A firm mass at the angle of the mandible

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THE CHALLENGE

An 8-year-old girl was brought in the oral and maxillofacial surgery department with swelling of her mandibular left jaw that her mother stated had been present for 3 weeks. At first, the patient noticed pain while brushing her teeth. Over the next 3 weeks, the patient's mother noticed increasing swelling that progressively increased in firmness. The patient endorsed constant pain with increased discomfort on palpation. At no point in the course had the patient experienced fever, nausea, or vomiting. The patient was prescribed amoxicillin (250 mg/mL) by her family dentist 4 days before seeking treatment for a suspected odontogenic infection. When the swelling did not resolve, she was referred to the oral and maxillofacial surgery department.

The patient's medical and surgical histories were unremarkable, and she was up to date with all childhood vaccinations. She lived with her family, and they had birds, cats, and dogs and used to have chickens. However, the patient denied any recent bites or scratches from these pets.

Extraorally, the patient had a fixed, indurated swelling, that was 4 cm × 2 cm overlying and obscuring the angle of the mandible. There was an absence of overlying erythema, inflammation, or warmth. No animal scratch lines or bite marks were present (Figure 1). This swelling was exquisitely tender to palpation. Intraoral examination was unremarkable, with no grossly carious teeth, drainage, or other signs of infection. A panoramic radiograph was obtained and was unremarkable except for a mesial caries lesion on the mandibular right primary second molar (Figure 2). Computed tomographic (CT) imaging and magnetic resonance imaging (MRI) showed a mass in the submandibular space that was partially cystic at the inferior lateral margin and partially solid at the anterior medial margin. The lesion was separate from the submandibular gland with displacement of the submandibular gland posteriorly and medially (Figure 3).

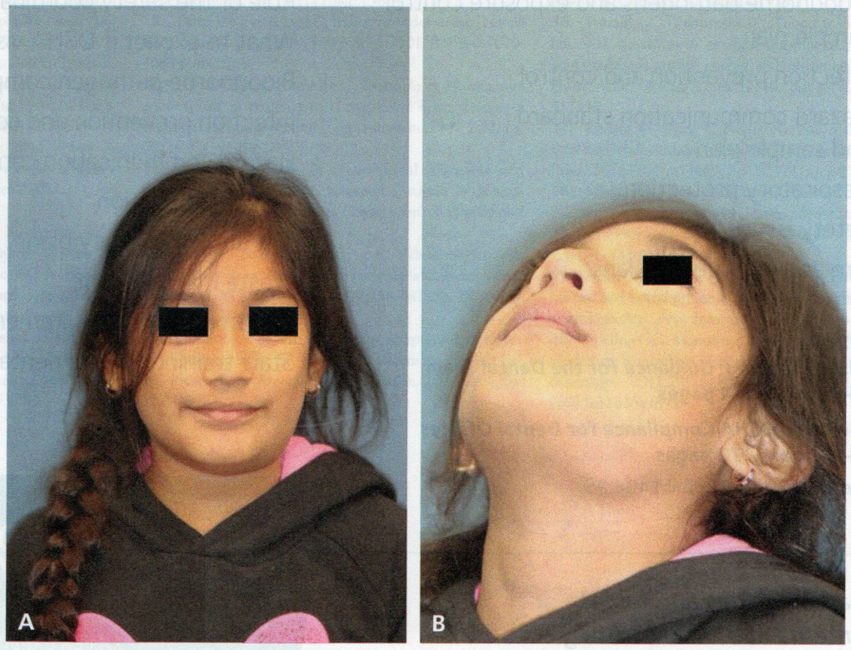

Figure 1. A. Facial asymmetry; submandibular left region was larger than the right. **B.** Indurated swelling of left inferior mandible, the posterior border of which obscured the angle. No erythema or warmth was noted on clinical examination.

(Please see next page for additional images.)

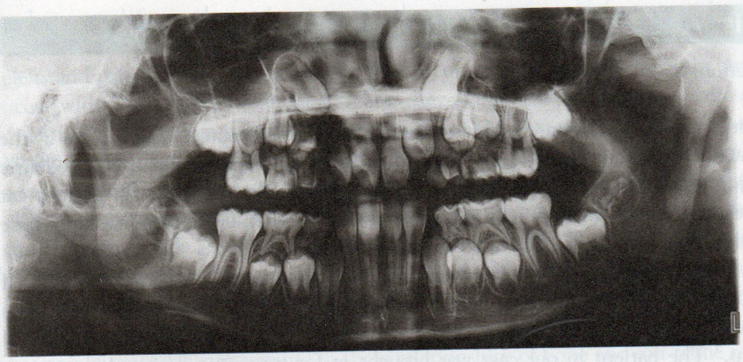

Figure 2. Panoramic radiograph unremarkable except for mesial caries on the primary mandibular right second molar.

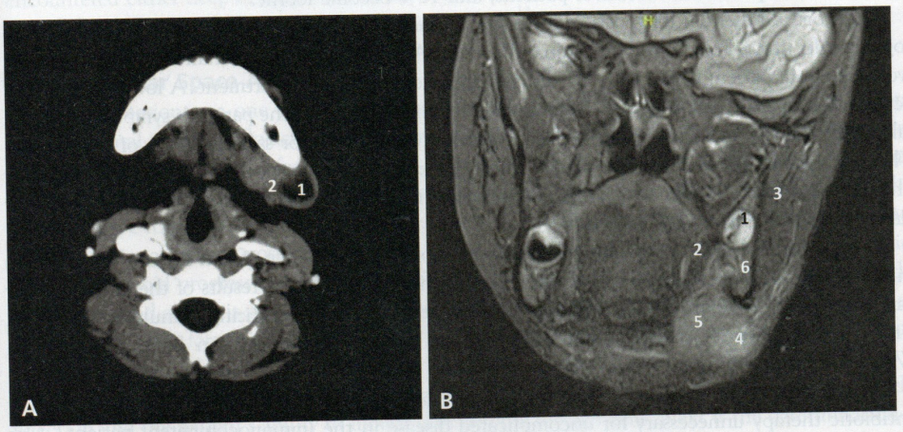

Figure 3. **A.** Axial computed tomographic image showing a mass within the submandibular left space with a cystic component along its inferolateral margin (**1**) and a solid component (**2**) along the anterior medial margin. **B.** Coronal magnetic resonance imaging further showing a mixed solid and cystic mass in the submandibular left space: developing mandibular left third molar (**1**), mylohyoid muscle (**2**), masseter muscle (**3**), solid component of mass (**4**), cystic component of mass (**5**) and angle of mandible (**6**).

Can you make the diagnosis?

A. Branchial cleft cyst
B. *Bartonella henselae* infection
C. Submandibular gland sialadenitis
D. Submandibular space abscess
E. Lymphoma

The diagnosis:

B. *B henselae* infection

B henselae infection, known as cat-scratch disease, is present in an estimated 22,000 cases in the United States annually, making it one of the top causes of regional lymphadenopathy in pediatric patients.[1] The major arthropod vector is the cat flea *Ctenocephalides felis*,[2] which enables cat-to-cat transmission. It is theorized that cat-to-human transmission occurs when flea feces, including those of *B henselae*, are inoculated into humans via a cat scratch.[3]

Of those patients who develop a *B henselae* infection, 65% have a visible inoculation site.[4] If visible, this appears within 2 weeks as a brownish red papule. Lymphadenopathy in the nodes draining the inoculation site follows; the most common sites are the lymph nodes of the cervical and axillary regions.[5] The patient in our case was brought in for treatment during this stage, as indicated by the submandibular swelling from cervical lymphadenopathy. At this phase, the lymph nodes are swollen and tender and have the potential to undergo suppuration. Aching, malaise, and anorexia develop in three-fourths of patients, and 10% become febrile.[6]

The broad differential diagnosis of a neck mass mandates prompt medical referral when odontogenic infection is ruled out by the general dentist. As mentioned in the challenge, the diagnostic work-up of our patient began with CT and MRI in the emergency department. A low probability of active odontogenic infection, due to the chronicity and mildness of the patient's symptoms, normal laboratory values, and nonresponsiveness to antibiotics, allowed for safe discharge of the patient. The patient was referred to and seen as an outpatient by a pediatric hematology and oncology physician 2 days later, after which she underwent further laboratory testing, including work-up for tuberculosis and deep fungal infection.

Results of an indirect fluorescent antibody assay showed the presence of anti-*Bartonella* antibodies in the patient's serum, confirming a *B henselae* infection. Inconclusive results of the antibody titer can prompt biopsy of an involved lymph node. When biopsied, necrotizing granuloma formation with microabscesses is observed, and the presence of *Corynebacterium* can be confirmed with Warthin-Starry staining.[7]

Cat-scratch disease has an excellent prognosis. Most cases resolve without treatment, rendering antibiotic therapy unnecessary for uncomplicated disease in the immunocompetent patient.[8] Our patient underwent a 4-day course of clindamycin for suspected staphylococcal or anaerobic infection under the care of a pediatric hematology and oncology physician. After antibody panel confirmation of cat-scratch disease, a 4-day course of azithromycin was completed, with the only noticeable change in the lesion being increased pruritis. The lesion resolved entirely 1 week after the azithromycin treatment was completed and approximately 1 month after the beginning of symptoms.

Although not present in this case, complicated disease may occur with central necrosis of 1 of the affected lymph nodes. This may lead to suppuration of the lymph node, severe tenderness to palpation, and chronic purulent drainage; the overlying skin may have a violaceous hue. In these cases, lymph node excision is indicated accompanied by postoperative antibiotics, either macrolides or tetracyclines. The benefits of excision are 2-fold: (1) the source of infection is removed, and (2) tissue samples can be submitted to rule out concomitant tuberculosis infection.[9]

DIFFERENTIAL DIAGNOSIS

Branchial Cleft Cyst

Branchial cleft cysts can arise in the lateral upper neck, producing a clinical appearance like that of our patient. These cysts occur near the sternocleidomastoid muscle either anterior or deep to the muscle in the superior lateral neck.[10] Unlike in our patient, these lesions are soft and not tender. An episode of acute enlargement, formation of an abscess, or both during an upper respiratory infection may lead the patient to seek treatment from a health care provider. In more advanced cases, dysphagia, torticollis, or respiratory compromise may occur. The cysts are typically noticed in the third to fifth decade of life.[11]

Branchial cleft cysts arise from branchial arch remnants. At the gestational age of 4 weeks, 6 branchial arches develop in the cephalad region of the embryo. Separating the outer surfaces of the

arches are clefts, and pouches separate the inner surfaces.[10] In appropriate development, an ingrowth of mesenchyme replaces these clefts and pouches. If this process is incomplete and the clefts and pouches remain, sinus tracts, fistulae, or cysts result.[12] Although branchial cleft cysts can occur within each of the branchial arches, they almost always originate in the second arch.[10]

In many cases a comprehensive history and physical examination may be all that is necessary to establish the diagnosis in the pediatric patient.[11] In contrast, in adults a fine-needle aspiration would be prudent to rule out metastasis from malignancies of the head and neck region that may clinically resemble a branchial cleft cyst. This is less likely in children because metastatic disease to the head and neck is rare in the pediatric patient.[13] On histopathologic analysis, the cysts are characterized by squamous, pseudostratified, or combined squamous and pseudostratified columnar respiratory epithelium. Lymphoid tissue, sebaceous glands, and salivary tissue may underlie the epithelium.[12] Keratinous debris may be found in the cystic cavity.[14] CT is the reference standard for imaging because it has the ability to show relationships of bone and soft tissue to the cyst as well as to detect a fistula.[11]

Surgical excision of these cysts is curative. A transverse cervical incision is made, and the cyst is encountered either deep or superficial to the cervical fascia. To prevent the risk of recurrence, it is essential that any fistula be completely excised as well.[11]

Submandibular Space Abscess

Orofacial infections are one of the leading reasons why patients seek treatment from the general dentist or oral and maxillofacial surgeon. In our case specifically, the general dentist prescribed amoxicillin, suspecting an infectious etiology. Odontogenic infections are initiated by the normal oral flora including gram-positive cocci of both aerobic and anaerobic varieties as well as anaerobic gram-negative rods.[15] If left untreated, the infection begins to spread periapically through the path of least resistance. In the posterior mandible, this is generally the lingual cortex. Infections inferior to the mylohyoid progress to the submandibular space. The infection then progresses through the inoculation and cellulitis stages. When anaerobic bacteria begin to predominate, tissue liquefaction begins and there is formation of purulence. This stage is known as the abscess stage, and on clinical examination the induration of the cellulitis stage gives way to fluctuance.[16]

Management of this pathology is multifaceted. First is the assessment of the severity of the infection and the patient's ability to mount host defense mechanisms. Next is the determination of whether the case may be treated by the general dentist or oral surgeon, and whether surgical intervention is indicated.[17] If odontogenic infection causing neck swelling is suspected, an initial survey with a panoramic or periapical radiograph is indicated, which may detect a radiolucency or periapical abscess. In-office cone-beam CT may detect focal cortical erosion near the odontogenic source of infection.[18] CT with contrast, a modality available in the hospital setting, shows rim enhancement characteristic of abscess formation.[19]

A submandibular space abscess requires antibiotics, hospitalization, and surgical intervention to establish extraoral drainage. Penicillin is the first-choice antibiotic for most clinicians. However, the choice of antibiotic is of significantly less importance than proper diagnosis and surgical intervention.[20] In surgery, an incision is made below the angle of the mandible. Dissection is carried to the inferior border of the mandible, and the space is irrigated. The causative tooth is extracted, and a drain is inserted to allow purulence to drain postoperatively.[21] On discharge from the hospital, reevaluation 2 days postoperatively is advantageous as it allows time for purulent drainage to stop and for the clinician to evaluate the ability of the patient's immune system to handle the infection.[22]

Submandibular Gland Sialadenitis

Sialadenitis may be bacterial or viral in nature. Bacterial sialadenitis etiologies are primarily obstructive in nature, arising from congenital strictures, adjacent tumor compression, and most commonly sialolithiasis. The submandibular gland is the origin of 85% of sialoliths. It is theorized that this is caused by salivary flow stasis due to superior flow against gravity and acute bends throughout the course of the duct. It is also theorized to play a role is the alkalinity, viscosity, and calcium salt concentration of the salivary output of the gland.[23]

A clue to this diagnosis is a diffusely swollen salivary gland with increased discomfort around mealtimes in an adult patient. Purulent discharge from the floor of the mouth originating in

Wharton duct is another key clinical finding, and these symptoms in combination allow for an expedited diagnosis of bacterial submandibular sialadenitis and preclude the necessity for a biopsy. *Staphylococcus aureus* and streptococci are among the most common offenders.[23] Bacterial sialadenitis is rare in the pediatric patient, typically manifesting as a *Mycobacterium tuberculosis* infection of the parotid gland, with even more rare cases of submandibular sialadenitis reported.[24] With this patient's negative interferon gamma release assay for the diagnosis of tuberculosis (QuantiFERON-TB; QIAGEN) test result and submandibular presentation of swelling, this was determined unlikely.

Survey with a panoramic or occlusal radiograph can detect the presence of a sialolith for further workup with a CT or MRI scan.[23] Most submandibular stones (80%) are radiopaque, making radiography a sensitive tool.[25] When diagnosis of acute bacterial submandibular gland sialadenitis is made, prompt hydration and antibiotic therapy are indicated. Additional corticosteroids, sialagogues, glandular massage, and potential surgical intervention are indicated in the chronic form.[23]

Mumps is the most common cause of viral sialadenitis. The most common agent for this is paramyxovirus.[26] Other, rare viral etiologies of sialadenitis include coxsackievirus A and B and cytomegalovirus.[24] The spread of mumps is most likely to occur in crowded areas such as military barracks, prisons, and kindergartens. After the development and implementation of the live attenuated measles, mumps, and rubella vaccine in the late 20th century, the annual incidence has decreased to less than 0.1 per 100,000.[27]

Mumps has an incubation period that typically lasts more than 2 weeks. This is followed by a prodromal 1- to 2-day period that includes constitutional symptoms of headache, chills, fever, and preauricular tenderness. This is followed by fast-developing and painful swelling of the parotid gland either unilaterally or bilaterally. Paired with this clinical history, mumps can be conclusively diagnosed by a real time reverse transcription polymerase chain reaction test.[23]

The patient's vaccination status and presentation without associated parotitis made a mumps etiology unlikely. This is because although mumps may affect the submandibular gland, it is rare for mumps to affect the submandibular gland while sparing the parotid gland. Submandibular sialadenitis sparing the parotid gland and accompanied by orchitis and meningoencephalitis has been documented in unvaccinated children or children of undetermined vaccination status.[28] Treatment of mumps is supportive consisting of bed rest, hydration, and oral hygiene.[23]

Lymphoma

Lymphoma is the responsible entity for 50% of all childhood head and neck cancers and is overall the third most common malignancy of childhood.[29] These lymphomas are divided into Hodgkin and non-Hodgkin lymphoma.[30]

Symptoms of acute lymphoma are pain, fever, and other related symptoms. When these symptoms are absent, size, time, and extension are important to consider regarding a suspected mass of lymphoma cells. Increased size of the lesion, especially lesions greater than 2 cm in diameter, should raise suspicion for lymphoma. Another feature concerning lymphoma is adenopathy persisting longer than 4 weeks, as well as the presence of extension into more than 1 anatomic area. The more prevalent non-Hodgkin lymphoma most commonly occurs with painless lymphadenopathy.[31] Symptoms of Hodgkin lymphoma are inflammatory in nature, characterized by chronic pruritis.[32] If any of these factors are present, a definitive diagnosis is arrived at by biopsy sampling the largest accessible lymph node.[31]

Chronic inflammation-inducing microbes are the most common etiologies of lymphoma.[33] Non-Hodgkin lymphomas affecting the cervicofacial region in pediatric patients are further subdivided by the cells they affect, as well as the location. The latter includes extranodal lymphatic, extralymphatic, and lymph node.[31]

Histologically, non-Hodgkin lymphomas are characterized by relatively uniform sheets of proliferating lymphocytic-appearing cells with varying degrees of differentiation that are infiltrative and destructive within the lymph node itself or in adjacent tissue. When there appears to be germinal center formation with cells of B-lymphocytic origin, the lymphoma is termed follicular. Without this appearance the lymphoma is termed diffuse.[34] Hodgkin lymphoma is characterized by the Reed-Sternberg cell.[35] Further characterization by immunohistochemical study is considered a standard of care for both Hodgkin and non-Hodgkin lymphoma because of the diagnostic and treatment value it affords.[36]

Owing to the heterogeneity of non-Hodgkin lymphoma, prognoses are variable. Treatment generally consists of chemotherapy. Hodgkin lymphoma in the pediatric population has 5-year event-free rates from 80% through 95% and is treated with radiotherapy and chemotherapy.[31]

CONCLUSIONS

Because of the variety of processes that might underlie a neck mass, a definitive diagnosis is difficult to obtain. It is critical for any oral health care provider to obtain a comprehensive history and work with an interdisciplinary team to arrive at a proper diagnosis and appropriately treat the patient. ■

DISCLOSURE

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