

CERVICAL TOXOPLASMA LYMPHADENITIS: REPORT OF A CASE

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SUMMARY

Toxoplasmosis is a parasitic infection of worldwide distribution. It is caused by an obligate intracellular parasite, Toxoplasma gondii. The commonest form of this disease is the acquired simple lymphadenopathy. Such a case is described and the clinicopathological significance of the disease is discussed.

INTRODUCTION

Toxoplasmosis is a worldwide disorder caused by an obligate intracellular protozoan, *Toxoplasma gondii*. While infection is common, symptomatic disease is rare.¹ Serologic evidence have shown that 50% of the population in USA and 15–25% in Finland are seropositive for toxoplasmosis.²

Transmission of the disease to man has now been clarified. The definitive host appears to be the cat. Handling of contaminated cat litter provides a

possible faecal-oral pathway of spread to man. Infection is also frequently produced by contact with previously contaminated soil, land snails, earthworms, fleas and cock.³ It is also possible to produce a clinical disease through consumption of raw or incompletely cooked meat.⁴ Transplacental infection can also occur if the mother acquires the disease during pregnancy.

Toxoplasma organisms are rapidly killed by gastric juices. When cysts or oocysts are ingested, trophozoites emerge after the cyst walls are dissolved in the intestines. These burrow into the intestinal mucosa and are subsequently spread through the blood.¹ The parasite is capable of infecting virtually any tissue in the body with the possible exception of non-nucleated red blood cells.³

CASE REPORT

A 34-year-old Indian female presented with pain and swelling of the left submandibular region for a duration of two months. Pain was intermittent, throbbing and appeared to be of soft tissue origin. It was not relieved by simple analgesics. There were no known aggravating factors. Swelling and pain were not related to mealtimes. There were no other signs and symptoms.

Past dental history revealed that patient had a carious lower left third molar extracted about three weeks previously but the pain and swelling persisted.

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Past medical history showed that patient had right facial palsy 12 years ago, bilateral tubal ligation in 1975 and emergency appendicectomy in 1976. There were no known history of tuberculosis or any other serious illness.

Extra oral examination showed residual right facial weakness. At the site of complaint, there was an enlarged left submandibular swelling which was palpable bimanually. It was about 3 cm by 2 cm in diameter, mobile and painful on palpation. An enlarged lymph node of about 1 cm in diameter was found distal to the main swelling. An enlarged, 2 cm in diameter submental lymph node swelling was also detected. These lymph node swellings were discrete and rubbery. The overlying skin was warm. There was no fever.

Intraorally, the mucosa appeared normal and well-lubricated. The oral hygiene was good. The socket of lower left third molar was clean and healing well. Right and left submandibular salivary flow were satisfactory.

Radiographs of the mandible did not show any abnormality. A sialogram of the left submandibular salivary gland was done and the report was as follows: "The submandibular gland is enlarged, and its margin is a little irregular. Although no focal mass lesion is shown within the gland, an infiltrative tumour cannot be excluded. There is no evidence of any obstruction by a calculus or any evidence of sialectasis or chronic infection".

Patient was admitted to hospital on 6 July 1983. General physical examination and routine laboratory investigations were within normal limits. At operation under general anaesthesia, a dark brownish coloured lymph node was found attached to the submandibular salivary gland. The latter appeared unaffected by disease. Considering its attachment to the diseased lymph node and the sialogram report, the decision was taken to remove it together with the diseased lymph node. Post-operative healing was uneventful.

RESULTS

Histological findings

Macroscopically, the specimen consisted of three lobulated masses of soft tissue held together by fibrous attachments. The large lobe was the submandibular salivary gland and measured approximately 3.5 x 3.0 x 1.5 cm. The largest lymph node measured 3.0 x 2.0 x 1.0 cm. In both, the cut surfaces were firm and brownish and did not show any striking changes.

Microscopically, H + E sections of the submandibular salivary gland and lymph nodes were prepared. The former showed a normal salivary gland with intact glandular architecture.

For the lymph node, the essential features of reactive hyperplasia were observed. However, unlike hyperplasia, the enlarged lymphoid follicles were rather irregular in outline and also less distinctive (Fig. 1). They appeared to be infiltrated by epithelioid and histiocytic cells. The large active germinal centres also appeared disrupted. They exhibit considerable amount of mitosis. Scattered within the germinal centres were large numbers of macrophages with engulfed karyorrhectic debris (Fig. 2). Binucleated cells resembling Reed-Sternberg cells were similarly observed (Fig. 3).



Fig. 1 Enlarged and irregular lymphoid follicles with invading epithelioid clusters. (Haematoxylin and eosin) x 40.

Scattered throughout the pulp of the lymph node were clusters of pale-staining histiocytes. These were found predominantly in the peripheral region of the lymph node. They have vesicular nuclei and eosinophilic cytoplasm.

The subcapsular and medullary sinuses were dilated and contained a diffuse round cell infiltrate.

Another striking change observed was the presence of numerous blood vessels and irregular eosinophilic amorphous deposits throughout the node (Fig. 4). The nodal capsule was considerably thickened.

A tentative diagnosis of toxoplasma lymphadenitis was made on the basis of the histologic criteria of Anderson and Remington,⁵ Dorfman and Remington,⁶ and Stanfeld.⁷ The diagnosis was confirmed following the discovery of two toxoplasma cysts in two lymph node sections after an exhaustive search (Fig. 5, Fig. 6).

Laboratory Findings

The final diagnosis was made based on the serum immunoglobulin test which gave an antibody titre level of 1:16,384.

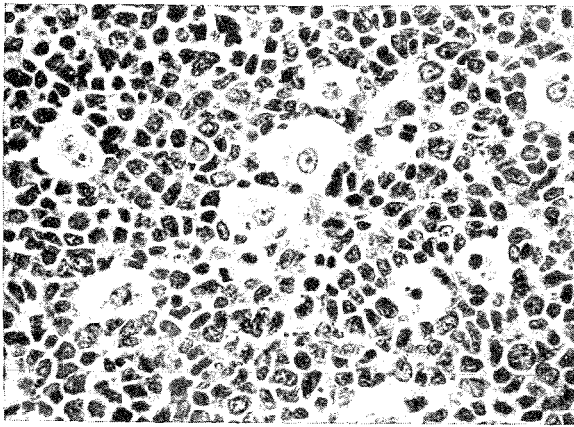


Fig. 2 Germinal centres showing mitoses and macrophages with engulfed karyorrhectic debris (Haematoxylin and eosin). x 400.

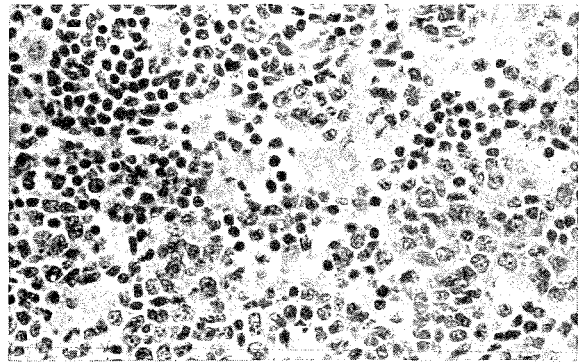


Fig. 4 Interstitial amorphous eosinophilic deposits. (Haematoxylin and eosin). x 400.

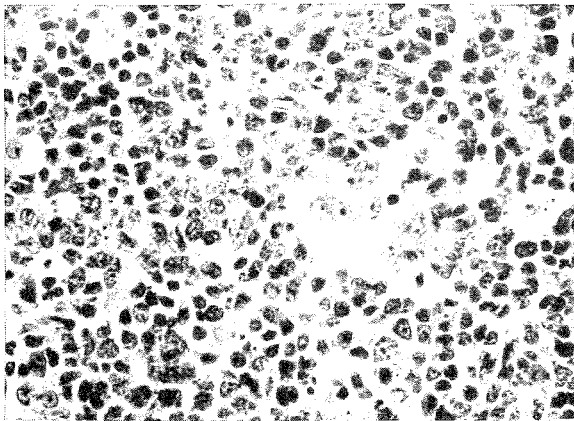


Fig. 3 Germinal centres showing a binucleated cell resembling a Reed-Sternberg cell. (Haematoxylin and eosin). x 400

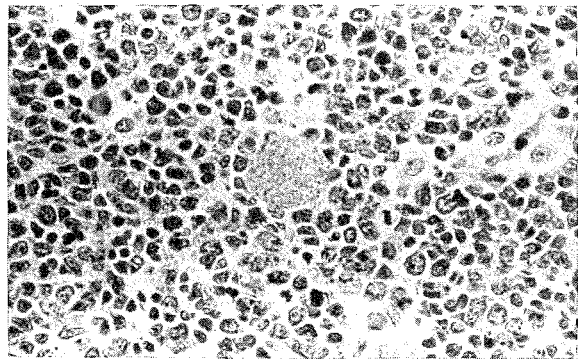


Fig. 5 Lymphoid follicle showing a distended toxoplasma cyst. (Haematoxylin and eosin). x 400.

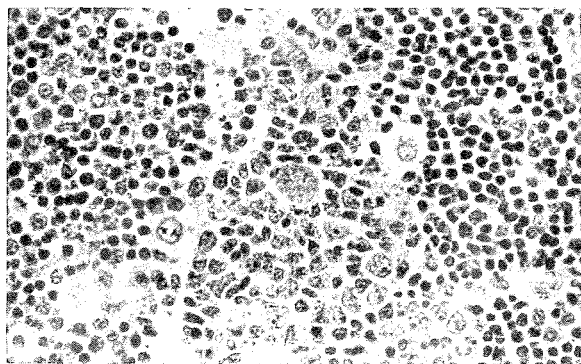


Fig. 6 Toxoplasma cyst at margin of a lymphoid follicle. (Haematoxylin and eosin), x 400.

Treatment

Once diagnosis was confirmed, patient was given a course of triple sulphonamide and pyrimethamine for two weeks. 2 g of sulphatriad and 50 mg of daraprim daily were prescribed. Patient developed nausea and vomiting with the sulphatriad. The serum folate level was 2 ng/ml. Folic acid supplement was given. Apart from some malaise, patient is well and the submental swelling had subsided considerably. Later her daughter aged eight years presented with fever (102°F) and similar swellings in the submandibular and submental regions. However serological investigations were negative. Although patient revealed that her neighbour had 25 cats, whether that contributed as a source of infection was not confirmed.

DISCUSSION

Acquired toxoplasmosis may present in three main ways: simple lymphadenopathy; lymphadenopathy with involvement of another organ; and generalised toxoplasmosis. Simple lymphadenopathy is by far the commonest. It is a disease with mild symptoms. In most cases the enlarged nodes were the only signs. Sometimes it may be associated with pharyngitis or a pyrexial illness requiring lengthy convalescence of one-and-a-half to two-years. In simple lymphadenopathy although any group of lymph nodes can be affected, the upper cervical nodes were commonly involved.⁴

In our present case, apart from the submental and left submandibular lymph node involvement, the apparent left submandibular salivary gland swelling could be attributed to the episodes of exacerbated chronic infected process occurring in the closely related lymph nodes.

The importance of toxoplasma lymphadenitis lies in its differentiation from much more serious conditions especially Hodgkin's disease and lymphosarcoma for which it may be mistaken on both clinical and histological grounds. Clinically, one of the characteristics which may lead to a suspicion of malignancy is the persistence of the lymph node enlargement, often for several months and sometimes for a year or longer. Although marked fatigue and general debility may be present, loss of weight is not a feature.⁷ Those with a pyrexial onset, pharyngitis and mild lymphocytosis may simulate infectious mononucleosis but the heterophil antibody test is consistently negative.³

Histologically, confusion with malignant lymphomatous conditions is liable to arise from the apparent disorganisation of the architecture of the node and the presence of active proliferating large cells variously interpreted as lymphoblasts or reticulum cells. Closer examination would show that the lymph node architecture is not, in fact, completely destroyed. The active proliferating cells show normal mitoses only. The crowding of the lymph sinuses with monocytoïd cells may simulate neoplastic infiltration. Although prominent histiocytic clusters of toxoplasma lymphadenitis may resemble those sometimes found in association with Hodgkin's disease and less often with lymphosarcoma and reticulosarcoma, giant reticulum cells characteristic of Hodgkin's disease are absent.

Another condition which the present case histologically resembles is angioimmunoblastic lymphadenopathy. This was considered in view of the presence of numerous blood vessels and scattered eosinophilic amorphous deposits which are characteristically found in this relatively newly described systemic disorder. However other features of this condition like hepatosplenomegaly, maculo-

papular rash, fever and haemolytic anaemia were not evident.¹

Although the concurrence of toxoplasmosis and lymphosarcoma or reticulosarcoma had been reported, it is difficult to decide whether this is a chance association or otherwise.⁷

Toxoplasma cysts are rarely found in lymph node sections.⁷ In the present case two such cysts were encountered after serial sectional studies. These cysts appeared to correspond to the true toxoplasma cyst and differ from pseudocyst in that there is a clearly defined cyst wall, apparently of parasitic origin. The contained toxoplasms are both smaller and much more numerous than those in the pseudocysts.

Apart from the finding of cysts in lymph nodes, it is generally agreed that the histological changes of toxoplasmic lymphadenitis are considerably characteristic.^{6,7} In his study, Miettinen *et al.*,² had shown that the histological specificity is about 85%. Out of 247 seropositive cases, seven presented with non-specific histology. In this study the most important features are nodal hyperplasia but with preserved general architecture, presence of histiocytic clusters and epithelioid cells both in the paracortical areas and germinal centres.

However characteristic the changes may be, the final diagnosis should never rest on histology alone.⁷ The final diagnosis should be made on the basis of

serological investigations. Isolation of organisms by animal inoculations can be done but had been shown to be not uniformly successful.

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