dis J 1992;10:887-8.
28. Hesseling AC, Johnson LF, Jaspan H, et al. Disseminated Bacille Calmette-Guérin disease in HIV-infected South African infants. Bull World Health Organ 2009;87:505-11.
39. Azzopardi P, Bennett CM, Graham SM, Duke T. Bacille Calmette-Guérin vaccine-related disease in HIV-infected children: a systematic review. Int J Tuberc Lung Dis 2009;13:1331-44.
40. Scientific Committee on AIDS and STI (SCAS), Centre for Health Protection, Department of Health, HKSAR. The use of BCG vaccine in HIV infected patients, 2009. http://www.info.gov.hk/aids/pdf/g215.pdf