Short reports

Atypical mycobacterial lymphadenitis in childhood—a clinicopathological study of 17 cases

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Abstract

Aims—To assess the clinical and pathological features of atypical mycobacterial lymphadenitis in childhood to define the salient clinical and histological features.

Methods—17 cases were included on the basis of positive culture or demonstration of bacilli of appropriate morphology and staining characteristics.

Results—The mean age at diagnosis was 4.86 years. All children were systemically well, with clear chest x rays. Unilateral cervical lymphadenopathy was the commonest mode of presentation. Differential Mantoux testing played no part in diagnosis. Clinical diagnosis improved with awareness. Treatment varied with surgeons opting for excision and paediatricians adding six months antituberculous chemotherapy. Acid- and alcohol-fast bacilli were identified in nine cases. Bacterial cultures were conducted in 16 cases and were positive for atypical or non-tuberculous mycobacteria in 14, the main organism being *M avium-intracellulare* complex (11 cases). Histologically, 12 cases had bright eosinophilic serpiginous necrosis with nuclear debris scattered throughout the necrotic foci. Langhans type giant cells featured in the majority of cases but infiltration by plasma cells and neutrophils was not consistent.

Conclusions—Atypical mycobacterial lymphadenitis of childhood represents a

rare but significant disease with characteristic clinical and histological features.

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Atypical or non-tuberculous mycobacteria have long been recognised as opportunistic pathogens in immunosuppressed individuals. Several series have emphasised their role in the causation of isolated lymphadenopathy in immunocompetent children.¹⁻³ Although usually a non-progressive condition it is important to differentiate between atypical and tuberculous lymphadenopathy, as inappropriate management can lead to sinus formation and unsightly scarring.⁴ During this study the clinicopathological features of 17 cases were reviewed in order to define main clinical and histological features which may aid diagnosis. We also studied treatment regimens to assess optimal management.

Methods

The archives of three centres were searched for cases of granulomatous inflammation or atypical mycobacterial infection between the years 1990 and 1994 in children aged 16 years or less. All cases diagnosed as toxoplasmosis, cat scratch disease, or non-specific granulomatous inflammation were excluded. The clinical notes were reviewed with regard to age and sex of patients, mode of presentation, provisional

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Table 1 Clinical details of the cases

Case	Anatomical site	Age	Sex	Mantoux	Culture result	Excision + drugs	Excision only	Sinus complicating treatment
1	Cervical nodes (unilateral)	3 y, 6 m	F	Not done	M mal	+	(6/12)	
2	Groin	1 y, 6 m	F	Not done	MAIS	+		+
3	Preauricular	3 y, 11 m	F	Not done	MAIS		+	
4	Preauricular	10 y	F	Not done	Negative		+	
5	Preauricular	2 y	M	Negative	MAIS	+		
6	Submandibular	4 y, 6 m	M	No record	MAIS		+	+
7	Cervical unilateral	1 y, 10 m	F	No record	MAIS	+		
8	Cervical sinus present	5 y, 4 m	F	Positive	M mal	+		
9	Cervical	6 y, 2 m	F	No record	MAIS		+	
10	Cervical	5 y, 4 m	M	Not done	MAIS	+		+
11	Cervical	9y 4m	F	Not done	MAIS	+		
12	Cervical	6 y, 1 m	M	Not done	Negative		+	
13	Cervical	13 y, 1 m	F	Not done	MAIS		+	
14	Cervical	3 y, 9 m	F	Not done	M mal		+	
15	Cervical sinus present	10 y, 9 m	F	No record	Negative		+	
16	Submental	2 y, 6 m	M	Not done	MAIS		+	
17	Cervical	1 y, 8 m	F	Not done	MAIS		+	

MAIS, *Mycobacterium avium-intracellulare*; M mal, *Mycobacterium malmoense*.

Table 2 Histological features

Case	Necrosis			Giant cells	Neutrophil polymorphs	Plasma cells	Peripheral palisading	Acid-fast bacilli
	Nuclear debris	Polymorphs	Type					
1		+	Serpiginous	++	++	++	-	-
2	+		Serpiginous	+	++	++	++	+
3	++	+	Serpiginous	+	+	+/-	+/-	-
4	++		Serpiginous	+	+/-	+/-	+/-	+
5	+/-	+	Serpiginous	+++	+/-	+/-	+/-	-
6	+		Serpiginous	+	+/-	+/-	+/-	-
7	+		Serpiginous	-	+/-	+/-	+/-	-
8	-		Coalescing calcified	+	+/-	+/-	+/-	+
9	+	+/-	Serpiginous	-	+/-	+/-	-	-
10	+		Serpiginous	+	+/-	+/-	-	-
11		+	Serpiginous	+	++	+/-	-	+
12	+		Serpiginous	-	+/-	++	-	+
13	+		Serpiginous basophilic	-	+/-	-	-	+
14			Coalescing	-		-	-	+
15			Serpiginous	+	+		++	+
16			Discrete granulomas	++	+/-	+/-	-	-
17	+		Focal necrosis	++	+/-	+/-	-	+

-, negative; +/-, minimal; +, present within necrotic focus; ++, extending beyond necrotic focus; +++, diffusely distributed throughout lesion.

diagnosis, diagnostic criteria including differential Mantoux testing, bacteriological culture, treatment regimen, and complications of treatment. Haematoxylin and eosin stained histological sections were examined and initial reports were reviewed. The criteria assessed were necrosis, granuloma formation, presence and type of giant cells, nature of associated inflammation, and Ziehl-Neelsen or auramine

staining for acid- and alcohol-fast bacilli. Only cases culture positive or with bacilli of appropriate morphology and staining characteristics are included in this study.

Results

The details of site of presentation, age, sex, Mantoux testing, and treatment regimen are summarised in table 1. Isolated unilateral lymphadenopathy of head and neck was the commonest presentation (16 cases), and two of these had sinus formation. The remaining case presented as a localised lymphadenopathy of the groin. The male to female ratio was 1:1.4, and the age range was 1.5 to 13.08 years (mean 4.86, median 3.89). Provisional clinical diagnoses included atypical mycobacterial lymphadenitis, thyroglossal cyst, lymphoma, branchial arch cleft, dermoid cyst, infected "sebaceous" cyst, tuberculosis, and reactive lymphadenopathy. Some clinicians offered more than one diagnosis. Family screening was performed in only one case as there was a strong clinical suspicion of tuberculosis.

Mantoux testing was documented in two children and was positive in one. No child was tested with *M avium-intracellulare* complex antigen. Chest x rays were unremarkable in all cases where reports were available (nine cases).

Bacterial culture was done in 16 cases and proved positive in 14, only two organisms were identified: *M avium-intracellulare* was found in 11 cases and *M mageritense* in three.

Thick irregularly shaped acid- and alcohol-fast bacilli were identified in nine cases. The organisms were extracellular and scant in number and were located at the periphery of the necrotic zone. Details of other histological features are summarised in table 2. In 15 biopsies there was serpiginous or stellate necrosis, variously described as bright eosinophilic, non-caseous, and caseous (figs 1 and 2). Prominent peripheral palisading around the necrotic focus was observed in only two cases. Nuclear debris was found throughout the necrotic foci, and neutrophils, where present, were distributed in a similar fashion. Three samples had more diffuse neutrophil infiltra-

Figure 1 Macroscopic view of lymph node showing central caseation.

Figure 2 Section showing Langhans type giant cells and central necrosis. Inset: irregularly shaped bacillus stained with Ziehl-Neelsen stain.

tion. Langhans type giant cells were often seen ($n = 12$).

The treatment regimen varied with clinical specialty. General surgeons opted for excision alone, while plastic surgeons and paediatricians instituted antituberculous treatment following excision biopsy. Three children developed sinuses with poor healing following needle aspiration or superficial biopsy. Complete excision with removal of the underlying node appeared curative with good cosmetic result.

Discussion

In this study we have reviewed 17 cases of non-tuberculous lymphadenitis presenting at three centres over a five year period. In the main, it is a disease of systemically well young girls, in whom it presents as isolated unilateral (cervical) lymphadenopathy of head and neck region. Other family members are not usually affected. Mantoux testing was rarely performed and contributed little to the final diagnosis. Also, though it may be tempting to perform needle aspiration in these cases, sinus formation and scarring may result. Our findings are similar to those of other studies.¹⁻⁵

Grange *et al* have recently postulated that the apparent increase in the condition may relate to increased awareness,⁶ a finding mirrored in this study by review of the provisional clinical diagnoses. Where clinicians had previous experience of the condition they were more likely to proffer the correct diagnosis. Further, our study confirmed that two principal organisms were concerned, *M malmoense* and *M avium-intracellulare* complex. Though surgical excision is curative and the organisms are highly resistant, antituberculous treatment continued to be prescribed.

In this study we found that the use of the standard Ziehl-Neelsen staining identified few organisms. These findings are confirmed in another recent study, where the Ziehl-Neelsen stain was compared with a modified Dieterle stain.⁷ In that study, the investigators found that while the number of organisms identified was increased using the Dieterle stain, the technique was limited by the morphological similarity of mycobacteria to nocardia. Furthermore, cat scratch disease was readily confused with *M avium-intracellulare* complex in the presence of Dieterle-positive staining, acid-fast negative organisms. These results emphasise the need for bacteriological confirmation of disease, and material should be sent for bacteriology at the time of biopsy.

It is interesting to observe the relatively consistent histological appearance of large stellate or serpiginous areas of necrosis with nuclear debris and neutrophils scattered throughout the necrotic or caseous foci. Despite contrasting histological findings in published reports,⁸ our results are in keeping with those studies concentrating on lymphadenitis in children, and a review of the initial reports showed that pathologists suggested the diagnosis in all

cases. Other investigators^{1-5,9} have also described "nuclear debris within an area of caseation" or necrotic focus, but in contrast to the findings of Jones and Campbell⁹ our cases showed bright eosinophilic rather than basophilic necrosis. Furthermore, although one study¹ intimated a paucity of Langhans type giant cells, we found them to be a consistent feature, in line with the published data of Margileth *et al*.⁵

Pinder and Colville,¹⁰ in attempting to delineate histological criteria for the differentiation of tuberculous versus non-tuberculous infection in the non-immunocompromised individual, observed that although no one definitive feature is diagnostic of non-tuberculous mycobacterial infection, some features may be helpful in distinguishing the two groups—for example, ill defined (non-palisading) granulomata, irregular or serpiginous necrosis with nuclear debris or polymorphs scattered throughout the area of necrosis, or non-specific granulomata without significant necrosis. Our study showed similar features but we found only one case with discrete granulomata and no necrosis.

Atypical mycobacterial lymphadenitis remains a rare but important cause of morbidity in Europe. The diagnosis should be considered in a well child under five years of age who presents with isolated unilateral lymphadenopathy, and treatment should involve excision to remove affected nodes. Against this clinical background histological findings of stellate or serpiginous necrosis with neutrophil polymorphs scattered throughout the necrotic foci can be regarded as highly suggestive of atypical mycobacterial infection, as opposed to other causes of necrotising granulomatous lymphadenopathy. However to achieve definitive diagnosis, material should be sent for bacteriology at the time of biopsy.

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