



# Cervical Toxoplasma Lymphadenitis in Immunocompetent Patients: A Report of Five Cases and Literature Review

Sang-Wook Park<sup>1</sup>, Hyun Cheol Cha<sup>1</sup>, Younjeong Lee<sup>1</sup>, Jung Je Park<sup>1,2,3</sup>

<sup>1</sup>Department of Otorhinolaryngology, Gyeongsang National University Hospital, Jinju, Korea

<sup>2</sup>Department of Otorhinolaryngology, Gyeongsang National University College of Medicine, Jinju, Korea

<sup>3</sup>Institute of Medical Science, Gyeongsang National University, Jinju, Korea

## ABSTRACT

Toxoplasma gondii is a protozoan parasite that can cause cervical lymphadenopathy, particularly in immunocompetent individuals. Although often self-limiting and asymptomatic, it can clinically mimic conditions such as tuberculosis or lymphoma, leading to unnecessary invasive procedures or treatment. We report five cases of toxoplasma lymphadenitis confirmed by histopathological and serological evaluation. All patients presented with painless cervical lymph node enlargement and lacked systemic symptoms. Key histological findings included reactive follicular hyperplasia, epithelioid histiocytes, and monocyteoid B-cell proliferation. Serological testing revealed positive Toxoplasma IgG in all cases and IgM in four. No patients required specific anti-toxoplasma therapy, and no recurrence was observed during follow-up. These cases highlight the importance of considering toxoplasmosis in the differential diagnosis of cervical lymphadenopathy. Recognition of its pathological and serological features is crucial for accurate diagnosis and preventing misdiagnosis and inappropriate management.

**KEY WORDS:** Toxoplasmosis; lymphadenitis; Toxoplasma gondii.

## Introduction

Toxoplasma gondii is a protozoan parasite first discovered in 1901 by Nicolle and Manceaux in North African rodents. The first human infection was reported in 1923 by J. Janju.<sup>1,2)</sup> Human infection occurs through various transmission routes, including ingestion of raw or undercooked meat from infected pigs, cattle, or birds, consumption of oocysts present in cat feces or contaminated soil, blood transfusion, organ transplantation, or congenital infection via the placenta.<sup>3-5)</sup>

Most infections in immunocompetent individuals are asymptomatic; however, when symptoms occur, cervical lymphadenitis is the most common clinical presentation. In

contrast, immunocompromised individuals and congenitally infected neonates may develop severe complications such as encephalitis, chorioretinitis, pneumonia, or myocarditis.<sup>6)</sup>

From 2010 onward, we encountered five cases of cervical toxoplasmosis diagnosed through histopathological and serological examinations in patients presenting with cervical lymphadenopathy. Here, we report these cases along with a review of the literature.

## Case Reports

### Case 1

A 49-year-old man presented with a left submandibular

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Corresponding author: Jung Je Park, Department of Otorhinolaryngology, Gyeongsang National University Hospital, Jinju 52727, Korea

Tel: +82-55-750-8698, Fax: +82-55-759-0613, E-mail: capetown@hanmail.net

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mass that had developed two months prior. He had no history of livestock or pet exposure, raw meat consumption, travel, or occupational risk factors. On physical examination, multiple firm, non-tender, mobile lymph nodes measuring  $2 \times 2$  cm were palpated in the left level II and V regions, with no additional abnormalities. Ultrasonography showed multiple hypoechoic lymph nodes measuring up to  $1.5 \times 1.5$  cm in the left level II and V regions, along with additional lymphadenopathy ( $>1$  cm) in both sides of the neck. Fine-needle aspiration cytology (FNAC) revealed abundant lymphocytes without malignant features. Neck computed tomography (CT) identified multiple homogeneous hypodense masses in the left level II and V regions, with the largest measuring  $1.7 \times 1.5$  cm (Fig. 1A). Excisional biopsy was performed, removing a well-circumscribed firm mass from level V. Pathological examination revealed chronic lymphadenitis with clusters of epithelioid cells, raising suspicion for toxoplasma lymphadenitis. Post-operative serological testing confirmed positive Toxoplasma IgG and IgM antibodies, leading to a definitive diagnosis. The patient remained asymptomatic, with no recurrence observed during six months of follow-up.

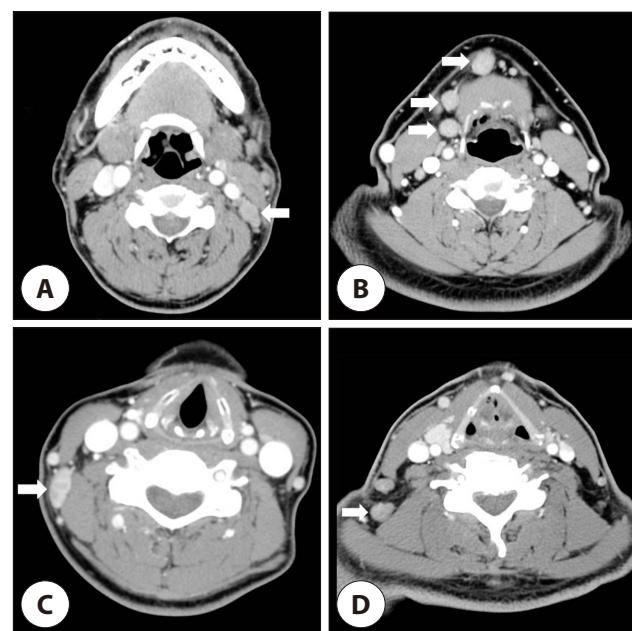
## Case 2

A 53-year-old man presented with a painless right cervical mass persisting for two months. His past medical history was unremarkable. Physical examination revealed a firm, mobile,  $1.5 \times 1.5$  cm mass at level I of the right neck. FNAC did not reveal malignant features. Neck CT showed multiple homogeneous hypodense lymph nodes, with the largest measuring  $1.7 \times 1.5$  cm at level I (Fig. 1B). Excisional biopsy was

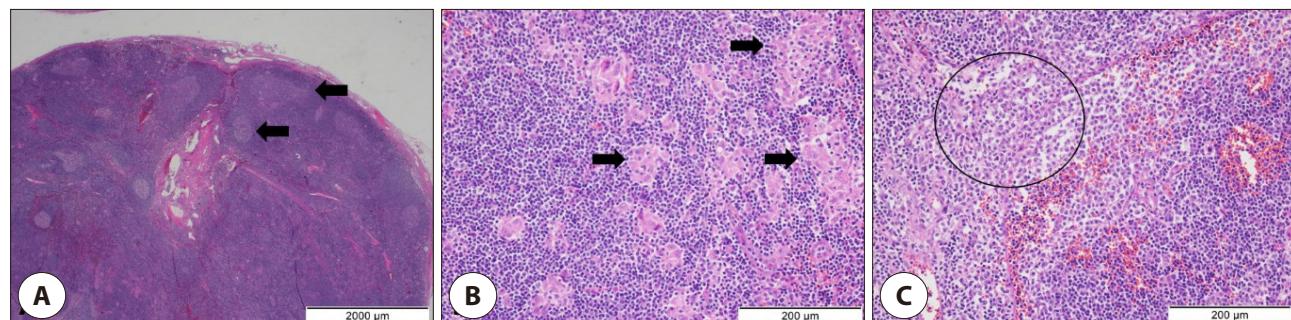
performed. Pathological findings included reactive follicular hyperplasia, epithelioid histiocytes, and monocyte B-cell proliferation, confirming toxoplasma lymphadenitis (Fig. 2). Postoperatively, serological testing confirmed positive Toxoplasma IgG and IgM antibodies. The patient remained asymptomatic, with no recurrence noted at the two-month follow-up.

## Case 3

A 56-year-old woman presented with a right cervical mass



**Fig. 1.** Axial enhanced neck CT scans of four toxoplasma lymphadenitis cases. A:  $1.7 \times 1.5$  cm sized ovoid mass with homogeneous low density in Lt. level V (arrow) of case 1, B: three round masses ( $1.7 \times 1.5$  cm,  $1.5 \times 1.5$  cm,  $1.3 \times 1.3$  cm) with homogeneous low density in Rt. Level I (arrow) of case 2, C:  $2 \times 1$  cm sized ovoid mass with heterogeneous enhancement in Rt. level V (arrow) of case 3, D:  $1.5 \times 1.3$  cm sized round mass with homogeneous low density in Rt. level V (arrow) of case 5.



**Fig. 2.** Histopathologic section of the Rt. level I mass of case 2. A: Low-power view of lymph node shows follicular hyperplasia (arrow; H&E stain,  $\times 20$ ), B: High-power view shows clusters of epithelioid cell (arrow; H&E stain,  $\times 200$ ), C: High-power view shows monocyte B-cells hyperplasia (round circle; H&E stain,  $\times 200$ ).

that persisted despite a 10-day course of antibiotics. Physical examination revealed two firm, non-tender lymph nodes measuring  $2.5 \times 1$  cm and  $1 \times 1$  cm in level V of the right neck. No additional abnormalities were noted. FNAC showed no malignant features, and *Mycobacterium Nested PCR* was negative. Neck CT revealed two oval, contrast-enhanced masses measuring  $2 \times 1$  cm and  $1.5 \times 1$  cm in the right level V region (Fig. 1C). Excisional biopsy was performed and pathological examination revealed follicular hyperplasia with multiple small granulomas, suggesting toxoplasma lymphadenitis. Postoperative serological testing confirmed positive Toxoplasma IgG and negative IgM, indicating a chronic infection.

#### Case 4

A 55-year-old man presented with bilateral cervical lymphadenopathy that had developed two weeks prior. His past medical history included raising poultry and dogs for over ten years, but he had no history of pulmonary tuberculosis or systemic symptoms. On examination, multiple lymph nodes (up to 1cm) were palpated in the posterior cervical region bilaterally. Laboratory tests showed normal findings, Interferon-gamma release assay (IGRA) negativity, and positive Toxoplasma IgG and IgM. To confirm the diagnosis, the excisional biopsy was done, and pathologic findings revealed chronic lymphadenitis with epithelioid cell clusters, leading to a diagnosis of toxoplasma lymphadenitis.

#### Case 5

A 47-year-old man was referred for suspected T-cell lymphoma based on an excisional biopsy. On examination, multiple non-tender lymph nodes ( $-1.5 \times 1.5$  cm) were palpated in levels II and V of the right neck. No other abnormalities were noted, and laboratory tests were within normal limits. Serological testing showed positive Toxoplasma IgG and IgM. Neck CT revealed multiple homogeneous hypodense lymph nodes in levels II and V, with the largest measuring  $1.5 \times 1.3$  cm at level V (Fig. 1D). Re-excisional biopsy was performed, and pathological findings included reactive follicular hyperplasia, epithelioid histiocytes, and monocyteoid B-cell proliferation, confirming toxoplasma lymphadenitis. The patient remained asymptomatic, with no recurrence observed over one year of follow-up.

## Discussion

Most patients infected with *Toxoplasma gondii* remain asymptomatic, with cervical lymphadenitis being the most common clinical manifestation. Involvement of posterior cervical lymph nodes is common, and some cases of intraparotid lymphadenopathy have also been reported in Korea.<sup>7)</sup> Other clinical symptoms may include maculopapular rash, arthralgia, myalgia, and hepatitis. In immunocompromised patients, toxoplasmosis may present as central nervous system infections, myocarditis, pneumonia, or chorioretinitis.<sup>6)</sup>

The diagnosis of toxoplasmosis requires both pathological and serological examinations. To obtain pathological specimens, fine needle aspiration (FNA), core needle biopsy (CNB), and excisional biopsy can be considered. Among these, FNA and CNB can be performed relatively easily under ultrasound guidance and are associated with a low risk of complications.<sup>8)</sup> However, FNA yields a smaller sample compared to CNB, and diagnosis may be challenging when based solely on aspirated cells.<sup>9)</sup> Although excisional biopsy provides the most accurate diagnosis, it often requires hospitalization and general anesthesia, leading to increased time and financial costs, as well as the potential for scarring.<sup>10)</sup> To avoid unnecessary excisional biopsies, it is preferable to first perform ultrasound-guided procedures and consider excisional biopsy only when a definitive diagnosis cannot be established.<sup>8,9)</sup>

On contrast-enhanced CT, tuberculous lymphadenitis shows central low attenuation due to necrosis and peripheral enhancement whereas pre-treatment lymphoma presents as homogeneously enhancing nodes without necrosis or calcification.<sup>11)</sup> Toxoplasma lymphadenitis usually presents as multiple posterior cervical nodes with homogeneous or only mild enhancement, and otherwise nonspecific features, therefore CT scan alone is insufficient to reliably distinguish it from tuberculous lymphadenitis or lymphoma.<sup>12)</sup> Definitive diagnosis should rely on histopathology and serology (toxoplasma IgM/IgG).

Three key histopathological features of toxoplasma lymphadenitis include: (1) reactive follicular hyperplasia, (2) clusters of proliferating epithelioid histiocytes mixed with lymphocytes and immunoblasts, and (3) monocyteoid B-cell

hyperplasia.<sup>13)</sup> Although these three histological findings exhibit high specificity (96.9%), they have a relatively low sensitivity (44.4%). Eapen et al. proposed diagnostic criteria that include (1) the presence of microgranulomas, (2) the absence of multinucleated giant cells, (3) the predominance of stage II giant granulomas, and (4) follicular hyperplasia. This set of criteria was shown to diagnose toxoplasma lymphadenitis with 100% sensitivity and 96.6% specificity.<sup>13)</sup>

Serological tests, particularly enzyme-linked immunosorbent assay (ELISA), are widely used for detecting Toxoplasma antibodies. The presence of IgG and IgM antibodies is commonly used to diagnose acute toxoplasmosis. IgG antibodies typically appear 2–3 weeks after infection, peak within 1–2 months, and persist for life.<sup>14)</sup> In contrast, IgM antibodies become detectable around two weeks post-infection, peak at one month, and gradually decline, usually disappearing within 6–9 months.<sup>15)</sup>

In general, toxoplasmosis is self-limiting, and symptomatic treatment is sufficient for most immunocompetent patients. However, in cases of severe acute infection, systemic involvement, or immunocompromised patients (including

pregnant women), treatment with macrolide monotherapy or a combination of pyrimethamine and sulfadiazine may be required.<sup>16)</sup>

In our study, all five patients were immunocompetent, and only one case had a history suggestive of potential toxoplasma exposure. None of the cases presented with clinical symptoms other than painless cervical lymphadenopathy. Three patients underwent IGRA testing for tuberculosis, with one showing a positive result. Given the relatively high prevalence of tuberculous lymphadenitis in Korea, careful differentiation is necessary. Serological testing revealed Toxoplasma IgG positivity in all five cases, with IgM positivity in four cases. All patients underwent excisional biopsy and improved without additional therapy. No recurrences were observed during the 6-month follow-up (Table 1).

Although the prevalence of toxoplasmosis in Korea remains relatively low, the increasing trends of pet ownership, meat-based diets, and international travel may contribute to a rising incidence. Therefore, clinicians should consider toxoplasma lymphadenitis as a differential diagnosis in patients presenting with cervical lymphadenopathy.

**Table 1.** Five cases of toxoplasma lymphadenitis

	Case 1	Case 2	Case 3	Case 4	Case 5
Sex	M	M	F	M	M
Age	49	53	56	55	47
Onset	2 months	2 months	10 days	2 weeks	1 weeks
Past history	Non specific	Non specific	Non specific	livestock farming	Non specific
Location	Lt. level II, V	Rt. level I	Rt. level V	Both level V	Rt. level II, V
Symptom	Painless neck mass	Painless neck mass	Painless neck mass	Painless neck mass	Painless neck mass
Radiology (neck enhanced computed tomography)	Multiple 1.7×1.5 cm ovoid well-margined mass with low attenuation	Multiple 1.7×1.5 cm round well-margined mass with low attenuation	Multiple 2×1 cm ovoid well-margined mass with heterogeneous attenuation	None	Multiple 1.5×1.3 cm round well-margined mass with low attenuation
FNAC	Negative for malignancy	Negative for malignancy	Negative for malignancy	None	None
Operation	excision	excision	excision	excision	excision
Toxoplasma IgG	Positive	Positive	Positive	Positive	Positive
Toxoplasma IgM	Positive	Positive	Negative	Positive	Positive
IGRA	Positive	None	Negative	Negative	None
Additional treatment	None	None	None	None	None
Recurrence	None	None	None	None	None

FNAC: fine needle aspiration cytology, IGRA: interferon-gamma release assay.

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## Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

## ORCID

Sang-Wook Park, <https://orcid.org/0000-0002-7579-2327>

Hyun Cheol Cha, <https://orcid.org/0009-0006-4474-7001>

Younjeong Lee, <https://orcid.org/0009-0007-6465-0183>

Jung Je Park, <https://orcid.org/0000-0001-6325-0398>

## Author Contribution

Conceptualization: Park JJ.

Data curation: Park JJ, Park SW.

Formal analysis: Park JJ, Park SW.

Methodology: Park JJ, Park SW.

Validation: Park SW.

Investigation: Park SW.

Writing - original draft: Park SW.

Writing - review & editing: Park SW, Cha HC, Lee Y, Park

JJ.

## Ethics Approval

Not applicable.

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