Diagnostic approach to intramasseteric nodules

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Intramuscular nodules can be the clinical presentation of several groups of lesions, such as reactive disorders and benign and malignant tumors. Here, we present three cases with similar clinical features and image aspects on Doppler ultrasonography. Two of the lesions were diagnosed as intramasseteric hemangioma and the third as intramasseteric metastasis from high-grade pleomorphic sarcoma of the thigh. The diagnosis of intramasseteric nodules is challenging, and various differential diagnoses must be considered. Clinical features, evolution time, and information from complementary examinations, such as Doppler ultrasonography and fine-needle aspiration cytology, are useful in making a precise diagnosis and providing appropriate treatment. (Oral Surg Oral Med Oral Pathol Oral Radiol 2017;123:e16-e21)

Masseter nodules are uncommon and often are misdiagnosed. To reach the right diagnosis, surgical exploration is an option, but access is difficult and might damage the facial nerve. For this reason, complementary imaging techniques, such as computed tomography (CT), magnetic resonance imaging (MRI), Doppler ultrasonography (DUS), and arteriography are important.[1-4]

Hemangioma is the most common diagnosis for nodules in the masseter muscle, accounting for approximately 36% of all hemangiomas that arise in the skeletal muscle of the head and neck region.[1,5] However, differential diagnosis from other diseases—particularly those that contain blood vessels and may have similar DUS images—is necessary. Although rare, distant metastasis to the masseter muscle is an important differential diagnosis of masseteric nodules and can be misdiagnosed as hemangioma.[6-9] Other uncommon intramasseteric tumors, such as schwanoma,[10,11] chondroma,[12] solitary fibrous tumor,[13] and angiolipoma,[14] have been reported, but such reports are scarce in the English language literature.

In this report, we present three cases of intramasseteric nodules and a literature review focused on differential diagnosis. Two of the lesions were diagnosed as intramasseteric hemangioma and the third as intramasseteric metastasis from high-grade pleomorphic sarcoma of the thigh. The aim of this case study was to provide a diagnostic approach for intramasseteric nodules, using DUS as an auxiliary tool, complementary to clinical examination, fine-needle aspiration cytology, and MRI/CT.

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CASES

Case 1

A 35-year-old man was referred to the oral diagnosis department for evaluation of a tender swelling in the left masseteric region (Figure 1A). The swelling had been growing slowly over the last 5 years. Clinical examination revealed a slight swelling in the right cheek that was painless, firm, and poorly circumscribed on palpation. The overlying skin was normal and freely movable. No cervical or perilesional lymphadenopathy was present. Ultrasonography was requested and revealed an ill-defined hypoechoic nodule 3 cm in diameter in the left masseteric muscle, comprising large-caliber blood vessels and revealing a high venous flow inside the lesion. DUS exhibited venous flow with reflux (Figure 1B). These findings were suggestive of soft tissue hemangioma. The sonographic appearance of the parotid glands was normal. The patient was informed of the diagnosis and has been in follow-up for 18 months without any alteration in the lesion.

Case 2

A 48-year-old man was referred for evaluation of a swelling in the masseteric region on the left side (Figure 1C). The patient had noticed the alteration 2 years previously and reported that the size remained stable. Clinical examination revealed a slightly defined, painless nodule measuring 2 cm at its maximum diameter and covered with normal skin. This patient's systemic health was unremarkable. During the DUS examination, a hypoechoic heterogeneous and hypervascular mass, 1.5 cm in diameter, was observed inside the masseter muscle (Figure 1D). There was no evidence of any alterations in the sonographic appearance of the parotid glands. These findings led to the diagnosis of hemangioma. Fine-needle aspiration cytology (FNAC) revealed a hemorrhagic smear consistent with the diagnosis of hemangioma. The patient has been in follow-up for 17 months without any alteration in the lesion.

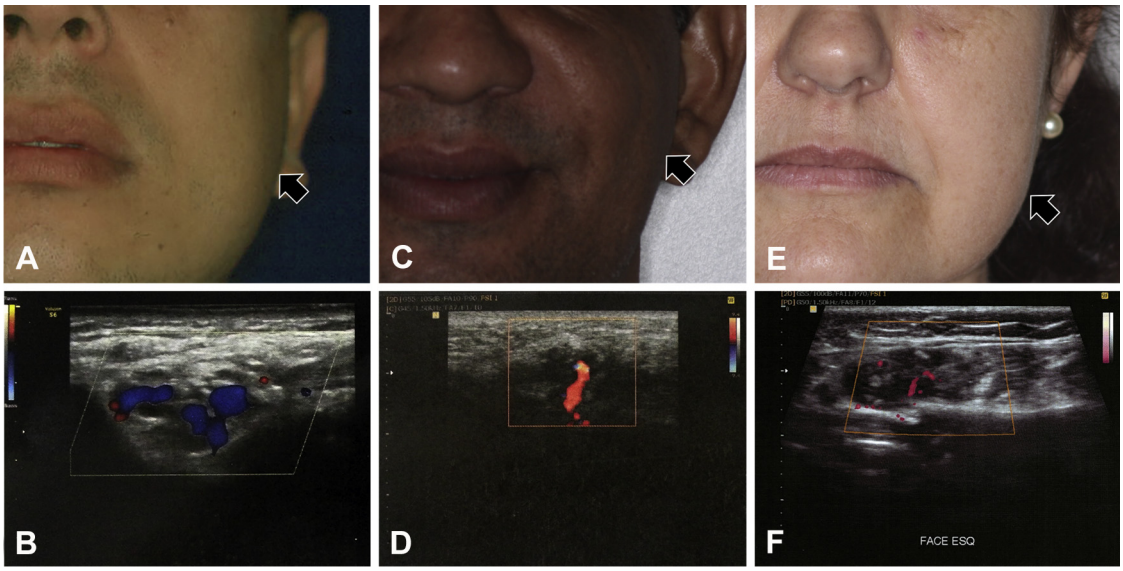

Fig. 1. **A,** Clinical photograph showing an almost imperceptible nodule in the left cheek *(arrow)*. **B,** Doppler ultrasonography (DUS) showing an ill-defined hypoechoic nodule with blood flow inside, suggesting the diagnosis of hemangioma. **C,** Clinical photograph showing almost no evident nodule on the left side *(arrow)*. **D,** DUS showing an ill-defined hypoechoic nodule with blood flow, compatible with the diagnosis of hemangioma. **E,** Clinical photograph showing a slight nodule in the left masseteric region *(arrow)*. **F,** DUS showing an ill-defined hypoechoic nodule with blood flow, suggesting the diagnosis of hemangioma.

Case 3

A 44-year-old woman was referred to the oral diagnosis clinic for evaluation of a painless and slightly defined masseteric nodule of 2 weeks' duration on the left cheek (Figure 1E). Her medical history included invasive ductal breast adenocarcinoma, which had been treated 17 years earlier with right radical mastectomy, axillary lymph node dissection, chemotherapy, and radiotherapy. In addition, she had had a high-grade pleomorphic sarcoma of the thigh, treated with two surgical resections, one for the primary tumor 9 years ago and the second for a local recurrence 5 years later. During clinical examination, a firm and nontender nodule, covered with normal overlying skin, was observed. DUS revealed an ill-defined hypoechoic nodule 1.2 cm in diameter, showing hypervascularization inside the lesion (Figure 1F). The sonographic appearance of the parotid glands was normal. After enhancement with contrast medium, CT revealed a solid and well-defined nodule of 2.4 cm located in the lower insertion of the masseter muscle. These findings suggested the diagnosis of hemangioma. However, FNAC was positive for malignant neoplastic cells. The patient was referred to a head and neck surgeon who removed the nodule with the patient under general anesthesia. Histopathologic and immunohistochemical analyses of the surgical specimen established the diagnosis of metastasis from a high-grade pleomorphic sarcoma. The excised nodule presented focally compromised margins upon microscopic observation. Therefore, postoperative radiotherapy was administered. Eight months later, the patient developed a new nodule in the thigh, and the histopathologic analysis confirmed another local recurrence of high-grade pleomorphic sarcoma. The tumor was again surgically removed but showed microscopic compromised margins. Another surgery was performed, and it showed free surgical margins.

DISCUSSION

Although intramasseteric nodules are uncommon, a variety of differential diagnoses must be considered. Imaging examinations, particularly those that are able to analyze soft tissues, such as DUS, CT, and MRI, are mandatory. FNAC is also useful and may provide additional information contributing to a correct diagnosis and treatment plan.

Differential diagnosis of masseter muscle nodules is difficult and includes differentiation from several diseases. The most frequent are benign processes, such as masseteric hypertrophy, hemangioma, other benign tumors, and infectious diseases. Primary malignant tumors and metastases may also occur but are extremely rare. On the basis of the cases presented in the literature, we propose a diagnostic algorithm for intramasseteric nodules, including the use of DUS and the indications for FNAC, taking the time of evolution into consideration (Figure 2). Although CT and MRI provide better-quality images and some cases need a combination of different imaging techniques to reach the right diagnosis, the information regarding blood flow provided by

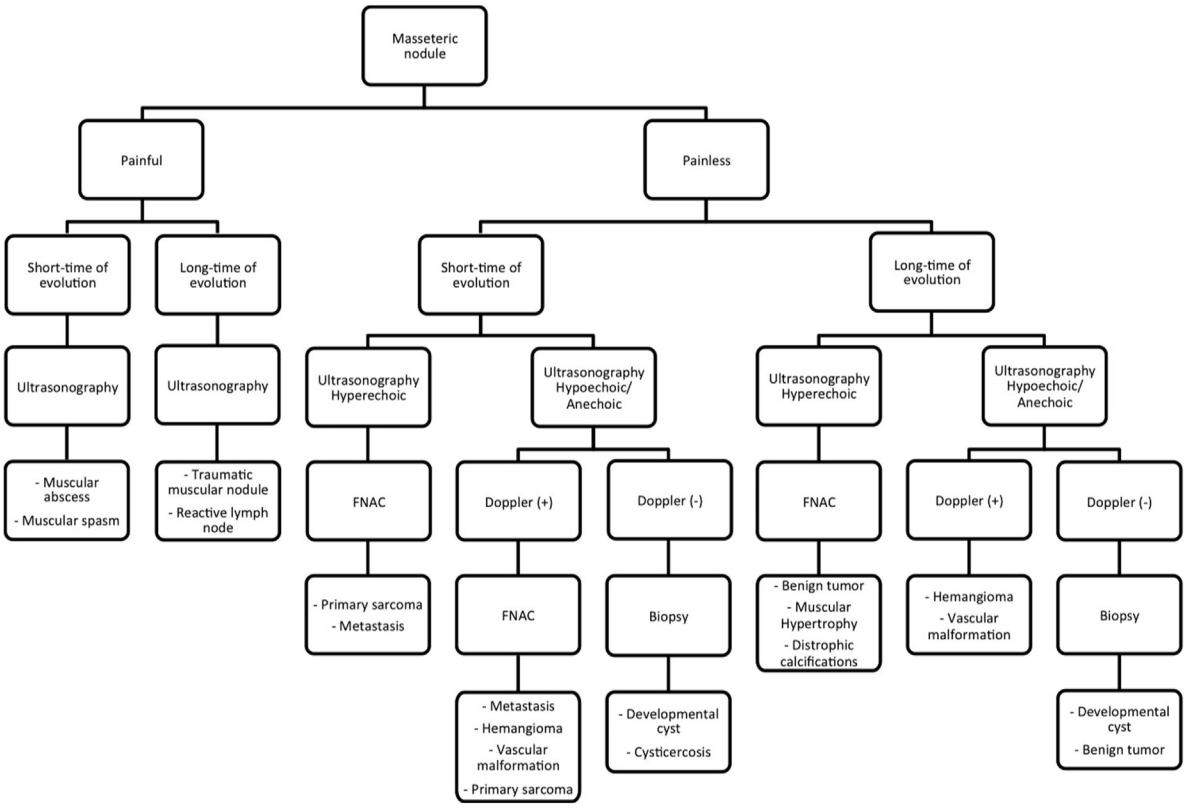

Fig. 2. Diagnostic algorithm for intramasseteric nodules.

DUS is very useful in establishing a diagnosis without the need for high-cost imaging examinations or biopsy.

Ultrasonography is a diagnostic imaging technique that provides information about muscles and neighboring tissues. DUS is a very practical complementary tool for diagnosis in this area, allowing detection of blood flow and the resistance of vessels, and can differentiate arteries from veins by waveform analysis, complementing the results obtained with the use of conventional ultrasonography.[3,15-17] The vascular flow through a lesion and the rate of blood passing between blood vessels are crucial for the diagnosis of lesions and vascular anomalies. Capillary, venous, and lymphatic malformations are identified as low-flow lesions, whereas arterial and arteriovenous malformations are identified as high-flow lesions.[2] Although CT and MRI are standard modalities used in oral and maxillofacial surgical practice, DUS is very useful for the diagnosis of lesions inside the masseter muscle. Ultrasonography is quick, easy, relatively inexpensive, and free of ionizing radiation; moreover, it is a painless, noninvasive, and nonthreatening method for the detection, evaluation, and follow-up of lesions. In addition, DUS can be used in deeply situated or large lesions and has Doppler capability.[2,18,19] Exposure times are relatively short compared with MRI, which often requires sedation in children younger than 10 years of age and in patients with claustrophobia.[18]

Many factors must be considered during evaluation of masseter muscles, such as the age and gender of the patient, size of the muscle, bite force, body variables (height, weight, and body constitution), type of occlusion, facial morphology, and temporomandibular joint disease.[18] Inflammatory reactive lesions are relatively common in the masseter muscle and can be characterized by muscle thickening and abscess formation, which can be demonstrated by using conventional ultrasonography[20]; however, DUS can show changes in vasodilatation. The vascularity in the tumors is important to differentiate hemangiomas from other lesions.[19,21]

Hemangiomas are congenital vascular lesions that often arise from proliferating endothelial cells. The vast majority is detected before the end of the third decade of life, and about half of all cases occur in the first decade of life.[22,23] Intramuscular hemangioma is relatively rare, accounting for less than 1% of all hemangiomas.[24-27] The intramasseteric location is the most common site of intramuscular hemangioma of the head and neck (approximately 36%) and presents clinically as a diffuse swelling in the cheek. Other sites include the trapezius, sternocleidomastoid, temporalis,

mylohyoid, mentalis, and buccinators muscles, as well as the lips and the tongue.[1,28] Compressibility, bruits, thrills, and pulsations are frequently absent as a result of surrounding muscular fibrosis, and overlying skin discoloration is also rare. These lesions are often asymptomatic for 2 or 3 decades, until a sudden growth spurt causes a palpable mass in the affected muscle, which is the most common initial presentation (98%).[28] Diagnosis of intramuscular hemangioma is usually difficult and usually not suspected clinically; as a consequence, over 90% of all intramuscular hemangiomas are misdiagnosed.[26-28]

Excessive muscle contraction and trauma seem to be important etiologic factors for intramuscular hemangiomas. Hormonal factors may also play a role, with a clear increase in volume correlated to menarche, pregnancy, and the menstrual cycle, which explains the slight female predominance in the incidence of intramuscular hemangiomas. However, involvement of the masseter muscle has a male predominance.[5,28] There are no racial factors, and 70% of the cases have unilateral presentation.[5]

The differential diagnosis includes a great variety of tumors and benign processes, such as lymphadenopathy, salivary gland tumors, sialoceles, congenital cysts, lymphangiomas, angiosarcomas, liposarcomas, rhabdomyosarcomas, osteogenic sarcomas, chondrosarcomas, hemangiopericytomas, benign muscular hypertrophy, muscle fiber herniation, myositis ossificans, diffuse angiomatosis, and metastases. Clinically, pain is dependent on speed of enlargement, pressure on adjacent anatomic structures, and thrombosis.[25] Spontaneous regression of hemangioma is rare, and management varies depending on the individual case, with consideration of tumor location, extension, growth rate, accessibility, patient's age, and aesthetics.

Complete surgical excision has been reported as the optimal management for intramuscular hemangioma, but it may be followed by recurrence.[1] For head and neck hemangiomas, periodic observation and parental support are the initial approaches in the treatment. Surgery is generally reserved for cases in which complete excision of the lesion is possible.[25] Enucleation of large deforming lesions can be difficult, and in these cases, alternative therapies, such as corticosteroids, cryosurgery, ligation of the feeding vessel, laser therapy, embolization, and sclerosing procedures, may be advised.[25,29]

The visibility of vessels on DUS varies, depending on the position, morphologic condition, and hemodynamics of the lesion. For these reasons, the DUS professional must have enough experience for an accurate interpretation. DUS shows colored areas corresponding to the blood vessels that supply the hemangioma. The flow diameter and velocities are increased on the affected side, and arterial resistance is decreased.[3] Hemangiomas can be distinguished from other soft-tissue lesions by their prominent vascularity and high blood flow velocity.[21] The resistance index and pulsatility index are reported to be useful in the differentiation of benign and malignant tumors in lymph nodes,[30,31] but there is no information about these parameters in intramasseteric nodules.

The presence of phleboliths in hemangiomas is another finding that has been reported. Phlebolith formation within intramuscular hemangioma is present in approximately 25% of cases.[32] Altuğ et al.[25] reported a case series of hemangiomas with phleboliths, indicating that phlebolith formation and calcification could be a feature of hemangiomas, and for this reason, diagnostic imaging tools, such as CT, MRI, and DUS have demonstrated significant accuracy for diagnosis.[27] It is easier to diagnose hemangioma when phleboliths are sonographically visualized within the lesion.[4] The pathogenesis of phleboliths is thought to involve thrombi produced by the slowing of peripheral blood flow, followed by organization and mineralization.[27]

Metastatic disease to the head and neck region usually involves bone or lymph nodes. Metastasis to skeletal muscles is rare, and involvement of the masseter muscle is extremely uncommon, with only few reported cases in the English language literature.[4,6,8,9,33,34] Approximately 40% of muscular metastases occur in the lower extremity, including the pelvic girdle; 26% occur in the upper extremity, including the pectoral girdle; and 30% occur in the trunk (chest wall, paraspinal muscles, abdominal wall).[8] Intramasseteric metastasis is usually not clinically apparent, and the incidence in autopsy series of patients with cancer is less than 1%.[4,35] Some studies have shown that the phenomenon could be more common than is usually appreciated, but it occurs as a late event. In contrast, approximately 50% of patients with leukemia or lymphoma have microscopic disease within muscles. Adenocarcinoma is the primary tumor most likely to metastasize to skeletal muscle, most commonly from the breast, lung, and colon.[4,8] Ultrasonographic examination shows masseter muscle metastases as ill-defined, hypoechoic, heterogeneous lesions aligned with the long axis of the muscle. Intramuscular hemangiomas have a similar sonographic appearance, and the differential diagnosis is clearer only in cases with phleboliths.[4] Clinically, metastasis has a short evolution time and hemangiomas have a long evolution time, which is important for the differential diagnosis.

The superficial location of metastases makes sonography the ideal imaging method. FNAC is generally confirmatory. The combination of ultrasonography and FNAC is the better method for diagnosing masseteric

metastasis.[4] Clinically, masseter muscle metastases are painless and are associated with widespread disease and a poor prognosis.[4] Skeletal muscle metastases are occasionally diffuse rather than focal, especially when the primary tumor is a breast carcinoma, which may be confused with masseter muscle hypertrophy.[4] To the best of our knowledge, the metastatic nodule seen in one of the current cases is the first case of a masseteric metastasis of pleomorphic sarcoma reported in the English language literature.

Muscular hypertrophy is commonly included in the differential diagnosis for intramasseteric nodules. It is generally diagnosed in young adult patients who experience unilateral or bilateral swelling; it is usually painful but can be painless, with or without limitation of mouth opening, and has a long evolution time. Ultrasonography generally shows a normoechoic or slightly hyperechoic image.[36,37] The cause of this disorder remains unknown, but bruxism and temporomandibular joint disorders have been associated with it.

Benign tumors are important differential diagnoses and commonly have a long evolution time with no signs of skin or mucosal alterations. Intramuscular lipomas have been reported in various muscles, and a few cases of masseteric lipoma and its variants have been described in the literature. Tsumuraya et al. reported a 58-year-old man with an intramasseteric lipoma of 2 years' evolution and without pain or any skin alteration.[38] Previously, Cassoni et al.[14] reported a case of intramasseteric angiolipoma in a 61-year-old woman, with 1 year of progressive growth. These authors reported that ultrasonography was consistent with lipoma and that FNAC was not diagnostic, revealing the presence of adipocytes in the first aspiration and mesenchymal cells in the second aspiration.[14] The diagnosis was confirmed in the histopathologic examination after surgical resection. Falleti et al.[12] reported a case of a masseteric chondroma in a 49-year-old man, with a 6-year history of a firm and painless swelling covered by normal skin. Ultrasonography revealed a uniform hypoechoic structure with calcifications.[12] He et al. reported a case of an intramasseteric schwannoma in a middle-aged woman with a 3-year history of a painless mass in her right cheek.[11] Nakamura et al. reported an intramasseteric schwannoma in a 12-year-old boy with 1 year of progression of the lesion.[10] Dogan et al.[13] reported a solitary fibrous tumor inside the masseter muscle of a 27-year-old woman, who reported a 4-month history of painless swelling in her left cheek. DUS revealed prominent vascularity of the mass; thus, differential diagnosis of intramasseteric hemangioma is important.[13]

Primary malignant masseteric tumors are extremely rare, but some cases have been reported in the literature. Franco et al. reported a case of alveolar rhabdomyosarcoma in a 32-year-old patient with 2 months of lesion evolution,[39] and Lin et al. reported a sclerosing rhabdomyosarcoma in a 40-year-old male.[40] Recently, a case was described of a peripheral primitive neuroectodermal tumor arising in the masseter muscle of a 14-year-old female patient with a painless, progressively enlarging mass present for 2 months.[41] The short time of progression is an important factor to consider with malignant tumors in the differential diagnosis of intramasseteric nodules.

Calcified nodules have been reported in some diseases, such as cysticercosis and tuberculosis. In our literature review, some cases of intramasseteric cysticercosis were observed, with a few days of evolution and evident inflammatory signs, such as pain and locally elevated temperature. Ultrasonography revealed a hypoechoic image with a well-defined cystic area.[42-44] A case of dystrophic calcinosis was reported by Mohiuddin et al. in a 17-year-old boy with multiple painless swellings of 2 years of evolution.[45] Additionally, myositis ossificans, which is a nonneoplastic bone formation within a muscle that generally occurs after trauma, is another differential diagnosis for intramasseteric swelling with inner calcifications.[46,47]

CONCLUSIONS

The diagnosis of intramasseteric nodules is challenging, and various differential diagnoses must be considered, including reactive disorders, benign tumors, metastases, and primary malignant tumors. Clinical features, time of evolution, and the use of auxiliary examinations, such as DUS and FNAC as complementary tools, are useful in obtaining the right diagnosis and for planning the right treatment for the patient.

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