

TOXOPLASMIC LYMPHADENITIS A CLINICOPATHOLOGICAL STUDY

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ABSTRACT

Forty three cases of toxoplasmic lymphadenitis were studied. They constituted 0.5% of all lymphnode biopsies and 4.2% of reactive lymphadenitis. The histological findings supporting a diagnosis of toxoplasmosis were correlated with serological studies. The condition primarily affects young men, causing cervical lymphnode enlargement and varying degrees of fatigue, malaise, cough and fever. It is usually self-limited. This study emphasizes the need for clinicians to consider toxoplasmosis in the differential diagnosis of lymphadenopathies (JPMA 41: 303, 1991).

INTRODUCTION

Since the parasite was first identified in 'gundi' (*ctenodactylus gundi*), later in rabbits and dogs¹ in North Africa, *toxoplasma gondii* has been the subject of much study. The interest was heightened with reports by Janku² who described these parasites in the tissue of an infant with hydrocephalus, who died soon after birth. The histopathologic changes in lymph nodes affected by toxoplasmosis was first described by Robb-Smith³. No study has been published about toxoplasmic lymphadenitis in Pakistan. Lymph node biopsies in patients with suspected tuberculosis or malignancy at various medical centres of northern Pakistan provided us an opportunity to undertake this study.

MATERIAL AND METHOD

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 NWFP. During the past eight years (January, 1983 to December, 1990), lymph node biopsies from 43 patients were diagnosed as consistent with toxoplasmic lymphadenitis. The histological diagnosis was made on the basis of already established criteria³⁻⁶ without prior knowledge of serological results. The clinical data was recorded and patient's serum was collected for toxoplasma antibodies. Blood complete picture and tuberculin test were also carried out. Paraffin section of the cases for light microscopy were fixed in B5 solution or 10% neutral formalin. In addition to routine stains of H&E, PAS and giemsa stains were also used. The serum was stored at -20°C until processed for analysis. IgG antibodies were detected in sera by direct agglutination method. The serological diagnosis was made on the basis of criteria⁷⁻¹¹ described.

RESULTS

(a) Clinical findings

Forty-three cases of toxoplasmic lymphadenitis constituted 0.5% of all lymph node biopsies and 4.2% of reactive lymphadenitis diagnosed during the period of study. The ages of the patients ranged between 6 to 42 years (mean 18.8 years). Out of 43 patients, 28 were males and 15 females (M:F ratio 1.8:1). The common occupations included students (48.8%), soldiers (18.6%), housewives (11.6%), teachers (9.3%) and drivers (6.9%). The most common manifestation was lymphadenopathy without

any symptoms (44%) followed by adenopathy with fatigue and fever (30%). The remaining patients (25%) had adenopathy with cough, malaise and anorexia. Skin rash and visceromegaly were not present in any case. The duration of the symptoms prior to diagnosis ranged from 1 to 24 months (mean 3 months).

TABLE I. Sites of lymphadenopathy

Site	Male	Female	Total (%)
Cervical	18*	12	30 (69.7)
Submental	2	-	2 (4.6)
Axillary	1	1	3 (6.9)
Supraclavicular	1	-	1 (2.3)
Inguinal	2	-	2 (4.6)
Cervical and axillary	4	1	5 (11.6)

*Six patients presented with bilateral cervical lymphadenopathy.

Table I represents the sites of lymphadenopathy. The details of clinical diagnosis are listed in Table II.

TABLE II. Toxoplasmic lymphadenitis.

Clinical Diagnosis	No. (%)
Tuberculosis lymphadenitis	24 (55.8)
Hodgkin's disease	7 (16.2)
Malignant lymphoma	5 (11.6)
Chronic lymphadenitis	2 (4.6)
Infectious mononucleosis	1 (2.3)
Reactive change	1 (2.3)
Not available	3 (6.9)

(b) Laboratory findings

Thirty-eight patients had normal blood count, five had leukocytosis (16.2 to $19.7 \times 10^9/l$). The lymphocytes constituted 48 to 65% of the total count. A mild increase in ESR was seen in all cases (23 to 35 mm at the end of 1st hour - Westergren method). Tuberculin test was positive in twenty-four (55.8%) patients. Toxoplasma antibody (IgG) was positive in all cases. The details of titre are listed in Table III.

TABLE III. Serological Data

Antibody Titre	No. of Cases (%)
1:128	6 (13.9)
1:256	9 (20.9)
1:512	23 (53.4)
1:1024	5 (11.6)

(c) Pathological observations

The excised lymph nodes measured 1 to 3 cm in diameter and firm in consistency. Histologic findings included reactive follicular hyperplasia, associated with presence of irregular clusters of epithelioid histiocytes, located usually in cortical and paracortical zones. These cells characteristically encroached upon and blurred the margins of germinal centres. Epithelioid cells were also seen frequently within the germinal centres (Figures 1 and 2).

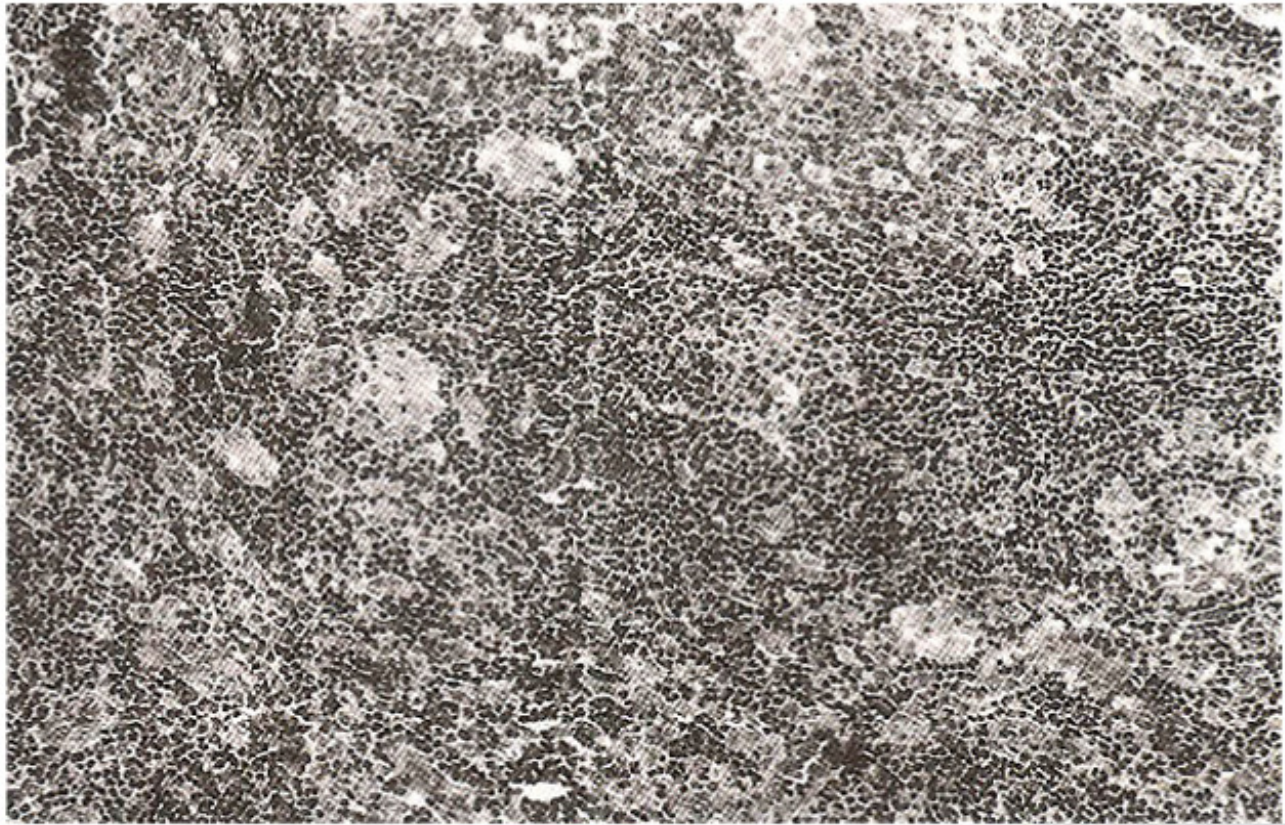


Figure 1. Toxoplasmosis lymphadenitis. Enlarged germinal centre has irregular contours. Clusters of epithelioid cells encroach on germinal centre and are scattered in cortex and paracortex (H&E x 40).

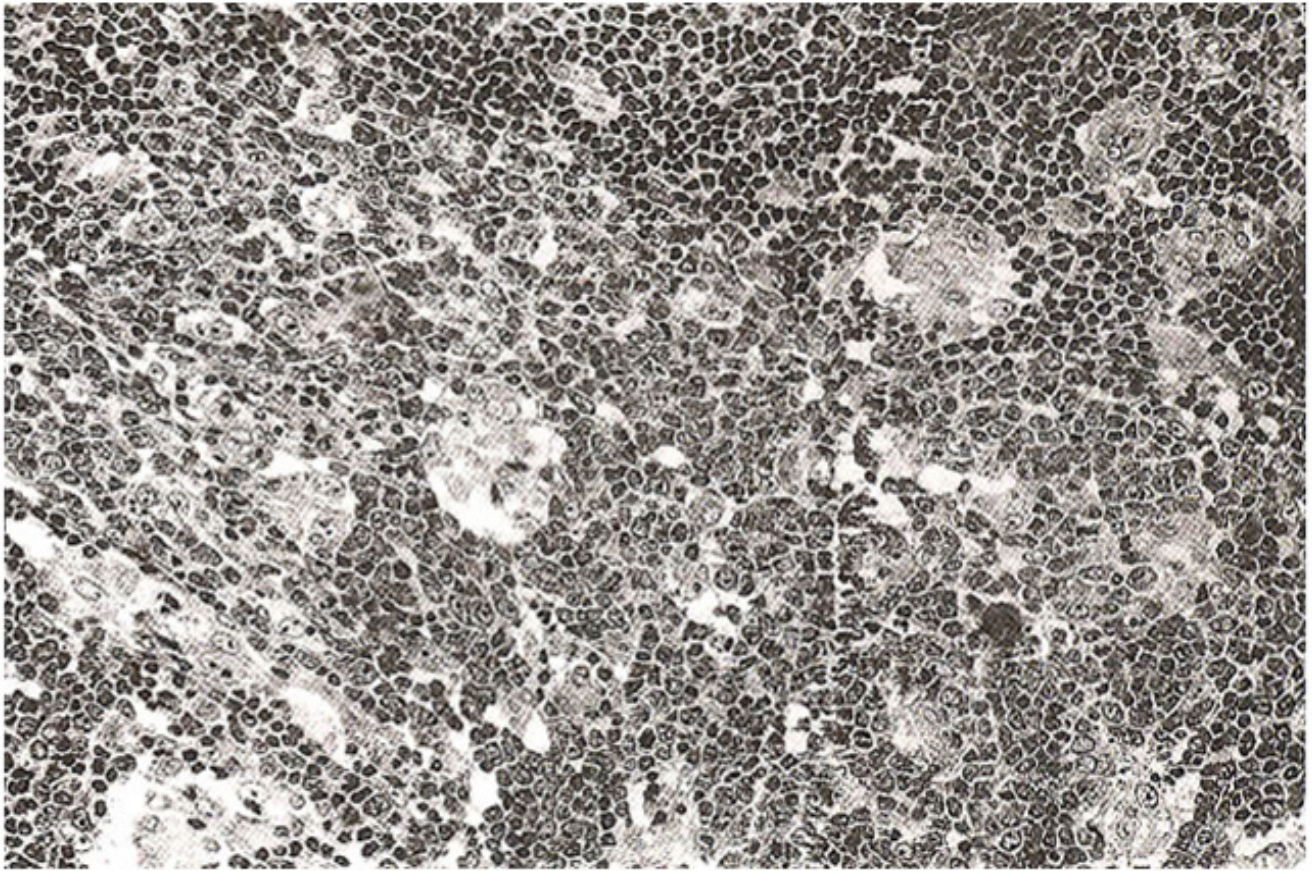


Figure 2. Toxoplasmosis lymphadenitis. Collections of epithelioid cells in the paracortical area encroach upon and are seen within the reactive follicle centre (H&E x 250).

An additional feature was distention of cortical and marginal sinuses by monocytoïd cells. The special stains yielded no 'cysts'.

(d) Prognosis and followup

The disease resolved spontaneously (4-12 weeks) in twenty-six cases (60.4%). The remaining seventeen cases responded to combination of sulphadiazine (3 gm/day) and pyrimethamine (25-50 mg/day) for 14 to 28 days. The disease resolved without any residual complications.

DISCUSSION

Toxoplasmosis is an infectious disease affecting man and other warm blooded vertebrates throughout the world, although the frequency of such infections varies considerably from country to country and within a country^{1,2,4,7,10,12-14}. It is caused by protozoan parasite *toxoplasma gondii*, an obligate intracellular protozoan. The parasite is coccidian of cats, the definitive host. Toxoplasmosis in humans has developed through several stages. In the past, it was regarded as a minor infection. However, extensive media attention in the late eighties made the medical and scientific communities appreciate the growing importance of toxoplasmic infection in humans. McCabe and Remington¹²⁻¹⁴ divided clinical toxoplasmosis into various types. Toxoplasmic lymphadenitis is the most common clinical type of acquired toxoplasmosis^{16,17}. However, other types may be associated with lymphadenopathy. Toxoplasmosis with lymphadenopathy as the presenting symptom has been well described^{4,15,17}. The lymphadenopathy is usually generalized; however, the cervical and suboccipital are often most prominent. They are painless^{3,4}. The duration of lymphadenopathy is extremely variable, ranging from

days to over a year. Our cases generally conformed to this pattern. Nonpruritic maculopapular rash and visceromegaly was reported in other studies^{3,4,13,17}, but was not seen in our cases. Present cases demonstrate a spectrum of symptoms, from completely asymptomatic patients to the prolonged illness with fever, anorexia, chills and cough. Malaise, fatigue and weakness are often quite pronounced. This clinical pattern was also reported in other studies^{3,4,6,13,17}. In this study, the disease primarily affected young men. The likelihood of toxoplasmosis increases with age, perhaps because of an increased cumulative exposure to infection as one gets older^{7,13}. The young men in our community are particularly exposed to undercooked meat, unpasteurized milk and/or contaminated water. The histological changes in lymph nodes affected by toxoplasmosis were described by Robb-Smith, but he was unaware of the underlying cause³. Pringer-Kuchinka and Sexan independently but simultaneously described the characteristic histologic changes that occur in toxoplasmic lymphadenitis^{3,4,6,17}. They emphasize the striking degree of reactive follicular hyperplasia associated with numerous mitosis in the germinal centres and presence of many freshly necrotic cells, so that the centres are littered with karyorrhectic particles of nuclear debris. The inter-follicular, cortical and paracortical zones contain clusters of epithelioid cells (histiocytes with vesicular nuclei and abundant eosinophilic cytoplasm). These cells are not arranged in well delimited tuberculioid follicles and very rarely associated with giant cells (foreign body/langhans type). They often and characteristically encroach upon and blur the margins of the reactive follicles and occur singly or in clusters in the germinal centre. These characteristic histological pictures of toxoplasmic lymphadenopathy were constantly seen in our cases. Occasionally similar collections of histiocytes are seen in lymph nodes of patients with Hodgkin's disease^{3,17}. Although necrosis is common Hodgkin's disease, it is not characteristic of toxoplasmic lymphadenitis^{6,15}. In other lymphadenitis like that of Whipple's disease¹⁸, infectious mononucleosis³, Kikuchi's lymphadenitis¹⁵ and Leishmaniasis⁶, aggregates of histiocytes similar to those seen in toxoplasmic lymphadenitis are also found. These clusters of histiocytes, therefore, may suggest the diagnosis, but do not make it definitive. If associated with high serological titer, they enable a surgical pathologist to diagnose toxoplasmic lymphadenitis with confidence^{1,3,4,15}. Since toxoplasmic 'cysts' are rarely observed in histologic section^{3-5,16-18}. The prognosis was excellent in our cases. The disease resolved in weeks to months without any residual complication. Occasionally disease recurs or may persist^{4,17}. The acute infection during pregnancy may result in severe consequences of congenital toxoplasmosis^{14,19}. Seroepidemiological study at Karachi¹⁰ confirms toxoplasma antibodies, 39.8% in pregnancy wastage group and 25.5% in congenitally abnormal group. Another study from northern Pakistan²⁰ reported that infection rate in pregnant women was highest in Punjab (63%) followed by Azad Kashmir(48%) and NWFP (38%). This indicates the widespread prevalence of parasite in our population. To conclude, toxoplasmosis is not an uncommon cause of lymphadenopathies as this is found in 4.2% of reactive lymphadenitis. It must be considered in the differential diagnosis of lymphadenopathy. The distinctive histopathological changes in affected lymph node could prevent the misdiagnosis of more serious conditions like Hodgkin's disease. The morphology, however, must be correlated with high serological titre, in order to make a definitive diagnosis.

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