NECROTIZING NON-GRANULOMATOUS LYMPHADENITIS: A CLINICOPATHOLOGIC STUDY OF 40 THAI PATIENTS

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Abstract. The purpose of this study was to describe the clinicopathological features of 40 cases of necrotizing non-granulomatous lymphadenitis in Thai patients. The clinical features, histomorphology and special stains were evaluated in 40 Thai patients from the pathology records of King Chulalongkorn Memorial Hospital from January 2001 to December 2003 in those diagnosed as having necrotizing non-granulomatous lymphadenitis. Of the 40 patients, 17 cases (42.5%) had Kikuchi-Fujimoto disease (KFD), 8 cases (20%) had tuberculosis (TB) lymphadenitis and 1 case (2.5%) had systemic lupus erythematosus (SLE) with associated lymphadenitis. Fourteen cases (35%) did not have a specific diagnosis due to a lack of follow-up data. KFD most commonly occurs in young women, and is characterized by the presence of coagulative necrosis and karyorrhexis often centered in the paracortex, an absence of neutrophils and plasma cells, proliferation of various cells composed of lymphocytes, histiocytes, immunoblasts and plasmacytoid monocytes and the absence of a granuloma. Tuberculous lymphadenitis usually occurs in women with a mean age of 34.25 years. The lymph nodes reveal extensive coagulative necrosis involving the cortex, paracortex and medulla, proliferation of mixed inflammatory cells, including neutrophils, lymphocytes and plasma cells in the necrotic area and the presence of proliferating histiocytes at the periphery of the necrotic area. The lymph nodes of SLE-associated lymphadenitis reveal large numbers of plasma cells and hematoxylin bodies. We suggest that necrotizing non-granulomatous lymphadenitis is not specific for any disease, but rather a common histologic change found in diseases, such as TB, SLE, and KFD. Further investigation to obtain a definite diagnosis should be done for appropriate treatment.

INTRODUCTION

Several diseases can present with necrotizing non-granulomatous lymphadenitis. Incorrect interpretation of this pathological term may lead to inappropriate treatment which can cause adverse effects to the patient. Neoplastic conditions, especially lymphoma (Saito *et al*, 2001) and metastatic carcinoma, must be excluded first (Strickler *et al*, 1987). Some benign conditions, including infectious diseases and autoimmune diseases, are also in the differential as well. In some instances, special studies, immunohistochemical and gene rearrangement studies are often required to determine a specific diagnosis (Vega *et al*, 1999).

We present a clinicopathological study of 40 Thai patients with necrotizing non-granulomatous lymphadenitis to draw attention to these diagnostic problems. We highlight the features which may aid in the definite diagnosis. In this study, we exclude some histologic features, including granuloma, malignancy and lymph node infarction.

MATERIALS AND METHODS

Case selection

The study population consisted of 40 cases of necrotizing non-granulomatous lymphadenitis retrieved from surgical pathology files of the department of Pathology, King Chulalongkorn Memorial Hospital, from January 2000 to December 2002, which had available clinical data and paraffin-embedded tissue specimens. Cases associated with granulomatous inflammation, lymph mode infarction and malignancy were excluded. In all forty cases the clinical data, histomorphology and special stains were reviewed.

From a retrospective review of the medical records, we evalvated the following features: age, sex, presenting symptoms, length of clini-

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cal history before the biopsy, site and largest size of lymphadenopathy, laboratory findings, including culture for tuberculous organisms (C/S TB) and polymerase chain reaction for tuberculous organisms (PCR-TB), treatment, status at last follow-up and total length of follow-up.

The hematoxylin and eosin stained sections of lymph node biopsies of all cases were re-examined. The following features were recorded: area of lymph node involvement, degree of necrosis, presence of tissue necrosis and apoptosis, presence of extracapsular involvement, presence of vasculitis, presence of neutrophils and plasma cells in the necrotic area and presence of histiocytes around the necrotic area. The degree of necrosis was graded as 1+ (occupying 1-25% of the lymph node), 2+ (26-50%), 3+ (51-75%) and 4+ (76-100%).

Two special stains for all cases were reperformed: a stain for acid-fast bacilli (AFB) and Gomori Methanemine silver stain (GMS).

Statistical analyses

Statistical analyses were performed using SPSS for Windows (version 13; SPSS Inc, Chicago, IL, USA). The correlation of degree of necrosis in different diseases was assessed with the chi-square and Fisher's exact tests. All p-values were based on 2-hypothesis testing, and statistical significance was defined as a probability value (p-value) <0.05.

RESULTS

Of the 40 patients included in our study, 7 were males (17.5%) and 33 were females (82.5%) with an overall mean age of 30.5 years (16-81 years). All of them had a presenting complaint of lymphadenopathy (100%). Pain was the second most common symptom and was seen in 15 patients (37.5%). Twelve patients (30%) had fever, 3 patients (7.5%) had weight loss and 2 patients (5%) had cough. One patient presented with alopecia and arthralgia and the another presented with oral ulcers, genital ulcers and arthritis. The average duration of symptoms was 7.4 weeks (2-52 weeks). The most common sites of lymphadenopathy were cervical (30 patients, 75%), followed by cervical with submandibular (4 patients, 10%), supraclavicular (3 patients,

7.5%), cervical with axillary (2 patients, 5%) and submandibular lymph nodes (1 patient, 2.5%). The mean duration from lymphadenopathy to biopsy was 7.4 weeks (2-52 weeks). The mean size of lymph node at diagnosis was 1.7 cm (1-4 cm.). Most patients had multiple lymphadenopathy (34, 85% patients).

Follow-up data were available in 27 patients (67.5%), none developed recurrent lymphadenopathy. The symptoms disappeared within 3-30 weeks (mean 11.2 weeks) of the date of the biopsy.

An extensive infectious work-up was done, 40 cases were evaluated with AFB and GMS stains, 22 cases with PCR-TB and 2 cases with C/S for TB. All patients were negative for GMS. AFB was positive in 2 cases (5%), PCR-TB was positive in 8 cases (36%) and C/S for TB was positive in 1 case (50%). The diagnosis of TB lymphadenitis was established in 8 cases; anti-TB drugs were given.

A systemic lupus erythematosus (SLE) work-up was done in one female patient who presented with fever, cervical and submandibular lymphadenopathy, oral ulcers, genital ulcers and arthritis, including antinuclear antibodies (ANA) and anti-double stranded deoxyribonucleic acid antibodies (anti-ds DNA). Both tests were positive, so SLE was diagnosed according to American Rheumatology Association criteria. She received steroids.

The clinical features, laboratory findings and follow-up date are shown in Table 1.

The histomorphologic features of all cases showed a necrotizing process, 2 cases had only apoptosis (5%), 12 cases had coagulative necrosis (30%) and 26 cases had both apoptosis and coagulative necrosis (60%). The necrosis involved the paracortex in 13 cases (32.5%), both the cortex and paracortex in 20 cases (50%) and the cortex, paracortex and medulla in 7 cases (17.5%). The degree of necrosis was evaluated subjectively using a scale ranging from 1 to 4. The results were as follows: grade 1, 5 cases (12.5%), grade 2, 16 cases (40%), grade 3, 13 cases (32.5%) and grade 4, 6 cases (15%). The proliferating cells in the necrotic area were both neutrophils and plasma cells in 15 cases (37.5%), and only neutrophils in 4 cases (10%).

Table 1
The clinical features, laboratory findings and follow-up data of 40 cases.

Case No.	Age (yrs)	Sex	Presentation			Lymphadenopathy			Investigation			Follow-up		
			Fever	Pain	Other	Dur (wks)	Size (cm)	Site	No	PCR-TB	C/S TB	Outcome	Dur (wks)	Reclassi-fication
1	33	F	+	-	-	4	2	Cer	m	-	NA	C	6	KFD
2	44	F	-	+	-	5	2	Sm	m	-	NA	L		unknown
3	37	F	+	+	-	3	1	Cer,Ax	m	NA	NA	L		unknown
4	33	F	-	-	-	3	2	Cer	m	-	NA	L		unknown
5	40	F	-	-	-	4	2	Cer	m	NA	NA	C	13	KFD
6	31	F	-	-	-	3	2	Cer	m	-	NA	C	3	KFD
7	57	F	-	-	cough	20	1	Suc	m	NA	NA	L		unknown
8	30	M	+	-	wt loss	8	4	Cer,Sm	m	+	+	C	17	TB
9	26	F	-	+	-	4	2	Cer	m	NA	NA	C	3	KFD
10	16	M	+	+	-	8	2	Cer	m	-	NA	L		unknown
11	36	F	-	-	-	4	2	Cer	m	-	NA	C	12	unknown
12	37	F	-	+	-	4	1	Cer	m	-	NA	C	3	KFD
13	22	F	-	-	-	8	1	Cer	m	NA	NA	C	3	KFD
14	28	F	-	+	wt loss	4	2	Cer	s	-	NA	L		unknown
15	36	F	-	-	-	4	1	Suc	m	NA	NA	L		unknown
16	28	F	+	-	-	4	2	Cer	m	-	NA	C	8	KFD
17	23	F	-	-	-	16	2	Cer	s	-	NA	C	16	KFD
18	30	F	-	+	-	4	2	Cer,Sm	m	-	-	C	10	KFD
19	22	F	-	+	-	3	2	Cer,Sm	m	+	NA	L		TB
20	45	F	+	-	-	4	2	Cer	m	NA	NA	C	26	unknown
21	17	M	-	-	-	4	4	Cer	m	-	NA	C	30	unknown
22	20	F	+	+	-	4	2	Cer	m	+	NA	C	14	TB
23	32	F	+	+	-	8	3	Cer	m	+	NA	C	15	TB
24	81	F	+	-	-	3	1	Cer	m	+	NA	C	22	TB
25	24	F	-	+	-	3	1	Cer	m	NA	NA	L		unknown
26	43	F	-	-	-	9	1	Cer	s	NA	NA	C	12	KFD
27	24	F	-	+	-	4	1	Cer	m	-	NA	C	3	KFD
28	21	M	-	+	-	4	1	Cer	m	NA	NA	C	3	KFD
29	19	F	+	+	-	12	2	Cer,Ax	m	-	NA	L		unknown
30	20	F	-	-	-	3	1	Cer	m	NA	NA	C	4	KFD
31	30	F	-	-	-	3	1	Cer	s	NA	NA	C	9	unknown
32	30	F	-	-	wt loss	52	3	Cer	m	+	NA	C	27	TB
33	19	F	-	-	-	4	2	Cer	m	NA	NA	C	6	KFD
34	31	M	+	-	-	2	1	Cer	m	+	NA	L		TB
35	28	M	+	-	cough	4	3	Cer	m	+	NA	L		TB
36	30	F	-	-	other1	4	1	Cer	m	NA	NA	L		unknown
37	28	F	+	-	other2	44	2	Cer	m	NA	NA	C	20	SLE
38	24	F	-	-	-	4	2	Cer,Sm	m	NA	NA	C	2	KFD
39	21	M	-	-	-	3	3	Cer	s	NA	NA	C	10	KFD
40	25	F	-	+	-	5	2	Cer	s	NA	NA	C	5	KFD

Dur: duration, No: number, wks: weeks, TB: tuberculosis, PCR: polymerase chain reaction, C/S: culture
M: Male, F: Female, m: multiple, s: single, wt: weight, C: cure, L: lost to follow-up, NA: not applicable, +: Positive, -: Negative
Cer: cervical lymph node, Sm: submandibular lymph node, Ax: axillary lymph node, Suc: supraclavicular lymph node,
Other 1: alopecia and arthralgia, Other 2: oral ulcer, genital ulcer and arthritis, KFD: Kikuchi-Fujimoto disease, SLE: systemic lupus erythematosis.

Table 2
The histomorphologic features and special stains of 40 cases.

Case No	Nec_are	Nec_degree	Nec_type	Proliferated cells in necrosis			Perinodal involvement	Vasculitis	Special stain		Reclassification
				Neu	Plas	Sur_His			AFB	GMS	
1	C,P	3	A,Co	-	-	-	-	-	-ve	-ve	KFD
2	P	2	A,Co	-	-	-	-	-	-ve	-ve	unknown
3	C,P	2	Co	+	-	-	-	-	-ve	-ve	unknown
4	P	1	A	-	-	-	-	-	-ve	-ve	unknown
5	C,P	2	A,Co	-	-	-	-	-	-ve	-ve	KFD
6	P	2	A,Co	-	-	-	-	-	-ve	-ve	KFD
7	C,P	4	Co	+	+	-	-	-	-ve	-ve	unknown
8	C,P,M	4	Co	+	+	+	-	-	-ve	-ve	TB
9	P	2	A,Co	-	-	-	-	-	-ve	-ve	KFD
10	P	1	A	+	-	-	-	-	-ve	-ve	unknown
11	C,P,M	4	Co	+	+	+	-	-	-ve	-ve	unknown
12	C,P	3	A,Co	-	-	-	-	-	-ve	-ve	KFD
13	C,P	3	A,Co	-	-	-	-	-	-ve	-ve	KFD
14	C,P	2	A,Co	+	-	-	-	-	-ve	-ve	unknown
15	P	1	A,Co	-	-	-	-	-	-ve	-ve	unknown
16	P	1	A,Co	-	-	-	-	-	-ve	-ve	KFD
17	C,P	2	A,Co	-	-	-	-	-	-ve	-ve	KFD
18	P	2	A,Co	-	-	-	-	-	-ve	-ve	KFD
19	C,P,M	4	Co	+	+	-	-	-	-ve	-ve	TB
20	C,P,M	3	A,Co	+	+	+	-	-	-ve	-ve	unknown
21	C,P,M	4	Co	+	+	-	-	-	-ve	-ve	unknown
22	C,P	4	Co	+	+	-	-	-	-ve	-ve	TB
23	C,P	2	Co	+	+	-	-	-	+ve	-ve	TB
24	C,P	3	Co	+	+	+	-	-	-ve	-ve	TB
25	C,P	3	Co	+	+	+	-	-	-ve	-ve	unknown
26	C,P	2	A,Co	-	-	-	-	-	-ve	-ve	KFD
27	P	2	A,Co	-	-	-	-	-	-ve	-ve	KFD
28	P	2	A,C0	-	-	-	-	-	-ve	-ve	KFD
29	C,P	3	A,Co	-	-	-	-	-	-ve	-ve	unknown
30	P	2	A,Co	-	-	-	-	-	-ve	-ve	KFD
31	C,P	2	A,C0	+	+	-	-	-	-ve	-ve	unknown
32	C,P,M	3	A,Co	+	+	+	-	-	-ve	-ve	TB
33	P	1	A,Co	-	-	-	-	-	-ve	-ve	KFD
34	C,P	3	A,Co	+	+	-	-	-	+ve	-ve	TB
35	C,P,M	3	Co	+	+	+	-	-	-ve	-ve	TB
36	P	2	A,Co	+	-	-	-	-	-ve	-ve	unknown
37	C,P	3	Co	+	+	-	-	-	-ve	-ve	SLE
38	C,P	2	A,Co	-	-	-	-	-	-ve	-ve	KFD
39	C,P	3	A,Co	-	-	-	-	-	-ve	-ve	KFD
40	C,P	3	A,Co	-	-	-	-	-	-ve	-ve	KFD

Nec: necrosis, Neu: neutrophils, Plas: plasma cells, Sur His:histiocytes around necrosis, C: cortex, P: paracortex, M: medulla, AFB: acid-fast stain,

GMS: Gomori Methanemine Silver stain, A: apoptosis, Co: coagulative necrosis, +: present, -:absent, +ve: positive, -ve: negative,

TB: tuberculosis, KFD: Kikuchi-Fujimoto disease, SLE: systemic lupus erythematosis,

Degree of necrosis: 1 (1-25% of the lymph node), 2 (26-50%), 3 (51-75%), and 4 (76-100%).

Twenty-one cases (52.5%) showed an absence of neutrophils and plasma cells in necrotic areas. There was proliferation of histiocytes around the necrotic areas in 7 cases (17.5%). Vasculitis and perinodal involvement were not seen in any of the cases. The histomorphologic features are detailed in Table 2.

After extensive work-up and follow-up, 8 cases (20%) were considered to be TB lymphadenitis, 1 (2.5%) was SLE and 17 cases (42.5%) were thought to be Kikuchi-Fujimoto disease (KFD), although viral lymphadenitis was not excluded. Once the diagnosis of KFD was made in 17 cases, only symptomatic treatment was given. The remaining 14 cases had no definite diagnosis. Of the 14 cases, 10 had incomplete investigations and lacked follow-up data, 4 cases were unknown because all 4 cases were negative on PCR-TB, but were treated with anti-TB drugs. The symptoms improved in all cases, and no recurrent lymphadenopathy was found.

In the 8 cases considered to be TB lymphadenitis, the patients consisted of 3 males (37.5%) and 5 females (62.5%) with an overall mean age of 34.25 years (20-81 years). The patients presented with multiple lymphadenopathy (8 cases, 100%), fever (6 cases, 75%), pain (3 cases, 37.5%), weight loss (2 cases, 25%) and cough (1 case, 12.5%). The mean duration from lymphadenopathy to biopsy was 10.5 weeks (2-52 weeks). The most common sites of lymphadenopathy were the cervical lymph nodes (8 cases, 100%), followed by the submandibular lymph nodes (2 cases, 25%). The mean size of the largest lymph node at diagnosis was 2.4 cm (1-4 cm). All the patients were treated with anti-TB drugs. Follow-up data were available in 5 patients. All five patients had improved symptoms within 14-27 weeks of the date of biopsy (mean 19 weeks). The lymph nodes had coagulative necrosis in all the cases (100%) and apoptosis in 2 cases (25%). Necrosis extended to the cortex and paracortex in 4 cases (50%) and involved the cortex, paracortex and medulla in 4 cases (50%). Grading of the necrosis was as follows: grade 2, 1 case (12.5%), grade 3, 4 cases (50%) and grade 4, 3 cases (37.5%). There were both neutrophils and plasma cells infiltrating the necrotic areas in all the cases (100%).

Proliferating histiocytes around the necrotic area was observed in 4 cases (50%). Neither vasculitis nor perinodal involvement was found in any of the cases (0%).

One case of SLE was documented. A 28-year-old female presented with multiple cervical and submandibular lymph nodes for 44 weeks. She had fever, oral ulcers, genital ulcers and arthritis. She received steroids, and the clinical symptoms improved within 20 weeks. No recurrent lymphadenopathy was found. The lymph nodes showed coagulative necrosis, grade 3, involving the cortex and paracortex. Neutrophils and plasma cells were present in the necrotic areas. No vasculitis or perinodal involvement were observed. A striking feature was the presence of hematoxylin bodies in the necrotic areas.

Seventeen cases were considered to be KFD due to compatible clinical course and histomorphologic features. The patients were 2 males (11.8%) and 15 females (88.2%) with an overall mean age of 27.5 years (19-43 years). Most patients presented with lymphadenopathy (17 cases, 100%), pain (7 cases, 41%) and fever (1 case, 5.9%) with a mean duration of 5.1 weeks (3-16 weeks). The most common sites for lymphadenopathy were cervical lymph nodes (17 cases, 100%), followed by submandibular lymph nodes (1 case, 5.9%). Generalized lymphadenopathy was not present. The mean size of the largest lymph nodes was 1.7 cm (1-3 cm). Of the 17 patient, 13 presented with multiple lymphadenopathy (76.5%) and 4 with single lymphadenopathy (23.5%). Once the diagnosis of KFD was established, only symptomatic treatment was given. Their symptoms completely resolved with a mean follow-up duration of 6.5 weeks (3-16 weeks).

The lymph nodes in KFD had a necrotizing process comprising tissue necrosis and apoptosis in all the cases (100%) involving the cortex and paracortex in 9 cases (53%) and only the paracortex in 8 cases (47%). The degrees of necrosis were as follows: grade 1, 2 cases (11.8%), grade 2, 10 cases (58.8%) and grade 3, 5 cases (29.4%). None of the cases had neutrophils or plasma cells in necrotic areas. There was a proliferation of histiocytes, plasmacytoid

monocytes, immunoblasts and lymphocytes in the necrotic areas. Proliferating histiocytes around the necrotic areas were observed in none of the cases. Vasculitis and perinodal involvement were not seen.

We compared the degree of necrosis between TB lymphadenitis and KFD. There was no statistical difference in the degree of necrosis between TB lymphadenitis and KFD (P=0.121).

DISCUSSION

The term "necrotizing non-granulomatous lymphadenitis" is not a distinct disease entity. Several diseases can present with necrotizing lymphadenitis, including KFD, autoimmune disease (SLE and Kawasaki disease), infectious disease, metastatic adenocarcinoma and lymphoma (Strickler *et al*, 1987). It is important to be aware of the characteristic clinical presentation and morphologic findings to exclude malignant disorders as well as non-neoplastic conditions that may require more aggressive and specific therapy. Some diseases are self-limited, such as KFD, so identification of this disease prevents over treatment.

It is also important to distinguish lymph node infarction from necrosis due to other causes, although, in practice, this is not always easy (Bhargava *et al*, 1989). There are some features that are suggestive for lymph node infarction, including the presence of ghost cells in the necrotic area surrounded by granulation tissue, a variable degree of dilatation of the deep nodal sinuses, and preserved connective tissue framework in the necrotic areas (Kojima *et al*, 2002).

KFD is a benign and self-limited condition of unknown cause, usually characterized by cervical lymphadenopathy, sometimes accompanied by mild constitutional symptoms. Less common manifestations include fever, axillary and mesenteric lymphadenopathy, cutaneous rash (erythematous macules, papules, plaques and nodules), arthralgia, aseptic meningitis, parotid gland enlargement, and bone marrow hemophagocytosis (Onciu and Medeiros, 2003).

Initially described in Japan, KFD was first reported almost simultaneously by Kikuchi and Fujimoto in 1972 (Fujimoto *et al*, 1972; Kikuchi,

1972). KFD is known to have a worldwide distribution with a higher prevalence among Japanese and other Asians. Affected patients are most often adults younger than 40 years (ranging from 19 months to 75 years). In general, a female preponderance has been reported (female/male ratio, 4:1) (Bosch *et al*, 2004).

A previous study in Thailand of 23 patients with KFD at Sonklanagarind Hospital from 1987 to 1996 revealed 18 females and 5 males with ages ranging from 9 to 57 years (Thongsuksai and Kayasut, 1999). We speculate KFD may be an underdiagnosed disorder. Some young patients with KFD who have a short history of low-grade fever and small cervical lymphadenopathy are given a presumptive diagnosis of a viral process. In this study, we found KFD in about 42.5% of all cases.

Laboratory investigations in KFD are usually unremarkable except for mild neutropenia and lymphocytosis in some cases (Menasce *et al*, 1998). The pathogenesis is still poorly understood but it is thought to represent a hyperimmure reaction induced by different antigenic stimuli or an autoimmune process, such as SLE (Felgar *et al*, 1997).

KFD typically is self-limited, and lasts 1 to 4 months. A low, but possible, recurrence rate of 3% to 4% has been reported, usually manifested as recurrent lymphadenopathy at the site of initial presentation or, less commonly, at another distant site (Lin *et al*, 2003). A few cases have been described with recurrent disease during an 8 to 9 year period (Bosch *et al*, 2004).

The lymph nodes involved by KFD are most commonly less than 3 cm in their greatest dimension, although there have been reports of enlarged lymph nodes up to 6 to 7 cm, most commonly in children (Onciu and Medeiros, 2003).

The characteristic histopathologic findings of KFD are irregular paracortical areas of coagulative necrosis with abundant karyorrhexis, absence of granulocytes and paucity of plasma cells. The degree of necrosis varies considerably from one case to another. These processes are associated with a mixture in variable proportions of benign histiocytes (so-called crescentic or c-shaped forms), immunoblasts, plasmacytoid monocytes, and small to large lymphocytes. The

lymph node capsule is usually intact and may show partial thickening in the areas overlying necrotic lesions (Onciu and Medeiros, 2003).

Our data are similar to previous reports. Of 17 patients with KFD, most were young females who presented with acute or subacute cervical lymphadenopathy. All cases were self-limited, showing no recurrent lymphadenopathy at the time of last follow-up, and their symptoms had disappeared within 16 weeks of biopsy.

There are a few important clues to support KFD. First, the lymph node shows a necrotizing process often centered in the paracortex and characterized by coagulative necrosis associated with karyorrhexis. Second, granulocytes are absent, and plasma cells are rare or absent. Third, this process is associated with a proliferation of various cells consisting of a mixture of lymphocytes, crescentic histiocytes, immunoblasts and plasmacytoid monocytes. Finally, the lymph node reveals no granulomas.

Viral-associated lymphadenitis can be characterized by histiocytic infiltrates and necrotic debris, findings that are characteristic for KFD. Histiocytic infiltrates are usually less striking than in KFD, neutrophils often are observed, and viral inclusions may be found (Onciu and Medeiros, 2003; Bosch et al, 2004). It is difficult to determine a virus as the cause of necrotizing non-granulomatous lymphadenitis except for prominent viral inclusions. Extensive investigations, such as serology and in-situ hybridization to detect numerous types of virus must be performed. However, it is not practical or possible to perform viral studies in every case. We did not explore this aspect in our study.

In TB lymphadenitis, most patients were younger than 40 years and presented with cervical lymphadenopathy (scrofula) (Dandapat et al, 1990; Thompson et al, 1992). A draining sinus that communicates with the skin (scrofuloderma) may form (Moore et al, 2003). The symptoms may exist for weeks to years. Multiple necrotizing granulomas, often confluent, are typical microscopic features. The caseating center is surrounded by epithelioid histiocytes, Langhans' giant cells, and lymphocytes. Nevertheless, granulomas and caseous necrosis are absent in some cases (Ramanathan et al, 1999),

especially in the immunocompromized host (Karunatilake et al, 2002). Those with TB lymphadenitis must be distinguished from the other causes of necrotizing lymphadenitis. Demonstration of the organisms by special stains, cultures, or PCR is necessary to establish the diagnosis (Ikonomopoulos et al, 1999).

In this study, most of the patients with TB lymphadenitis were females presenting with cervical lymphadenopathy and fever. Features commonly seen in TB lymphadenitis are extensive necrosis involving the cortex, paracortex and medulla, the presence of lymphocytes, plasma cells and neutrophils in the necrotic area and protiferating histiocytes around the necrotic area. However, the histologic features alone are not sufficient to diagnose TB lymphadenitis. An extensive TB work-up is necessary to identify the organism and diagnose TB lymphadenitis.

SLE can be associated with lymphadenitis characterized by prominent foci of necrosis. The lymph node changes in SLE are generally of a non-specific nature. Features that can be seen in SLE-associated lymphadenitis but not in the others, including hematoxylin-bodies and the Azzorpardi phenomenon. Moreover, the presence of large numbers of plasma cells, DNA deposition on vessel walls and extensive areas of acellular coagulative necrosis devoid of karyorrhectic material favors SLE-associated lymphadenitis. However, these features may not be identified in every case of SLE-associated lymphadenitis, and the diagnosis cannot always be ruled out on histologic morphology alone. The diagnosis of SLE-associated lymphadenitis is based on the clinical features and laboratory investigations (Kojima et al, 2000; Hu et al, 2003).

One case was diagnosed as SLE-associated lymphadenitis in this study. Some histologic features of SLE-associated lymphadenitis overlap with those seen in KFD or other necrotizing non-granulomatous lymphadenitis. There are some clues, including the presence of large numbers of plasma cells and the presence of hematoxylin bodies. However, the diagnosis of SLE-associated lymphadenitis cannot be done based on histomorphology alone. It is always based on clinical features, laboratory investigations and pathologic findings.

Kawasaki disease is an uncommon disease, and may present with necrotizing non-granulomatous lymphadenitis. It is described in children younger than 5 years, which is characterized clinically by cervical lymphadenopathy, fever, conjunctivitis, erythyma of the lips and oral cavity and a skin rash. Affected lymph nodes display geographic necrosis and fibrinoid thrombosis of small vessels. The inflammatory cell infiltrate is composed of neutrophils and histiocytes. Plasmacytoid cells are not prominent (Taubert and Shulman, 1999). There was no Kawasaki disease in our cases.

In conclusion, our data demonstrate that necrotizing non-granulomatous lymphadenitis is only a common pathological change found in some diseases, such as TB, SLE and KFD. It is not a specific disease entity. Further investigations to exclude treatable causes are recommended.

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