Isolated Mediastinal Lymphadenitis Caused by Toxoplasma Infection in an Immunocompetent Adult

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Abstract

A 71-year-old female with no respiratory symptoms was admitted to our hospital for preoperative assessment before cataract surgery. All physical examination and laboratory findings were normal, but a chest x-ray showed bilateral hilar enlargement. Computed tomography (CT) of the chest revealed multiple lymphadenopathy involving the paratracheal, precarinal, subcarinal, aorticopulmonary and hilar nodes. Tuberculous lymphadenitis was suspected because there was a family history of tuberculosis and the patient's tuberculin skin test was positive. Excisional biopsy of the right scalene lymph node was performed, and pathologic examination revealed the characteristic features of toxoplasmic lymphadenitis. Testing showed that the patient was negative for immunoglobulin IgM antibodies to Toxoplasma, but had high Toxoplasma IgG avidity, which supported chronic Toxoplasma infection. Follow-up CT studies at 6 months, 1 year, 2 years revealed no changes in the lymphadenopathy. No further diagnostic testing was done and no therapy was administered. This case is noteworthy because it documents the rare finding of mediastinal lymphadenopathy in Toxoplasma infection and shows that it is appropriate to follow this condition without treatment in immunocompetent patients who are asymptomatic.

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Introduction

Toxoplasma gondii infection is usually a self-limiting subclinical illness in immunocompetent adults. The seroprevalence is high (reportedly up to 40%) in the adult population worldwide, especially in warm and humid climates. Acquired infections occur through ingestion of undercooked infected meat, inhalation of tissue cysts shed by infected animals or by penetration of the skin with oocysts (1). Lymphadenopathy is the most common manifestation of the disease in healthy adults. It is estimated that 5-8% of all cases of lymphadenopathy of unidentified origin are caused by *Toxoplasma gondii*. However, the true incidence is not known because affected individuals may show no definitive clinical signs of toxoplasmic lymphadenitis (2). The posterior cervical lymph nodes are the most frequently affected site. To our knowledge, involvement of the mediastinal nodes in this disease has not been reported previously. We report a case of toxoplasmic lymphadenitis in which the isolated mediastinal lymph node involvement showed characteristic histologic findings. The patient was seropositive.

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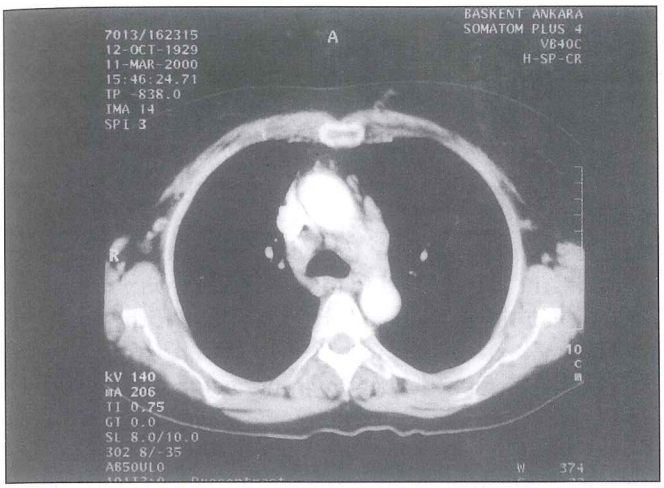

Figure 1. *Computerized tomography of the chest showing multiple lymphadenopathy in the mediastinum.*

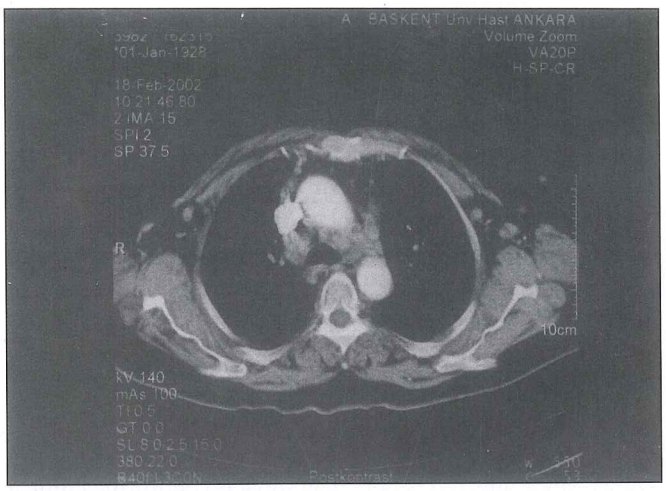

Figure 2. *After a period of two years, no change was observed in mediastinal lymph nodes.*

Case Report

A 71-year-old woman was admitted to our hospital in March 2000 for preoperative pulmonary evaluation prior to cataract surgery. She had no complaints related to the respiratory system or other organ systems. Her son had been treated for pulmonary tuberculosis 2 years previously. All physical examination findings were normal and no peripheral lymphadenopathy was noted. Laboratory investigations revealed a normal complete blood count (white blood cell count 7800/mm^3, red blood cell count 4 730 000/mm^3, platelet count 230 000/mm^3), and normal findings for hemoglobin (12.3 g/dL), erythrocyte sedimentation rate (25 mm/h), and C-reactive protein (2.4 mg/dL). The results of liver and renal function tests, serum electrolyte levels and glucose levels were also normal. A routine chest x-ray showed bilateral hilar enlargement. Computerized tomography (CT) of the chest revealed enlarged paratracheal, precarinal, subcarinal, aorticopulmonary and hilar lymph nodes, with the largest one measuring 18 mm in diameter. No pulmonary parenchymal involvement was present (Figure 1).

Ultrasound examination of the upper and lower abdomen showed no abnormalities. Serum angiotensin-converting enzyme and calcium levels were measured to rule out sarcoidosis and both were within normal limits (32 U/L and 8.6 mg/dL, respectively). Tuberculin skin testing (PPD) produced 19 mm induration. Bacille Calmette-Guerin (BCG) scar formation was absent in her left arm. Tuberculous lymphadenitis was suspected due to the family history of tuberculosis, PPD positivity and the fact that this disease is endemic to Turkey. On this basis, an excisional biopsy of the right scalene lymph node was performed for pathologic examination and *Mycobacteriun tuberculosis* (M.Tb) culturing.

The specimen was processed by standard procedures and 3 Fm-thick sections stained with hematoxylin and eosin stain were examined. The slides showed a polymorphous cell population composed of various sizes of mature lymphocytes with prominent germinal centers, epithelioid histiocytes in the paracortical areas and reactive follicular hyperplasia. No caseating or non-caseating granuloma, giant cell, or inflammatory exudate were observed. The histologic findings were suggestive of toxoplasmic lymphadenitis (Figure 2). The results of cultures for *Mycobacterium tuberculosis* were negative.

Serologic testing (EIA Kit, Labsystems) revealed high avidity for immunoglobulin (IgG) antibodies to *Toxoplasma*. This confirmed the pathologic diagnosis, and pointed to chronic *Toxoplasma* infection. Serology for IgM antibodies to *Toxoplasma* was negative, excluding acute infection.

The patient could not remember having had any contact with cats or other animals. Since the patient had asymptomatic clinical status and was immunocompetent, no specific toxoplasmosis therapy was administered. Follow-up CT scans at 6 months, 1 year and 2 years showed no change in the mediastinal lymphadenopathy (Figure 2). She underwent cataract surgery in April 2000 with no complications, and was in good clinical condition at the writing of this report.

Discussion

The majority of toxoplasmic lymphadenitis cases involve the posterior cervical lymph nodes, but other cervical nodes as well as the supraclavicular and occipital lymph nodes may also be affected (1,2). Involvement of the inguinal, axillary, and intramammary nodes has also been reported, but these are not common sites (3,4).

The clinical forms of *Toxoplasma* infection include acquired infection in an immunocompetent patient, acquired or reactivated infection in an immunosuppressed patient, ocular infection, infection during pregnancy, and congenital infection (1,5). It is reported that 80-90% of

immunocompetent patients with *Toxoplasma* infection remain asymptomatic (1) Our patient of toxoplasmic lymphadenitis was also asymptomatic. In symptomatic cases, the presentation ranges from enlargement of a solitary lymph node to generalized lymphadenopathy and fever (1). Our patient exhibited enlargement of the mediastinal lymph nodes exclusively and her condition was diagnosed accidentally during a preoperative assessment. In contrast to previous reports stating that toxoplasmic lymphadenitis is much more common at younger ages our patient was in the geriatric age group (2,6). *Toxoplasma* IgG seroprevalence of adult immunocompetent population in our country is reported to be similar (43%) to that reported from other regions (7). The course of toxoplasmic lymphadenitis is not known since affected people may show no definitive clinical sign of the disease.

The histopathologic triad of reactive follicular hyperplasia, clusters of epithelioid histiocytes and focal sinusoidal distention by monocytoid B cells is considered diagnostic for toxoplasmic lymphadenitis. One study showed that the sensitivity and specificity of this triad were 62.5% and 91%, respectively (6). In our case, examination of a right scalene lymph node biopsy revealed this histopathologic triad. As noted above, these features are highly specific for the diagnosis of toxoplasmic lymphadenitis and can be used with confidence. However, the literature stresses that toxoplasmosis can only be definitively diagnosed when histopathologic findings are supported by serologic results. In one report 89% of patients with toxoplasmic lymphadenitis showed significant levels of IgG antibodies to *Toxoplasma* (2). Our patient was seropositive and also exhibited the histopathologic triad, thus her diagnosis was confirmed.

Patients with toxoplasmosis generally test positive for IgM antibodies within the first week of infection and these levels peak within a month. A negative IgM test basically rules out infection of less than three weeks in an immunocompetent person. IgG antibody levels begin to rise approximately 2 weeks after infection reach a plateau within 2 months and then decline steadily over many years. Traditional serological testing with measurement of IgM and IgG levels is somewhat limited in its ability to reveal the duration of *T. gondii* infection in patients with lymphadenopathy, pregnant women, and older children suspected of having congenital toxoplasmosis (1). To address this problem, a variant of the *T. gondii* IgG avidity test is used in these three groups. High IgG avidity suggests that an individual is in the chronic phase of toxoplasmosis (5). In our case the typical histopathologic findings high IgG avidity, and long follow-up period (2 years) with no change in lymph node status supported the diagnosis of chronic toxoplasmic lymphadenitis.

The histologic differential diagnosis of toxoplasmic lymphadenitis includes several types of lymphadenitis characterized by granulomas or aggregated monocytoid cells. Sarcoidosis lymphadenopathy features well-formed granulomas. However unlike toxoplasmic lymphadenitis it is usually accompanied by multinucleated giant cells. Tuberculous lymphadenitis features caseous epithelioid cell granulomas accompanied by necrotic material (8,9). In addition the clinical findings of persistent and unchanged lymphadenopathy over 2 years in our asymptomatic patient did not suggest lymphoma. In line with the principle of "first do not harm" we decided to follow the case with no further diagnostic intervention, and administration of therapy.

It is usual to encounter self-limited, asymptomatic, unexplained lymphadenopathy in normal individuals. Fine-needle aspiration cytology has become an important first line of non-invasive investigation for patients with palpable peripheral lymph node enlargement (4). However, we opted for excisional biopsy in our case because we felt that fine-needle aspiration would not provide an adequate sample.

Tuberculosis is the leading cause of unexplained lymphadenitis in Turkey. Particularly tissue culturing is reported to be essential for diagnosis of tuberculosis, even if takes 6-8 weeks for this method to yield results. In our case, we were able to diagnose toxoplasmosis specifically and rapidly because the patient was seropositive for *Toxoplasma* and showed characteristic histopathologic findings. Cultures for *Mycoplasma tuberculosis* also remained negative. This was very important because it prevented unnecessary anti-tuberculosis therapy.

The drugs that are currently recommended for treatment of *T. gondii* infection act primarily on the tachyzoite stage. Pyrimethamine is considered the most effective anti-*Toxoplasma* agent. Immunocompetent adults with toxoplasmic lymphadenitis are usually not treated unless there is clinically overt visceral disease or the symptoms are severe or persistent (1). Based on our patient's symptom-free status, we elected not to treat but to follow her clinically and radiologically.

In conclusion, lymphadenitis due to *Toxoplasma* infection is relatively common and should be considered in the differential diagnosis of unexplained lymphadenopathy at any site. It is appropriate to follow this condition without treatment in asymptomatic immunocompetent patients.

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