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Correspondence to Dr C A Johnson, Department of Pediatrics, Bowman Gray School of Medicine, 300 South Hawthorne Road, Winston-Salem, North Carolina 27103, USA.

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Caseating regional lymphadenitis complicating BCG vaccination: a report of 6 cases

PAUL K H TAM, A B STROEBEL, H SAING, J T K LAU, AND G B ONG

Department of Surgery and Department of Microbiology, University of Hong Kong, Queen Mary Hospital, Hong Kong

SUMMARY Six infants had caseating regional lymphadenitis complicating BCG vaccination. There was a delayed onset and a lack of immediate vaccination complications. Three infants had frank abscesses. Additional affected nodes undetected clinically were found at operation in all cases. All lymph nodes contained tubercles, 3 showing acid-fast bacilli, 2 of which grew *Mycobacterium bovis*. Complete excision followed by antituberculous chemotherapy produced satisfactory results.

Although the efficacy of BCG vaccination in protection against tuberculosis is still a subject of much debate,[1] the procedure has generally been regarded as safe. Complications have been reported as uncommon.[2] Development of regional lymphadenitis has been described. However these data were concerned mainly with epidemiology.[3] Detailed information on microbiology, pathology, management and its result were lacking.

We have recently noted an increase in incidence of this form of complication in our hospital—six cases in 6 months (June 1981–November 1981) and would therefore like to report our experience.

Patients

All 6 infants in this series received BCG vaccination during the first week of life. Vaccination was administered by a special nurse, with the French vaccine, at a dose of 0·005 mg, intradermally in the left arm. Each infant presented with an axillary mass on the side of the vaccination, and one had a supraclavicular mass in addition. The onset varied from 3 to 8 months after vaccination, averaging 6 months (Table). Only one infant gave a history of immediate post-vaccination complication consisting of a rash over the vaccination site which had subsided after a week.

On examination, all the infants were well and active. Only one infant had a low grade fever of 37·5°C. Three infants had frank axillary abscesses which were pointing, while the other 3 infants had solitary axillary masses which were mainly solid but with areas of fluctuation clearly demonstrable.

Management and results

Excision was performed for all the infants under general anaesthesia. Clinically solitary lesions were invariably found to be associated with some other enlarged nodes deeper down and all these were removed. Frank abscesses were not incised but rather excised *in toto* with elliptical incisions. The wounds were sutured in 3 infants and left open in three.

On cutting open, all enlarged nodes showed caseation at centres. Histopathology of the abscess walls and lymph nodes of all 6 infants showed the presence of tubercles with caseous necrosis, epithelioid cells, and Langhans' giant cells.

The caseous material obtained either in the frank abscess or in the centres of enlarged nodes was examined microscopically and cultured for acid-fast bacilli. Acid-fast bacilli were demonstrated in only 3 of 6 patients. Only 2 of these were culture positive and in each *Mycobacterium bovis* was isolated.

Immunological parameters including total lymphocyte counts, T- and B-cell counts, and lymphocyte response to phytohaemagglutinin and serum immunoglobulin levels were examined and found to be normal. IgG antibodies directed against the antigen 6 fraction of *Mycobacterium tuberculosis* were increased only in the 3 cases in whom frank abscess formation was present.

Table *Case summary. All patients had BCG vaccination with French vaccine intradermally on left arm at a dose of 0·005 mg during the first week of life*

Case	*Sex*	*Age (months)*	*Immediate local complication*	*Operative findings*	*Pathology*	*AFB microscopy*		*AFB culture*
						LN	*Pus*	
1	F	7	—	1½ × 1½ caseating LN, 1 smaller LN	Tubercles, central necrosis, epithelioid cells, Langhans' giant cells, dystrophic calcification	−	+ (Few)	−
2	M	8	—	1-cm diameter abscess, pointing to skin, 1 caseating LN beneath	Granulomas, central caseation, epithelioid cells	−	−	−
3	M	3	—	1-cm diameter abscess, 1 underlying LN 1-cm diameter	Caseating granulomas, Langhans' giant cells	+ (Both abscess wall + LN)	+	+ (*Mycobacterium bovis*)
4	M	5	+ (Rash locally)	1-cm diameter axially abscess, + 3/4-cm diameter supraclavicular abscess	Numerous caseating centres, epithelioid cells, well-formed Langhans' giant cells	−	−	−
5	F	6	—	1 enlarged fluctuant LN, other enlarged LNs deeper down	LN destroyed by caseating granulomas, extending to fibrofatty tissue and dermis	−	−	−
6	F	4	—	Matted LNs, some with central necrosis	Tubercles, central caseous necrosis, epithelioid cells	−	+	+ (*Mycobacterium bovis*)

AFB = acid-fast bacilli. LN = lymph node.

A course of antituberculous treatment consisting of isoniazid 10 mg/kg a day and rifampicin 15 mg/kg a day for 6 months, and streptomycin 20 mg/kg a day for 2 months was given postoperatively to all the patients. All the wounds healed after excision whether sutured or not. No recurrence was detected on follow-up which ranged from 3 to 9 months.

Discussion

The risk of caseating regional lymphadenitis complicating BCG vaccination has not received much attention recently. In situations where epidemiological studies are carried out and this possibility specifically looked for,[3] there is little difficulty in recognising the condition. However, in the more usual circumstances when the attending physician is seeing the patients for the first time, such a diagnosis may not be obvious. The difficulty is due to (1) a delayed onset of symptoms (in this series it ranged from 3 to 8 months with an average of 6 months); (2) the usual absence of immediate vaccination complications as illustrated by the occurrence of local erythema in only one of the 6 infants.

The parents will therefore be unable to relate the present symptom of an axillary mass with the long-past history of vaccination and will not volunteer such information unless specifically asked for. Hence when an infant of such an age presents with axillary lymphadenopathy which is not generalised, the possibility of BCG vaccination complication should be considered and the history of BCG vaccination on the arm of the same side be ascertained. Examination of early cases will show enlarged lymph nodes which are mainly solid but even then some areas of fluctuations can generally be demonstrated if specifically looked for. Advanced cases will show frank abscesses.

After a clinical diagnosis is made, the treatment should consist of complete excision under general anaesthesia and not just incision and drainage as it may result in a persistent discharging sinus. The experience in this series also shows that clinically solitary lesions are associated with more enlarged lymph nodes deeper down not palpable clinically but showing involvement on histology. All accessible nodes should therefore be removed. Complete excision, even in the presence of frank abscess formation, ensures ready healing regardless of whether the wound is sutured.

Only 3 patients showed an IgG antibody response to the antigen 6 fraction of *M. tuberculosis*. This is in contrast to the response seen in patients with infections caused by *M. tuberculosis*[4] and seems to indicate that serological means of diagnosis is unsatisfactory in these patients.

Even though acid-fast bacilli could only be demonstrated in half the cases, there should be no doubt about the diagnosis if the clinical presentation, histological findings, and response to antituberculous therapy is taken into consideration.

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Correspondence to Dr Paul Tam, Department of Surgey, University of Hong Kong, Queen Mary Hospital, Hong Kong.

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Transient pseudo-precocious puberty by probable oestrogen intake in 3 girls

A M PASQUINO, R BALDUCCI, M L MANCA BITTI, G L SPADONI, AND B BOSCHERINI

Department of Paediatrics, University of Rome, Italy

SUMMARY We report the clinical and laboratory findings in 3 prepubertal girls with transient signs of sexual precocity. Accidental oestrogen intake from contaminated food was the most likely cause, the luteinising hormone—releasing hormone test showing suppressed secretion of follicle-stimulating hormone and luteinising hormone at the time of maximal oestrogenisation.

In prepubertal girls oestrogen intake can cause transient signs of pseudo-precocious puberty, particularly breast enlargement, with intense pigmentation of the mammillary areola and sometimes vaginal bleeding. Initially, this condition can be difficult to differentiate from true precocious puberty or from other forms of pseudo-precocious puberty.

Oestrogen intake can occur in various ways—such as by ingestion of accidentally contaminated drugs,[1 2] application of dermal ointments containing oestrogens,[3] inhalation of stilboestrol dust,[4] or ingestion of contaminated meat.[5]

Three prepubertal girls had transient pseudo-precocious puberty with clear evidence of oestrogenisation. The luteinising hormone—releasing hormone (LH-RH) test is useful in the diagnosis of such patients.

Case reports

Case 1. This 7-year-old girl had enlarged breasts with hyperpigmentation of the areola and genitalia. A month later she had vaginal bleeding lasting 3 days. Oestrogen ingestion by tablet or its absorption by ointments, creams, or powders was excluded. Her height (114 cm) and weight (18 kg) were on the 3rd centile. Physical examination showed slight breast enlargement (Tanner's 2nd stage) with intense pigmentation of the mammillary areola and anogenital region; there was no pubic hair. Bone age was slightly retarded (5·9 years according to Greulich and Pyle). *X*-ray films of the skull and fundus oculi were normal. Rectal examination showed no adnexal masses or uterine enlargement. Vaginal smear showed clear evidence of oestrogenisation. Levels of E_2 were normal for age (<10 pg/ml). Serum gonadotrophin levels after LH-RH injection (50 μg intravenously) were very low (Table).

Breast enlargement and areolar pigmentation had disappeared 5 months later and vaginal bleeding did not recur. Vaginal smear now showed absence of

Table *Serum gonadotrophin levels after LH-RH injection (50 μg intravenously)*

	At peak oestrogenisation				*After complete oestrogenisation regression*			
	FSH (mIU/ml)		*LH (mIU/ml)*		*FSH (mIU/ml)*		*LH (mIU/ml)*	
Case	*Basal*	*Maximum*	*Basal*	*Maximum*	*Basal*	*Maximum*	*Basal*	*Maximum*
1	1·8	2·9	1·8	1·9	2·4	19	2·5	9·3
2	<1·5	<1·5	<1·5	<1·5	19	51	1·5	7·5
3	1	3	1·5	7·5	—	—	—	—