A 16-Year-Old Adolescent Boy With Unilateral Cervical Lymphadenopathy Suspicious for Malignancy

Yael R. Barr, MD; Suimin Qiu, MD, PhD

A 16-year-old African American adolescent boy presented with a tender left cervical mass. He reported that he had first noticed the mass several months ago, but it had significantly enlarged and become mildly painful in the 2 weeks prior to his seeking medical advice. History was remarkable only for intermittent headache, without fever or any other constitutional symptoms such as weight loss, night sweats, or malaise.

Physical examination revealed an afebrile young man with a mobile, soft tissue mass measuring $2 \times 1.5$ cm above the superior trapezius muscle. There was no erythema or drainage. Small, nontender nodes were also palpated. A chest radiograph revealed no evidence of mediastinal mass or lymphadenopathy. The cervical mass was excised and sent for pathologic evaluation, with the clinical diagnosis of cervical lymphadenopathy suspicious for malignancy.

Received was an enlarged lymph node measuring $1.5 \times 1 \times 0.8$ cm, with intact capsule and white-tan parenchyma on cross sections. Microscopic examination revealed diffuse effacement of the lymph node's normal architecture by focal stellate-shaped microabcesses with necrotizing, noncaseating necrosis; brisk cellular debris (Figure 1); tingible-body macrophages; and abundant neutrophils surrounded by a rim of granulomatous inflammation (Figure 2). The neutrophilic infiltration was more apparent in the germinal centers. Warthin-Starry silver stain (Figure 3) was used for the diagnosis, with a higher-magnification inset (upper right) to highlight the finding. The diagnosis was confirmed by specific immunohistochemical stain (Figure 4).

What is your diagnosis?
Pathologic Diagnosis: Cat Scratch Disease With Necrotizing Granulomata

Neck masses are frequently encountered in both the young and adult patients, and they have a wide differential diagnosis. Benign causes include infectious or inflammatory processes as well as congenital anomalies and benign neoplasms. Malignancies, including a primary tumor (salivary gland, thyroid, or primary lymphoid malignancy) or metastatic carcinoma, should also be considered in the differential diagnosis, especially in the older patient. Among children and adolescents, cat scratch disease (CSD) is one of the common causes of a benign neck mass. Additionally, Hodgkin lymphoma is often listed in the differential diagnosis, because it is also more common in young individuals with a neck mass.

Cat scratch disease is a zoonotic disease caused by the bacterium Bartonella henselae, which is harbored by young cats and kittens. It has many forms of clinical presentation, the most typical being a subacute, tender, regional lymphadenopathy, developing 2 weeks after being scratched or bitten by a carrier cat. The inoculation site (usually on the hands, arms, or chest) usually shows a primary granulomatous skin lesion 3 to 10 days after inoculation, before involvement of the regional lymph nodes becomes clinically apparent. The lymph nodes most commonly involved are the cervical and axillary lymph nodes, and usually only a single node is involved. Most patients will lack constitutional symptoms or laboratory abnormalities and will not appear ill. The histologic hallmark features of classic CSD lymphadenitis include reticular or stellate necrotizing granulomatous lesions that early in the disease are found close to the capsule, which is fibrotic, thickened, and inflamed. Reactive hyperplasia of the adjacent follicular centers is common. As the disease progresses, lesions are seen in the central portion of the lymph node as well. Giant cell reaction is not prominent, but vascular proliferation in the paracortical areas usually is.

The diagnosis is aided by identifying the small, pleomorphic, gram-negative bacilli with silver impregnation techniques such as the Warthin-Starry silver stain or the Steiner stain, although the sensitivity of this test is considered low and the mature lesions only rarely show the bacteria. The bacteria are seen either within macrophages, as demonstrated in this case with abundant intracellular organisms, or in the extracellular debris, and the bacteria are especially abundant within the necrotic foci and along the proliferating blood vessels. Other ancillary tests useful for diagnosis include serology for anti–B henselae immunoglobulin (Ig) M and IgG titers, detection of Bartonella DNA in lymph node specimens using polymerase chain reaction, and immunohistochemical stains. The present case was confirmed by immunohistochemical staining, as shown in Figure 4 (Biocare Medical, Walnut Creek, Calif).

Because it is a fastidious organism (having complex nutritional requirements) it is usually not possible to culture Bartonella from an affected lymph node.

Other disease processes that could cause a similar clinical and histologic picture include other infectious granulomatous diseases, such as lymphogranuloma venereum, tularemia, mycobacterium tuberculosis, brucellosis, and fungal infection. Noninfectious diseases to be considered in the differential diagnosis include Kikuchi necrotizing lymphadenitis and Kawasaki disease. Of those, lymphogranuloma venereum probably has the most histologic resemblance, but involvement is usually seen in the inguinal lymph nodes, not the cervical or axillary lymph nodes. Tularemia is also very similar, but typically the patients have more apparent constitutional symptoms. In addition, the necrotic areas in the cortex are often more demarcated but lack the well-defined rim of histiocytes found in CSD. Mycobacterial infections will usually show caseating necrosis and will lack the zonation of CSD; such infections are often confirmed by acid-fast stain. Kikuchi lymphadenitis normally shows no neutrophilic infiltration, although necrosis and histiocyte proliferation are seen. Kawasaki disease is characterized by follicular depletion and microthrombi, features that are not found in CSD.

Although traditionally considered to be a disease of children and adolescents, some authors, such as Ridder et al., have challenged this observation and have shown that CSD can occur at any age. In their article, the mean age of patients was 33 years (range, 4–89 years), and they recommended that CSD be kept in the differential diagnosis for the adult with lymphadenopathy.

One should keep in mind that the classic presentation of CSD occurs in immunocompetent patients. Immuno compromised patients tend to present with atypical extranodal forms of CSD, including Parinaud oculoglandular syndrome, bacillary angiomatosis, peliosis hepatitis, bacteremia, osteomyelitis, pulmonary disease, splenic involvement, endocarditis, and aseptic meningitis.

Typical CSD is benign and self-limiting and often resolves spontaneously. Antibiotic treatment may be given; the most often used antibiotics are the macrolides, such as erythromycin, azithromycin, and clarithromycin.

Upon further questioning of our patient, he acknowledged having a new kitten at home; he played with and was frequently scratched by the kitten. Because of the history of cat exposure and the unequivocal pathologic diagnosis, serologic testing was not done on this patient. The patient was treated with antibiotics (clindamycin) and made an uneventful recovery. However, when adequate clinical information is not available, the accurate diagnosis in surgical pathology may be challenging.

References