HISTIOCYTIC NECROTIZING LYMPHADENITIS A CLINICOPATHOLOGICAL STUDY

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ABSTRACT

Seven cases of Histiocytic necrotizing Lymphadenitis (HNL) were studied. They constituted 0.56% of all lymph nodes biopsies. The condition primarily affects young women causing cervical lymph node enlargment and leukopenia. The basic lesion is characterized by proliferation of lymphocytes and histiocytes with nuclear debris in the para cortex and cortex. This study examined various bacterial, viral and immunological factors which could possibly be responsible for this condition. However, it failed to find positive association with any of them. The existence of this disease in Pakistan is documented. (JPMA 41: 86, 1991).

INTRODUCTION

The disease was first described by Kikuchi et al[1]. Since then many cases have been reported from Japan[1-3], Europe[4-6] and USA[7]. The etiology and pathogenesis of lesions is not yet known. No case has been described from Pakistan. This paper describes the clinical pattern, morphological features, prognosis and association of possible etiological factors in our patients.

PATIENTS AND METHODS

Armed Forces Institute of Pathology receives specimens not only from military hospitals but also from civilian population of the northern Punjab and adjacent part of N.W.F.P. The study comprised of 7 cases of HNL studied at the Institute. The clinical data was obtained from the attending clinicians or patients. Paraffin sections of the cases for light microscopy were fixed in B5 solution or 10% neutral formalin. In addition to routine stains of H&E, special stains were used for demonstration of organisms and PAS was used for cytoplasmic immunoglobin. The diagnosis was made on the basis of histological criteria described in the previous reports[1,2,4].

Following laboratory investigations were also carried out:-

Blood complete picture, culture of sputum, throat and blood, tuberculin test, antibody titre for typhoid, brucella, toxoplasma, mycoplasma, monospot test for heterophile antibodies, influenza, measles, rubella adenoviruses, HIV and EB viruses, liver function tests, serological test for rheumatoid factor and anti-DNA antibodies was also carried.

Cases were followed over a period of one year.

RESULTS

1. Clinical findings

Of 1231 lymph node biopsies, 7 (0.56%) showed HNL. The ages of the patients ranged between 10 and 42 years, with a mean of 23.7 years. Out of 7 patients, 6 were females and 1 male. All patients had cervical lymph node involvement (frequently post cervical), with one case of adenopathy in inguinal region. Duration of lymphadenopathy ranged from 20 days to 60 days. There was low grade fever. None of them had skin rash. Generalized lymphadenopathy alongwith splenomegaly was not present in

our cases. Non specific signs/symptom like sneezing, catarrh, malaise were present in most of the cases. The main clinical findings alongwith history is shown in table.

TABLE. Clinical Findings.

S.No	Age	Sex	Site	Duration (days)	Fever (38°C)	Skin Rash	Past History	Family History	Exposure to Drugs/Vaccine	History of Allergy	Clincal Diagnosis
1.	24	M	Cervical	30	+	-	Nothing significant	Nothing significant	Analgesic off & on	Nil	Tuberculosis
2.	18	F	Cervical	35	+	-	Severe Bron chitis 8 wks back.	do	Bronchitis was treated with erythrocin	Sulpha drugs and Gold ornaments	RTI
3.	42	F	Cervical	42	+	-	Acid peptic disease	IHD	Antacids	Hair Dyes	Tuberculosis
4.	23	F	Cervical	21	+	-	Nothing significant	Tuberculosis	Nil	Nil	Tuberculosis
5.	35	F	Cervical	18	+	-	Respiratory tract infection off & on	Nothing significant.	Nil	Nil	Tuberculosis
6.	10	F	Inguinal	28	-	-	Typhoid fever 8 months back	do	Amoxil used for typhoid	Sulpha drugs	Non specific chronic lymphadenitis
7.	14	F	Cervical	14	+	-	Nothing significant	do	Nil	Nil	Tuberculosis

Four patients were housewives, two were students and one was serving soldier.

2. Laboratory findings

Laboratoryfindings in most ofthe patients included neutropenia (1.9 to 3.4 x109 / 1). Lymphocytes constituted 43 to 62% of total count. Atypical lymphocytes were seen in three cases making up 1-2% of the differential count. Platelet count was within limits in all cases. A mild to moderate increase in ESR was seen. Blood culture, throat and sputum cultures did not yield any pathogenic organisms. Transaminases were raised only in two cases. Tuberculin test was positive in five cases.

3. Antibody titre

Antibodies against toxoplasma were negative in all cases. One case each had positive titre for influenza and measles. virus. R A factor was positive in one case and anti-DNA antibodies (LE) were positive in 2 cases.

4. Light microscopy findings

There was proliferation of transformed lymphocytes which had oval or slightly indented vesicular nuclei, small nucleoli and pale amphophilic cytoplasm. They were found focally, mainly in paracortex and subcapsular cortex. Histiocytes and nuclear debris were intermingled with these lymphocytes. There were no neutrophils and plasma cells. Fibrin thrombi were present in the vessels alongwith necrosis in affected areas (Figures-1,2).

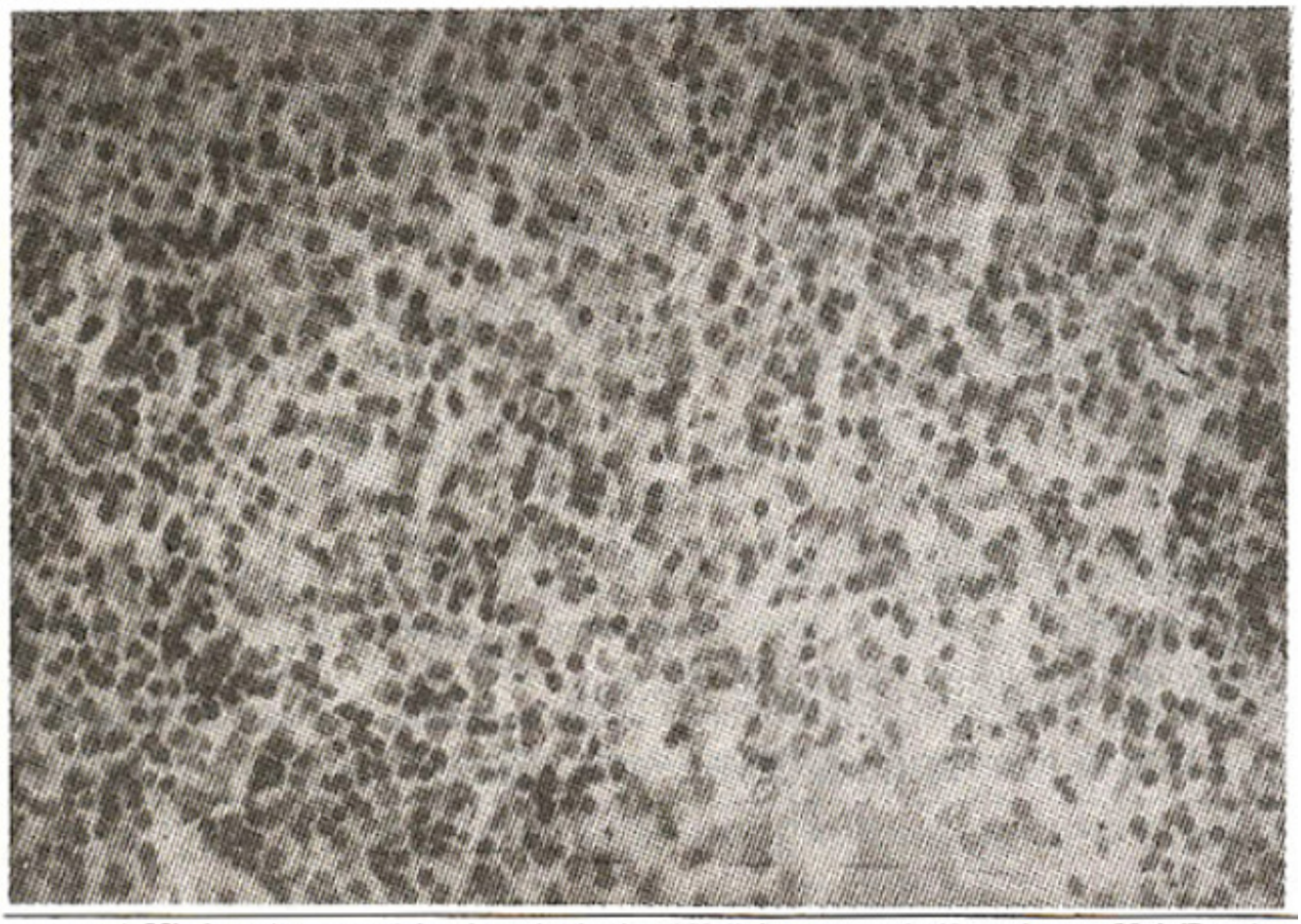

Figure 1. Histiocytic necrotizing lymphadenitis. Well demarcated affected area. H & E stain, X250.

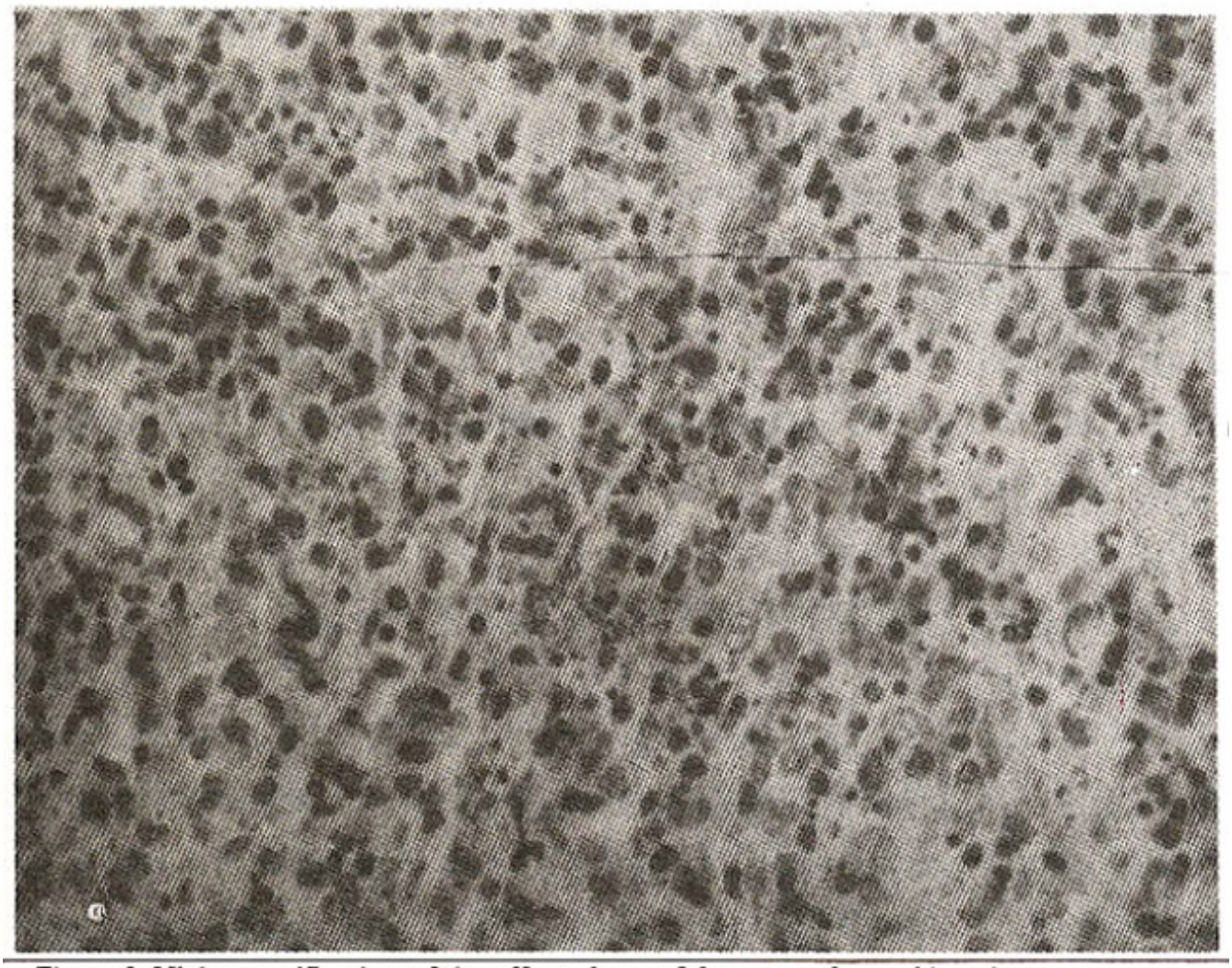

Figure 2. High magnification of the affected area. Many transformed lymphocytes, macrophages and histiocytes are present, accompanied by individual cell necrosis. A few immunoblasts are seen at places. H & E stain X 400.

Special stains were used but yielded no organisms, PAS stain was negative for cytoplasmic immunoglobins. Two of seven cases were referred from other Institutes. One case had been diagnosed as “Malignant Histiocytosis" and another as “Large cell Non Hodgkin’s Lymphoma". This misdiagnosis was apparently due to the presence of transformed lymphocytes and histiocytes in the affected foci.

Prognosis and follow-up

The disease resolved spontaneously (6-18 weeks) in all of the cases alongwith complete resolution of all clinical and laboratory findings without any residual complication. Regular follow up was carried out but no abnormal
findings were noticed in any case.

DISCUSSION

HNL has been reported from various parts of the world[1-3,5]. It is a unique lymphadenitis affecting mainly young women but male patients and older people may also be affected[7-9]. The patients usually present with enlargement of lymph nodes of short duration (3-12 weeks). The disease mainly affects

cervical lymph nodes but any other lymph node may be involved or there may be generalized lymphadenopathy alongwith splenomegaly[7,8,10,11]. Most patients have low grade fever, without any specific pattern. The general condition of patients is usually excellent[1,6]. Our cases generally confirmed to this clinical pattern. The disease typically resolves spontaneously in weeks to months without any residual complication. Occasionally disease recurs or it may persist upto 8-12 months[1,7,12,13] .In Dorfinan's comprehensive review, there have been no fatalities or malignant transformation. Some authors recommend longterm follow up of the patients[9,13]. Chan et al recently reported a fatal case of HNL[14]. The etiology of HNL is unknown. Viral etiology which is unidentified is claimed by various authors[2,7,15]. The observation was based on neutropenia alongwith relative lymphocytosis, no response to antibiotics and seasonal variation in incidence. Electron microscopic studies also suggest a viral edology. structures in the cytoplasm of lymphocytes and histiocytes) but do not confirm it[3,16,17]. Our cases were mostly reported in winter. We searched for positive antiviral titre but only two cases showed association with past viral infection. Chan et al[18] discussed the morphological changes in salmonella infection and similarities of lesion in their reported fatal case[14]. The blood culture and antityphoid antibodies were negative in all of our cases. No other microbial agents have shown relationship with the lesion. Immunohistological studies carried out by Kikuchi et al[3] demonstrated that proliferating lymphocytes in the lesion were composed mainly of both CD4 and CD8, with a predominance of CD8 in the early stage. These immunohistologica! features are also seen to be related to delayed type of hypersensitivity reaction as well as defence mechanisms against some agent. Tuberculin test was positive in all except two cases but positive tuberculin is reported in normal adults of our country. None of our patients gave history of vaccination. Use of any chemicals or drugs with past history of allergy was not reported. Rheumatoid factor (one case) and anti DNA antibodies (two cases) were positive in our study. Young women in their active reproductive life constitute main bulk of the patients. The skin rashes, fever, myocarditis, leukopenia, lymphadenopathy and positive anti-DNA antibodies, are all suggestive of autoimmune disorder. Defective Immuno-regulation alongwith immune-effector mechanism and altered estrogen metabolism are characteristic of SLE[19-22]. Tubuloreticular structures (TRS) have also been noted within lymphocytes of patients with SLE and other autoimmune disorders[12]. These clinical and morphological features are strongly suggestive of SLE-like condition induced by different etiological agents (chemical, microbial, physical, or immunological). We could not correlate these findings with etiology of HNL because plasma cells are scanty and there is no PAS positive cytoplasmic immunoglobulin. No significant increase in vascularization is seen. Lastly we stress the importance of correct diagnosis of HNL. Two of our cases were misdiagnosed even by experienced histopathologists. HNL has excellent prognosis but requires a correct diagnosis. A long term follow up of all patients is also recommended.

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