

Case Report

Toxoplasmosis presented as a submental mass: a common disease, uncommon presentation

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Abstract: Submental mass secondary to toxoplasmosis is not common in clinical work. A diagnosis of toxoplasmosis is rarely considered by physicians. Here we describe a 50-year-old woman presented with a progressive, painful, submental and left neck swelling for 1 month. After having obtained an insufficient evidence from the fine-needle biopsy, the patient finally received an excisional biopsy which highly indicated the possibility of lymphadenopathy consistent with toxoplasmosis. Diagnosis of toxoplasmosis was finally established by a combination of the pathological criteria, together with the positive serological finding. According to review the clinical presentations, pathological characteristics, diagnostic standard and treatment of this disease, the article aims to remind otolaryngologists who are evaluating a neck mass should be aware of the infectious cause of lymphadenopathy and the possibility of toxoplasmosis.

Keywords: Toxoplasmosis, lymphadenopathy, diagnosis, toxoplasma

Introduction

Neck masses in patients usually refer to one of three situations: inflammatory/reactive, congenital, neoplastic. Nevertheless, making an accurate diagnosis is not as easy as it looks, even for otolaryngologists. *Toxoplasma gondii*, an obligate intracellular parasite, is prevalent in most areas of the world [1]. The clinical presentations of this disease are depended on the immune status of the patient. In most of immunocompetent adults and children, there are always no signs and symptoms when they get infection. Having reviewed the literature, we found that a diagnosis of toxoplasmosis is rarely considered by physicians even if the most typical clinical manifestation of this disease is isolated cervical and occipital lymphadenopathy.

Here we report a case of toxoplasmosis manifested as a progressive mass of the submental region, with the clinical and pathological features described.

Case report

A 50-year-old female was referred to the ENT Department of West China Hospital, complain-

ing of a 1-month history of a progressive, painful, submental and left neck swelling. During the period, there was no fever, hearing loss and hoarseness or other symptoms. Presumed by another physician to have reactive lymphadenitis, she had already received a 2-week course of antibiotic treatment, with no significant improvement in her symptoms. A mildly painful nodular mass of the submental region and diffuse lymph nodes, which mainly placed in her left neck and posterior auricular, were revealed by bimanual palpation. There were no any obvious pathologic findings through systemic examinations and laryngoscopy. Ultrasound testing reported a structural abnormality of the submental lymph nodes while the thyroid gland showed normally. Computed Tomography (CT) localized a 2.0 cm × 1.3 cm lymph node in the submental space while the rest smaller ones were distributed in posterior cervical triangle and submaxillary space. Owing to the poor effect of antibiotic therapy, she was suggested to receive a fine-needle aspiration biopsy which indicated that a few epithelioid cells were surrounded by lymphocytes. According to pathological finding of the scanty tissue, pathologists could not make an accurate diagnosis, thus she underwent an excisional biopsy. During the sur-

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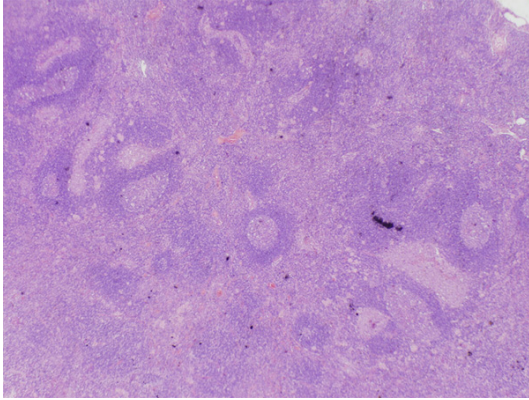


Figure 1. Follicular hyperplasia in toxoplasmic lymphadenitis (Hematoxylin and eosin [H&E], × 40).

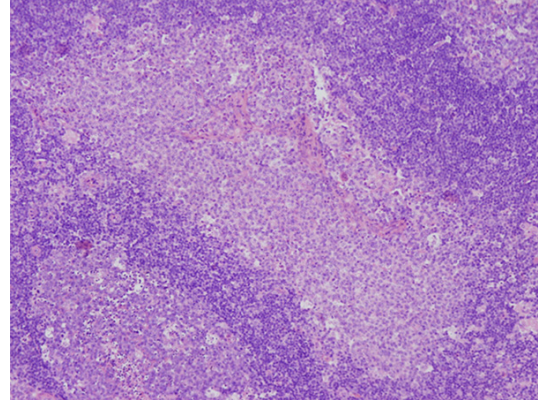


Figure 3. Monocytoid B-cells hyperplasia (Hematoxylin and eosin [H&E], × 100).

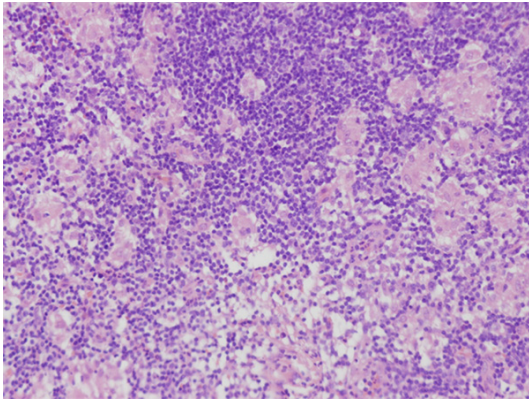


Figure 2. Small, noncaseating epithelioid in follicular areas (Hematoxylin and eosin [H&E], × 200).

gery, diffuse enlarged lymph nodes were noted to be located deep to the hyoid bone but superficial to the genioglossus muscle. In the intraoperative frozen pathological report, pathology tends to be a lymphoproliferative disease.

A subsequent formalin-fixed tissue sections were processed for routine microscopic examination. The most distinctive histopathological features seen on microscopic examination were: 1. Follicular hyperplasia. 2. Clusters of epithelioid encroached in the follicular center. 3. Monocytoid B-cells proliferation (**Figures 1-3**). The histopathological triad was highly suggested of a reactive lymphadenopathy secondary to toxoplasmosis. A serological test was scheduled consequently. The immunologic result confirmed a previous toxoplasmosis infection (IgG positive) but not a current infection (IgM negative). The final diagnosis was lymphadenitis consistent with toxoplasmosis.

The patient was referred to an infectious disease specialist, having taken sulfamethoxazole for 4 weeks. At the 4 years follow-up, there were no postoperative complications and the patient is asymptomatic with her lymphadenopathy resolved.

Discussion

Toxoplasma gondii is an obligate intracellular parasite which is prevalent in most areas of the world, having a non-seasonal worldwide distribution [1]. The prevalence rate of the disease depends on the environment, climate, living habits, sanitation level and so on. Prior seroepidemiological surveys in the USA showed 11% of persons aged 6 to 49 were seropositive for *T. gondii*, which exists in the environment in three forms: tachyzoite, bradyzoite (tissue cyst), oocyst [2]. Cats and other felines are the definitive hosts of the protozoan, while other warm-blooded animals, including humans, play a role of the intermediate hosts. Humans can be infected via transplacental transmission, ingestion of cysts, organ transplantation and blood transfusion. Transmission during breastfeeding or direct human-to-human transmission other than from mother to fetus has not been recorded [1, 3]. Our patient was probably exposed to *T. gondii* by intimate contacting with her cat, thus got infected through an oral-fecal avenue.

As mentioned above, toxoplasmosis mainly manifested in two forms: the congenital and the acquired forms. Clinically, the severity of acquired toxoplasmosis correlates with the immunologic status of the patient and the clinical setting [1]. Most of the immunocompetent

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patients often suffered an asymptomatic infection, while the immunocompromised ones are life-threatening. Symptomatic infections usually have a varied presentations and the common finding is an isolated cervical or occipital lymphadenopathy although any lymph node group can be affected. The intraparotid lymph nodes are involved when they represent an unusual presentation of toxoplasmosis [4, 5]. Some serious symptoms including toxoplasmic encephalitis, chorioretinitis, pneumonitis, acute respiratory failure seem to be more frequent among immunocompromised patients, especially in recipients of bone-marrow transplants and in patients with AIDS; or hematologic malignancy [6].

The histopathological triad of florid reactive follicular hyperplasia, clusters of epithelioid histiocytes, and focal sinusoidal distension by monocytoid B-cells has been considered to be distinctive changes of toxoplasmic lymphadenitis [7]. At the light microscopic level, the features are of extreme importance in differentiating lesions, such as: Hodgkin's lymphoma, cat scratch disease, etc., which mainly manifest as lymphadenopathy in the cervical and/or submental regions. Though it has been found to have a high specificity (96.9%), the sensitivity of this triad is only 44.4%. Eapen et al. have devised a composite criterion which including (1) presence of microgranulomas, (2) lower than grade 2 macrogranuloma, (3) absence of giant cells, and (4) follicular hyperplasia. This criterion can diagnose toxoplasmic lymphadenitis with a high degree of sensitivity (100%), specificity (96.6%), and positive likelihood ratio (29) [7]. The pathologists cannot identify the characteristic of nodal architecture that confirms the diagnosis, when a diagnosis of toxoplasmosis is suspected, unless the entire lymph node is removed and the architecture is well-preserved, so toxoplasma organisms are rare identified by examination of routinely stained tissue sections alone [8].

Despite its typical histological appearance of an involved lymph node, the diagnosis of toxoplasmosis is definitively confirmed after obtaining the positive results of tissue culture or to isolate the parasite from an infected tissue or body fluid by intraperitoneal inoculation of mice, which are described as the direct techniques while serological tests are the indirect tool. Clinicians prefer to choose the later one as

they are readily available, cheaper, and faster. Tuzuner et al confirmed the diagnosis of toxoplasmosis by serologic testing in 80 of 731 consecutively patients (10.94%) presenting with reactive lymph node hyperplasia [9]. For the diagnosis of a suspected patient of toxoplasmosis, IgM and IgG serology has been the main clinical test performed. Controversy exists in differentiating between a recently acquired infection and those obtained in the more distant past: IgM titers arise within the first 7 days of infection, elevate peak concentrations from 2 to 3 months, and then drop back to normal finally 6 to 9 months later; IgG antibodies become detectable 1 to 2 weeks after infection, persisting for the individual's lifetime [10]. In some cases, IgE and IgA could also be detected early in the infection, and IgA is more sensitive than IgM antibodies in the fetus and newborn, however, it can remain positive for years, so it has minor value for diagnosis of a recent infection; IgE antibodies only are used in combination with other serological methods [1].

Toxoplasmic lymphadenitis is a self-limited disease if it happened on immunocompetent adults and children. Symptoms are self-limited and resolve within 1 to 2 months in 60% of immunocompetent patients with no antimicrobial treatment [11, 12]. When patients suffers from unreasonable lymphadenopathy in the head and neck regions without any other systemic manifestation, a positive treatment is not necessary unless the clinical symptoms become severe or persistent or presented among the immunocompromised patients. It is especially important to control the parasitic infection in the immunocompromised hosts for its rarity and fatal consequences [6]. If needed, a typical drug combination of pyrimethamine, sulfadiazine and folinic acid for 4-6 weeks is the most widely used regimen, both from the point of economics and clinical efficacy. However, in immunocompromised patients, doses and lengths of treatment protocols should be adjusted according to their immunosuppression status [13].

In conclusion, despite high seroprevalence of the disease, toxoplasmosis is still an unrecognized disease. Thus, toxoplasmosis should be considered in the differential diagnosis of any cervical or unexplained lymphadenopathies. Diagnosis of toxoplasmosis should be estab-

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lished by a combination of the pathological criteria mentioned, together with the positive serological findings.

Disclosure of conflict of interest

None.

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