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Yeshwant B. Rawal
Marquette University, yeshwant.rawal@marquette.edu

Carl M. Allen
The Ohio State University

John R. Kalmar
The Ohio State University

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A Nodular Submental Mass

Yeshwant B. Rawal
Oral and Maxillofacial Pathology, University of Tennessee College of Dentistry, Memphis, Tennessee
Carl M. Allen
Oral and Maxillofacial Pathology, College of Dentistry, The Ohio State University, Columbus, Ohio
John R. Kalmar
Oral and Maxillofacial Pathology, College of Dentistry, The Ohio State University, Columbus, Ohio

Abstract

A 26-year-old male presented with a 2-month history of a mildly painful, slow growing, nodular mass of the submental region (Fig. 1). Examination revealed a 1.5 × 1.0-cm midline swelling of the submental region. The skin over the mass appeared normal. The mass was firm and slightly tender on palpation and appeared to be positioned within the submental space. Intraoral examination did not reveal any obvious pathologic findings and the nearby teeth showed no caries, periodontal disease, or mobility. The patient's medical history was unremarkable.

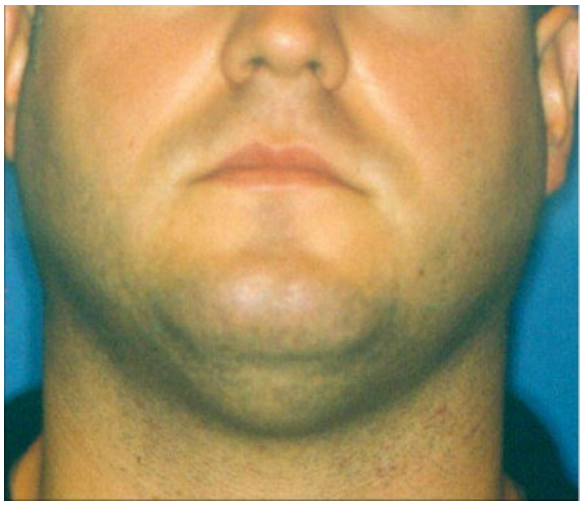
Fig. 1. Submental swelling in a 26-year-old male patient.

Differential Diagnosis

Diagnostic considerations for a slowly enlarging, mildly symptomatic submental mass could include a reactive lymphadenitis, epidermoid cyst, dermoid cyst, and lymphoma.

Clinical and radiographic examination however did not identify an obvious dental source of infection and no oral mucosal ulceration was noted. The skin over the nodule was not fixed and lacked erythema, edema, or a draining sinus, all potential signs and symptoms that might be encountered in the case of an inflamed epidermoid cyst.

Other potential causes of reactive lymphadenopathy could include cat scratch disease, infectious mononucleosis, and lymphadenopathy associated with HIV disease.

Cat scratch disease is a self-limiting lymphadenopathy associated with *Bartonella henselae* infection that commonly affects the cervical lymph nodes of young adults. Patient history usually confirms frequent contact with a cat.[1] The subacute, tender, regional lymphadenopathy typically develops 2 weeks after being scratched or bitten by a carrier cat or kitten. The inoculation site may be erythematous. Most patients lack constitutional symptoms other than solitary, painful lymphadenopathy. Our patient, however, denied any scratches from or significant contact with felines and no evidence of a facial erythematous papule suggestive of a recent scratch or bite was identified.

Infectious mononucleosis is a lymphoproliferative syndrome related to infection with the Epstein-Barr virus. It is particularly common in adolescents and young adults. The infection is spread primarily by saliva. Young adults almost always present with pharyngeal inflammation, tonsillar enlargement, cervical lymphadenopathy, fever, and malaise. Older adults are less likely to have pharyngitis and adenopathy but are more likely to have hepatosplenomegaly and jaundice. The clinical presentation is often highly suggestive, with definitive confirmation of the diagnosis usually based on positive serologic findings (“mono test”).[2] In our case, the patient lacked constitutional symptoms and exhibited no signs of tonsillar or oropharyngeal inflammation.

Persistent generalized lymphadenopathy (human immunodeficiency virus [HIV] lymphadenopathy) is a poorly understood diffuse lymphadenopathy involving 2 or more extrainguinal sites lasting longer than 3 months. Up to 70% of patients infected with HIV develop this condition within the first few months

following seroconversion, well before any other symptoms of HIV infection appear.[3] The lymph nodes in HIV lymphadenopathy are soft and symmetrically distributed, ranging in size from 1 to 5 cm.[4] Such findings are common in head and neck locations, especially the posterior triangle of the neck.[5] HIV-associated lymphadenopathy was not strongly considered because our patient presented with a solitary mass, was otherwise in apparent good health, and denied history of any recent flu-like symptoms such as fever, skin rash, sore throat, cough, or headache. Subsequent serum testing for antibodies to HIV, requested by the patient, was negative.

Lymphoma, particularly Hodgkin's lymphoma was also included in our differential diagnosis. Hodgkin's lymphoma is a B-cell lymphoproliferative neoplasm that comprises approximately 20% to 30% of all malignant lymphomas in the United States. It has a bimodal age distribution with a peak at 15 to 40 years and a second smaller peak in the seventh decade. There is a 1.5:1 male preponderance in all microscopic types except the nodular sclerosis type. The disease presents a painless enlargement of superficial (usually cervical) lymph nodes. Fever, night sweats, and weight loss may also be noted.[6]

Given the midline location, dermoid cyst was considered a likely diagnostic possibility. Dermoid cysts are keratinized stratified squamous epithelium-lined cystic lesions containing epidermal appendages such as hair follicles, sweat glands, and/or sebaceous glands. They form along embryonic fusion lines. Approximately 7% occur in the head and neck region, primarily involving the floor of the mouth (above the mylohyoid muscle) and the anterior neck (below the mylohyoid muscle).[7] They usually present in the second or third decade of life. Lesions in the floor of the mouth can displace the tongue, causing dysphagia, dysphonia, and dyspnea, whereas lesions below the mylohyoid muscle present a characteristic double chin.[8] Although usually asymptomatic, trauma or infection can cause local symptoms and/or tenderness.

Our final working diagnosis was dermoid cyst.

Diagnosis and Management

The patient was scheduled for an excisional biopsy. During surgery, the mass was noted to be located deep to the platysma muscle but superficial to the mylohyoid muscle and appeared to represent an enlarged lymph node. Formalin-fixed tissue sections were processed for routine microscopic examination. Sections stained with hematoxylin and eosin showed a lymph node that exhibited follicular hyperplasia of varying degree (Fig. 2). On closer inspection, the paracortical and marginal sinuses were distended with monocytoid cells (Fig. 3) that were positive by immunohistochemical analysis for the expression of the B-cell antigen CD20. Noncaseating granulomas were scattered across the follicles as well as encroaching onto the sheets of monocytoid cells in the sinuses (Fig. 4). These granulomas typically consisted of fewer than 25 epithelioid histiocytes (Fig. 5).

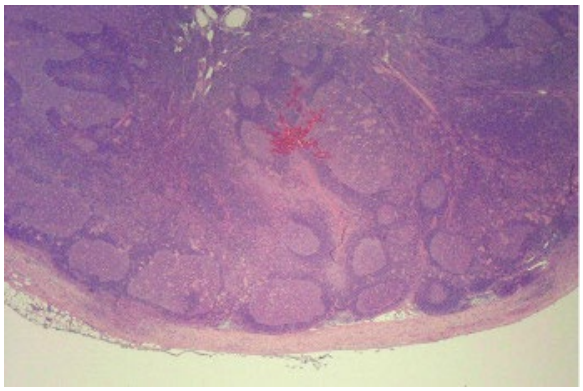

Fig. 2. Follicular hyperplasia of varying degree in toxoplasmic lymphadenitis (Hematoxylin and eosin [H&E], ×20).

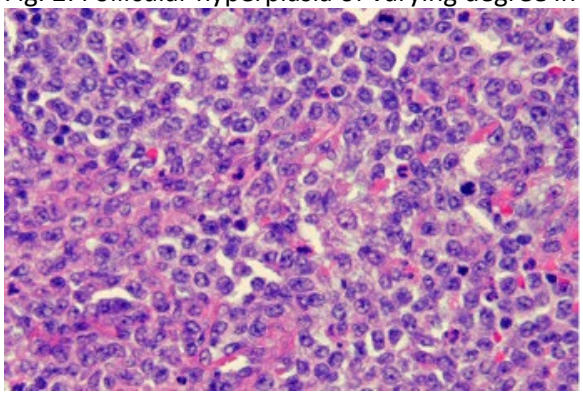

Fig. 3. Monocytoid B cells within paracortical sinuses (H&E, ×100).

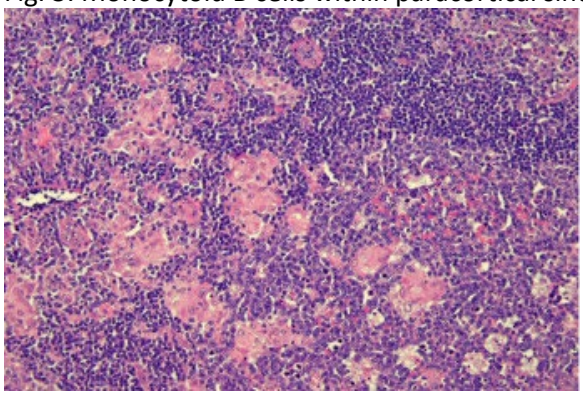

Fig. 4. Small, noncaseating epithelioid granulomas within follicles and encroaching into the sheets of monocytoid cells in the paracortical sinuses (H&E, ×40).

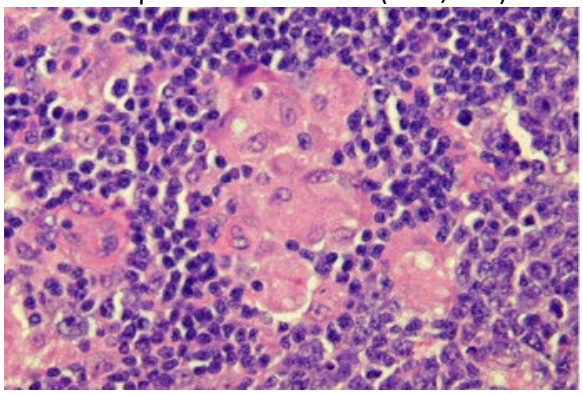

Fig. 5. Noncaseating granulomas composed of fewer than 25 epithelioid histiocytes (H&E, ×100).

The histopathological triad of follicular hyperplasia, monocytoid B-cell proliferation, and small, non-necrotizing granulomas consisting of epithelioid histiocytes was highly suggestive of a reactive lymphadenopathy secondary to toxoplasmosis. Careful examination of tissue sections using an antibody probe (*Toxoplasma gondii* P30 antigen, mouse monoclonal antibody, 1:60 dilution, Novocastra Laboratories Ltd, Newcastle upon Tyne, UK) revealed the presence of trophozoites within histiocytes (Fig. 6,*A*) as well as the presence of a toxoplasmic cyst (Fig. 6, *B*). Subsequent serology revealed α-toxoplasma immunoglobulin (Ig)G titer of 106 IU/mL (reference range: 6-200 IU/mL of serum), consistent with long-standing immunity or early seroconversion.

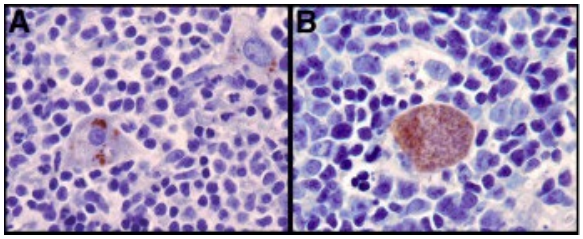

Fig. 6. (**A**) Trophozoites within histiocytes are detected using immunohistochemistry (×100). (**B**) A toxoplasmic tissue cyst is also seen in the involved lymph node (ABC technique with DAB peroxidase substrate; ×100).

The final diagnosis was non-necrotizing granulomatous lymphadenitis consistent with toxoplasmosis.

The patient was referred to an infectious disease specialist who prescribed pyrimethamine 25 mg, 4 times daily, for 3 weeks and then reduced to 25 mg, twice a day, for 5 weeks; sulfadiazine 1 g, 4 times a day, for 8 weeks, and leucovorin 25 mg every day for 8 weeks. There were no postsurgical complications and the patient is disease free after 4 years.

Discussion

Toxoplasma gondii, an obligate intracellular protozoan, can infect a variety of vertebrate hosts including humans. Toxoplasmosis has a nonseasonal worldwide distribution. Ninety percent of *T. gondii* infections in immunocompetent hosts are asymptomatic. Symptomatic infections usually cause a mononucleosis-like illness with low-grade fever, malaise, headache, and cervical lymphadenopathy. Encephalitis, myocarditis, hepatitis, and pneumonia may complicate infection in an immunocompromised host.[9]

Cats and other felines are the definitive hosts of *T. gondii*, in whom sexual reproduction results in the formation of infective oocysts. Other warm-blooded animals, including humans, are intermediate hosts that can harbor tissue cysts in their bodies.[10]

Humans can develop *T. gondii* infection by a number of avenues, including the ingestion of tissue cysts from infected, undercooked meat, ingestion of infective oocysts through oral-fecal contact, through blood transfusion from an infected person with circulating tachyzoites, and by transplacental passage of tachyzoites to a fetus (congenital toxoplasmosis).[9] Infection can be prevented by cooking meat thoroughly. Proper handling and disposal of cat litter also reduces the risk of toxoplasma transmission to humans.[10]

On further questioning, our patient revealed that he had returned a few months earlier from a vacation in Cuba. While on vacation, he had extensively relished pork dishes and cigars. We speculate that the pork indulgence may have been the source of the patient's infection.

Serological testing is considered the gold standard in the diagnosis of toxoplasmosis. IgG antibodies against *T. gondii* become detectable 1 to 2 weeks after infection and remain elevated indefinitely. IgM antibody levels increase within days and remain elevated from 2 to 3 months[9] before dropping down to undetectable levels within 6 to 9 months.[10]

Although *T. gondii* infection can be suspected from the histopathologic appearance of an involved lymph node, definitive diagnosis traditionally requires the demonstration of specific antibodies in the serum.[11] 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 diagnostic for toxoplasma lymphadenitis.[11] The marked follicular hyperplasia is associated with intense mitotic activity and phagocytosis of nuclear debris. The clusters of epithelioid histiocytes located within the hyperplastic follicles produce small noncaseating granulomas. These granulomas may also encroach upon the periphery of the follicles, thereby obscuring their margins, although the overall nodal architecture is well preserved.[6] Monocytoid B cells distend the marginal as well as the cortical sinuses. Additionally, immunoblasts and plasma cells may be seen in the medullary cords. Necrosis of the granulomas and the presence of occasional Langhans giant cells may complicate the diagnosis.[6] Toxoplasma organisms are rarely identified by examination of routinely stained tissue sections alone. As the current case demonstrates, immunohistochemistry may facilitate the detection of cysts and trophozoites in tissue section (Fig. 6).

At the light microscopic level, preservation of the nodal architecture as well as the presence of epithelioid granulomas within follicles are helpful features in excluding the possibility of lymphoma.[12] Lymphadenopathy secondary to cat scratch disease is usually characterized by central necrosis with neutrophils within the follicles. Clusters of perifollicular and intrafollicular epithelioid cells are also not seen in lymph nodes enlarged secondary to cat scratch disease.[6]

Controlling the parasitic infection is especially important in the immunocompromised host and in reducing the potential risk during pregnancy. Treatment with pyrimethamine and sulfadiazine, combined with folinic acid, is the most widely used approach, both from the point of economics and clinical efficacy.[13]

In conclusion, although in many cases the differential diagnosis for a submandibular-cervical mass is relatively straightforward, in the absence of an identifiable oral or odontogenic source of infection, toxoplasma lymphadenitis should be included in the differential diagnosis. This is true even in the absence of a significant history of feline contact.

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