Toxoplasma Lymphadenopathy in an Immunocompetent Host

Sanjay Kumar Mandal\textsuperscript{a}  Atanu Chandra\textsuperscript{b}  Jacky Ganguly\textsuperscript{c}  Uddalak Chakraborty\textsuperscript{d}

\textsuperscript{a}Department of Internal Medicine, Medical College Kolkata, Kolkata, India; \textsuperscript{b}Department of Internal Medicine, RG Kar Medical College and Hospital, Kolkata, India; \textsuperscript{c}Department of Neurology, Medical College Kolkata, Kolkata, India; \textsuperscript{d}Department of Neurology, Bangur Institute of Neurosciences, IPGMER and SSKM Hospital, Kolkata, India

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Abstract
Toxoplasma infection can be congenital or acquired. Infection with \textit{Toxoplasma gondii} can result in multi-organ involvement in immunocompromised patients; whereas in immunocompetent patients, it usually remains asymptomatic. \textit{Toxoplasma} is a rare cause of isolated lymphadenopathy especially in immunocompetent individuals, though it is a common manifestation of this protozoal infection. We present a 27-year-old male who presented to us with isolated cervical lymphadenopathy. Histopathology and serological studies confirmed the diagnosis of toxoplasma lymphadenopathy. It usually affects the posterior cervical group of lymph nodes, but in our case, it had also affected anterior group and presented without any constitutional symptom. The patient was treated with cotrimoxazole double strength tablet once daily for 1 month and responded well.

Introduction
\textit{Toxoplasma gondii} can be transmitted to humans by ingestion of uncooked/undercooked infected meat or ingestion of oocysts through fecal contamination [1]. In immunocompetent patients, the infection mostly remain asymptomatic; sometimes, it can give rise to mild, nonspecific febrile illness or can present as acute disease, mostly in the form of chorioretinitis [2]. But in immunocompromised patients, there can be systemic disease involving the lymph nodes, eyes, central nervous system, lungs, heart, gastrointestinal tract, skeletal muscle, and kidneys. Lymphadenopathy can occur in 10–20% of acute cases and may be accompanied by constitutional symptoms [3]. Hence, there can be lots of differential diagnosis due to its diverse presentation. Here, we have reported a case of a 27-year-old immunocompetent male presenting with isolated cervical lymph nodes involvement without any fever or other constitutional symptoms, as the sole manifestation of \textit{Toxoplasma} infection.

Case Report
A 27-year-old male patient presented with multiple nodular swellings over his neck for last 3 weeks. There was neither any history of fever nor any history of cough or shortness of breath. He...
had no history of any recent travel or any history of contact with cats, other pets, or animals. He had no complaint of any rash, bleeding manifestations, or pain in the abdomen. He also denied any history of high risk sexual behavior. On examination, patient was afebrile. No pallor or icterus was noted. Cervical lymph nodes were found significantly enlarged. Left submandibular lymph node was 2.5 × 2 cm²; left occipital lymph node was 3 × 2.5 cm²; submental was of 2 × 2 cm²; and right submandibular was of 2 × 1.5 cm². They were nontender, firm in consistency, neither fixed to the overlying skin nor to the underlying structure, without any sinus or discharge. Other areas of lymph nodes were uninvolved. Sternal tenderness was absent. There was no hepatosplenomegaly, and examinations of the other systems were unremarkable. Retinoscopy did not reveal any abnormality.

Basic blood parameters did not reveal any abnormality; serum lactate dehydrogenase and uric acid levels were within normal limits. Antinuclear antibody, serology for HIV 1 and 2, monospot test for Epstein Barr virus, and ELISA to detect antibody to Cytomegalovirus, serum rK39 rapid immunochromatographic test were all negative. Serum angiotensin-converting enzyme level was not elevated. The summary of laboratory investigations has been described in Table 1. Contrast-enhanced computed tomography thorax and abdominal ultrasonogram did not reveal anything unusual. Biopsy was done from left submandibular lymph node. It revealed a preserved nodal architecture with expansion of the interfollicular areas and infiltration by plasma cells, lymphocytes, and histiocytes (Fig. 1). Scattered immunoblasts were seen along with small noncaseating granulomas within hyperplastic follicles (Fig. 2). Hematoxylin and Eosin stain, Giemsa stain from the lymph node biopsy or immunohistochemical staining failed to detect presence of any organism. Ziehl-Neelsen staining for acid fast bacilli and Gene-Xpert/Mtb from lymph node biopsy, negative Mantoux test, histopathology findings; lymphoproliferative diseases (point against: hematological and histopathology finding not suggestive of this); and infectious mononucleosis (points against: negative monospot test and specific histopathology finding). The possibility of other infectious etiologies such as Cytomegalovirus infection and leishmaniasis were ruled out by relevant serological tests. The possibility of sarcoidosis was unlikely due to normal serum angiotensin-converting enzyme level and normal chest imaging. Hence, based on the serological studies for toxoplasma and the suggestive histopathology of

### Table 1. Summary of the relevant laboratory parameters

| Tests                       | Results | Normal range          |
|-----------------------------|---------|-----------------------|
| Hemoglobin                  | 13.3    | 12–16 g/dL            |
| WBC                         | 6,800   | 4,000–11,000/μL       |
| Platelet count              | 1.62    | 1.5–4.5 lakh/μL       |
| ESR                         | 18      | <30 mm (first hour)   |
| CRP                         | 0.6     | Up to 0.8 mg/dL       |
| Serum LDH                   | 251     | 140–280 U/L           |
| Serum uric acid             | 5.8     | 3.5–7.2 mg/dL         |
| Serum ACE                   | 21      | <40 μg/L              |
| ANA                         | Negative| –                     |
| HIV 1 and 2                 |         | –                     |
| Monospot test for EBV       |         | –                     |
| ELISA for CMV antibody      |         | –                     |
| rK39 rapid test            |         | –                     |
| Mantoux test                |         | –                     |

WBC, white blood count; ESR, erythrocyte sedimentation rate; LDH, lactate dehydrogenase; CRP, C-reactive protein; ANA, antinuclear antibody; HIV, human immunodeficiency virus; EBV, Epstein Barr virus; ACE, angiotensin-converting enzyme; ELISA, enzyme-linked immunosorbent assay.

Possible differential diagnosis in our case were tubercular lymphadenopathy (points against: negative Ziehl-Neelsen staining for acid fast bacilli and Gene-Xpert/Mtb from lymph node biopsy, negative Mantoux test, histopathology findings); lymphoproliferative diseases (point against: hematological and histopathology finding not suggestive of this); and infectious mononucleosis (points against: negative monospot test and specific histopathology finding). The possibility of other infectious etiologies such as Cytomegalovirus infection and leishmaniasis were ruled out by relevant serological tests. The possibility of sarcoidosis was unlikely due to normal serum angiotensin-converting enzyme level and normal chest imaging. Hence, based on the serological studies for toxoplasma and the suggestive histopathology of

Fig. 1. Lymph node biopsy showing infiltrations by lymphocytes, plasma cells, and histiocytes.

Fig. 2. Lymph node biopsy showing noncaseating granuloma.
lymph node biopsy, the diagnosis was confirmed as toxoplasma lymphadenopathy.

The patient was treated with cotrimoxazole double strength tablet once daily for 1 month. The patient visited our outdoor after taking the medication for 1 month. All the lymph nodes decreased in size. At 3-month follow-up, there were no palpable cervical lymph nodes. The patient’s Toxoplasma IgG and IgM levels returned to undetectable range after completion of treatment.

Discussion

Clinical presentation of T. gondii infection is dependent mainly on two factors—the age and immune status of the individual. In immunocompromised patients, toxoplasmosis can be life-threatening [3]. It occurs as a result of reactivation of chronic disease and mostly affects the central nervous system but multi-organ failure can result. In immunocompetent patients, primary infection is usually asymptomatic. Individuals infected with toxoplasma may present with asymptomatic cervical lymphadenopathy at the time of the acute systemic infection; and sometimes the clinical feature mimic infectious mononucleosis such as fever, myalgia, sore throat, rash, and infrequently, myocarditis [4]. Acute acquired toxoplasmosis is usually self-limited and rarely requires treatment. Disseminated toxoplasmosis has also been reported in immunocompetent individuals [5]. Painless submandibular lymphadenopathy without any systemic symptoms were reported in a few case reports [6, 7]. Mashaly et al. [8] found a considerable prevalence of toxoplasmosis among Egyptian patients with tuberculosis and the severity of pulmonary tuberculosis was seen to be increased in those with coinfection with Toxoplasma. Chiu et al. [9] described a 66-year-old immunocompetent female who developed new-onset cervical lymphadenopathy and difficulty in deglutition during her treatment for pulmonary Mycobacterium avium complex. Excisional biopsy from the lymph node revealed noncaseating epithelioid granulomas and Gomori methenamine silver stain demonstrating bradyzoite of Toxoplasma gondii. Patient was treated successfully with trimethoprim-sulfamethoxazole. An unusual case of submandibular lymphadenitis in a 16-year-old male patient secondary to Toxoplasma gondii infection was described by Saxena et al. [10].

Diagnosis of toxoplasma lymphadenopathy is mainly based on careful history, along with histologic and serologic data. Histologic analysis usually reveals preserved lymph node architecture with presence of hyperplastic follicles and germinal centers containing multiple mitoses [11]. Toxoplasma lymphadenitis has triad of three findings: reactive follicular hyperplasia, clusters of epithelioid histiocytes within germinal centers (most specific), and B-cell infiltration in sinusoids [12]. Infections other than toxoplasmosis such as leishmaniasis and HIV infection often simulate the biopsy findings of toxoplasma lymphadenitis, which were excluded in our patient by appropriate serological tests. Granulomas and necrosis are usually not features of Toxoplasma lymphadenitis. Noncaseating granuloma was seen in biopsy in our case. Serological investigations using the ELISA are most useful and trustworthy tool in confirming old or recent infection with toxoplasma [13]. Molecular tests such as polymerase chain reaction was applied to the biopsy material for confirmation of diagnosis in some case reports, although it could not be done in our patient due to logistic issues.

Pyrimethamine plus sulfadiazine (PS) is the preferred choice in the treatment of ocular toxoplasmosis and toxoplasma encephalopathy [14]. Trimethoprim plus sulfamethoxazole (TS) is a reasonable alternative to PS in case of intolerance or unavailability of the drug. Pyrimethamine plus azithromycin may be used in cases of allergy to sulfonamides. PS, TS, and intravitreal clindamycin and dexamethasone are the treatment options active ocular toxoplasmosis. In immunocompetent individuals with toxoplasmic lymphadenopathy, TS is the treatment of choice.

Conclusion

Toxoplasmosis (mainly in severe forms) is usually seen in immunocompromised individuals, but other common manifestations of this infection like lymphadenopathy may be present in immunocompetent individuals. Sometimes, this may not be associated with constitutional symptoms as in our case. Though tuberculosis and lymphoproliferative diseases are the two most common causes of lymphadenopathy in developing countries, possibility of other uncommon infections like toxoplasmosis should also be kept in mind.

Statement of Ethics

Our research complies with the guidelines for human studies and was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. However, ethical approval was not required for this article in accordance with the Institutional Ethics Committee. Written informed consent was obtained from the patient for publication of this case report and accompanying images after full explanation regarding his images being published for academic interest.

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Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

S.K.M., J.G., and U.C. contributed to conception, initial drafting of manuscript, critical revision of content, and final approval of manuscript. S.K.M., J.G., and A.C. contributed to patient management, conception, critical revision of content, and final approval of manuscript. All the authors are in agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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