

Pathology Mimicking Orofacial Pain



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KEYWORDS

- Orofacial pain • Facial swelling • Parotid gland swelling • Salivary gland tumors
- Pleomorphic adenoma

KEY POINTS

- Pathology arising from structures adjacent to the temporomandibular joint can present with temporomandibular disorder (TMD)-like symptoms including facial pain and trismus.
- The symptoms of salivary gland pathology involving the parotid gland can sometimes mimic TMD.
- A comprehensive history, thorough clinical examination, and appropriate imaging can help make an accurate diagnosis.
- Understanding the various types of pathology that can present with orofacial pain is crucial for timely diagnosis, treatment, and improved prognosis.

CLINICAL CASE

A 64-year-old retired school teacher presented with the chief complaint of right-sided jaw pain and fullness. She had had this condition for the past 7 years, but a week before presentation, she developed pain in the area without any inciting event, which prompted the referral to see an orofacial pain specialist with the suspicion of a possible temporomandibular joint (TMJ) disorder. She reported that the fullness had neither increased nor decreased over the years, and she had never been evaluated for this condition in the past. The pain was localized to the right TMJ and masseter area, with radiation of pain to the posterior aspect of her right ear. The pain was sharp, shooting in the beginning, with a 9/10 intensity that gradually transitioned into a dull ache of 4/10 over the next few days. The pain was constant and aggravated by coughing, sneezing, yawning, and chewing. She had tried ibuprofen, 400 mg, with no relief. She did not complain of any facial numbness, hypersensitivity, or facial weakness nor of any bite change, jaw joint noises, or jaw locking episodes. She had no systemic

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constitutional features (fever, malaise, night sweats) nor autonomic symptoms. She denied any history of head or neck trauma. She had a long-standing history of migraines but no new headaches, earaches, or neck pain. She did not complain of any toothache or dental sensitivity to hot or cold foods.

Her past medical history was relevant for hypertension, hyperlipidemia, arteriosclerotic vascular disease, bariatric surgery, gastroesophageal reflux disorder, insomnia, and migraines. Her medications included butalbital-acetaminophen-caffeine (50–325–40 mg as needed), trazodone (50 mg once daily), omeprazole (40 mg three times daily), rosuvastatin (20 mg once daily), spironolactone (50 mg once daily), valsartan (160 mg once daily), carvedilol (25 mg), diltiazem (120 mg once daily), hydralazine (25 mg three times daily), and quetiapine (50 mg once daily). She was a former smoker with a 12.5 pack-year history. No pertinent family history of cancer or any autoimmune diseases was reported.

Examination revealed mild facial asymmetry with a firm, tender swelling over the right deep masseter area approximately 3.5×4 cm (Figs. 1). This tenderness duplicated her chief complaint. There was no associated erythema, fluctuance, or purulent discharge or lymphadenopathy. Cranial nerves V and VII were intact. Slight pain on palpation of the bilateral masseters and neck muscles was noted but this was subclinical. She had a normal mandibular range of motion with 40 mm maximal interincisal opening and 8 mm bilateral excursions without any pain or joint noises. No intraoral lesions, swelling, or any signs of odontogenic infection were noted. The ducts of major salivary glands were patent with adequate salivary flow, and the oral mucosa was pink and moist. Her occlusion was stable with good bilateral posterior contacts.

A panoramic radiograph did not show any signs of condylar flattening, erosion, osteophyte, subcondylar sclerosis, or sclerosis. The cortical margins of the mandible were intact, and there were no signs of dental pathology or any pathology of the maxilla or mandible.

The development of recent onset of pain in an area of long-standing facial fullness raised the concern for a neoplastic process. Our differential diagnosis included parotid gland tumor, odontogenic infection, benign or malignant jaw tumors (such as ameloblastoma, osteosarcoma, Hodgkin disease, multiple myeloma, or metastatic disease),



Fig. 1. Clinical image depicting right-sided facial fullness/swelling that was diagnosed as pleomorphic adenoma, a benign parotid gland tumor. The arrow indicates right-sided facial fullness.

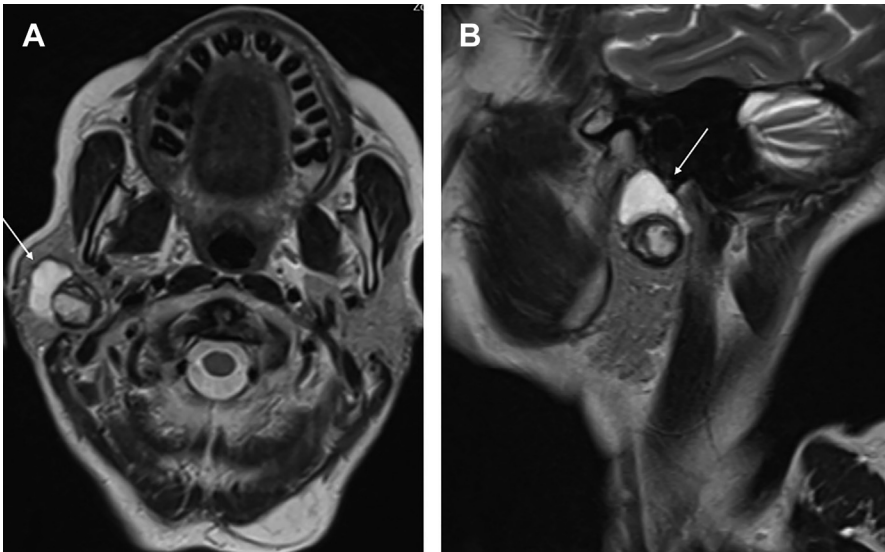


Fig. 2. Pleomorphic adenoma. MRI depicting a 2.5 x 2.4 x 2.8-cm avid homogenous enhancement in the superficial lobe of the right parotid gland in (A) axial T2 and (B) sagittal T2 sections. The arrow indicates the pleomorphic adenoma.

or an immune-mediated condition (such as Sjogren syndrome). In addition, she had subclinical myofascial masticatory and cervical pain.

An MRI was ordered that demonstrated a 2.5 x 2.4 x 2.8 cm heterogeneous cystic lesion in the superficial lobe of the right parotid gland. The patient was referred for fine-needle aspiration, which demonstrated a benign mixed tumor, consistent with pleomorphic adenoma. She underwent right total parotidectomy, and the pathology demonstrated completely excised pleomorphic adenoma. There were no postoperative complications, and her facial pain resolved as she recovered successfully from the surgery. In this case, it is important for clinicians to note that the associated TMD-like symptoms were secondary to the neoplasm of the parotid gland instead of a primary pathology involving the TMJ or the myofascial muscles of the joint space and its associated structures (Fig. 2).

SALIVARY GLAND TUMORS

Epidemiology

Salivary gland tumors constitute about 3% to 6% of head and neck tumors, making them rare neoplasms. The incidence of salivary gland tumors has been reported to be 0.4 to 13.5 cases per 100,000 people, with benign tumors being more common than malignant.^{1,2} Thirty-one different types of salivary gland neoplasms have been identified by the 2017 World Health Organization (WHO) classification, of which pleomorphic adenoma and Warthin tumor are the most common benign tumors and, mucoepidermoid carcinoma and adenoid cystic carcinoma are the most common malignant histologic types.³

Salivary gland tumors have a high predilection for parotid glands, followed by minor salivary glands, submandibular glands, and sublingual glands in that order.⁴ Among the minor salivary glands, there is increased predilection for the palate followed by the upper lip and buccal mucosa.⁵ Most of the parotid gland tumors are benign

(69%–88%), and most of the sublingual glands tumors are malignant (75%–100%).^{2,4,6–9} There is an equal prevalence of benign and malignant tumors in the submandibular glands, and most tumors of the minor salivary glands (60%) are malignant.^{2,4,6}

The 2 most common benign tumors—pleomorphic adenoma and Warthin tumor—have a gender predilection for women and men, respectively.^{8,10–13} A consensus is currently lacking regarding gender predilection for malignant salivary gland tumors. Benign salivary gland tumors are more common at around 50 years of age; malignant tumors commonly occur 10 years later.^{14–19} No predilection for ethnicity has been reported.

The exact cause of salivary gland tumors is unknown, but these tumors have been identified with high incidence in patients with a history of Epstein-Barr virus-related cancers, immunosuppression, childhood radiation therapy, and in atomic bomb survivors.^{20,21} Interestingly, smoking and alcohol use, which are significant risk factors for head and neck cancers, have not been found to influence the risk for salivary gland cancers.²² Genetic alterations are also implicated in the development of salivary gland tumors. Pleomorphic adenoma gene 1 and high-mobility group AT-hook 2 gene alterations are highly specific for pleomorphic adenomas and carcinoma ex-pleomorphic adenoma.^{23,24}

Clinical Features

Benign tumor of the salivary glands commonly presents as a slow-growing, well-circumscribed painless mass. Pleomorphic adenoma, Warthin tumor (usually present bilaterally), and myoepithelial tumors are the most common benign salivary gland tumors of the parotid gland.²⁵ Parotid gland tumors commonly involve the superficial lobe where they typically present as asymptomatic, slow-growing, facial swelling without any systemic symptoms. When the deep lobe is involved, patients may present with symptoms such as pharyngeal narrowing, sleep apnea, dyspnea on exertion, trismus, and pain.²⁵

Involvement of the facial nerve causing facial weakness, increased tumor growth, onset of pain or paresthesia, trismus, fixation of tumor mass, pharyngeal asymmetry, dysphagia, glossopharyngeal nerve palsy, bleeding from the parotid duct outlet, and lymphadenopathy should raise suspicion for a malignant process.^{26,27} A retrospective study including 131 patients with parotid gland carcinoma found facial nerve palsy and skin infiltration to be independent poor prognostic factors for the treatment outcome.²⁷ Mucoepidermoid carcinoma, adenoid cystic carcinoma, and acinic cell carcinoma are the most common malignant salivary gland tumors affecting the major salivary glands.²⁸ Adenoid cystic carcinoma has been associated with early and frequent perineural invasion and distant metastases, most commonly to the lungs.²⁹ The duration of the symptoms may vary from 2 to 48 months before referral to a specialist.³⁰

Diagnosis

A thorough clinical examination can help identify the red flags and prevent a clinician from missing these pathologies. Clinical examination has been shown to have an accuracy of approximately 85% in differentiating benign parotid gland tumors from their malignant counterparts.³¹ Imaging (such as ultrasound, MRI, computerized tomography, and PET scans) and histopathology (fine-needle aspiration [FNA] cytology or biopsy) are crucial in making the diagnosis of salivary gland pathology.^{32,33}

MRI is the diagnostic modality of choice and can help evaluate the extent of the tumor, local invasion, marrow infiltration, and perineural spread.³² PET can be used to

determine distant metastases.³³ Imaging modalities are extremely helpful, but they lack the ability to differentiate between benign and malignant salivary gland tumors. These tumors can be differentiated with histopathology using either FNA, which has a sensitivity of 73% and specificity of 91%,^{34,35} or core needle biopsy where a larger tissue sample is needed.³⁶

Management

The management of salivary gland tumors varies depending on the benign or malignant nature of the tumor, the staging, and the grade of the tumor. The 3 standard treatment modalities are surgery, radiation therapy, and chemotherapy. Surgical excision remains the cornerstone treatment of most salivary gland tumors, except when the risk to benefit ratio of surgery is high, as in the elderly.³⁷ Complications of surgery can include facial nerve palsy, Frey syndrome, and first bite syndrome.^{38–40} External beam radiation therapy is used in cases with unresectable or macroscopically persistent or recurrent disease.⁴¹ Chemotherapy with Taxol and platinum-based agents has been used for the treatment of unresectable advanced salivary gland cancers and cases with distant metastases^{42–44} but the impact of chemotherapy on overall survival remains unclear.

Prognosis

The recurrence rate of pleomorphic adenoma and Warthin tumor is in the range of 1% to 5% and 7% to 12%, respectively, primarily due to incomplete surgical excision, tumor spillage, and satellite lesions.^{45,46} The malignant transformation of pleomorphic adenoma into carcinoma ex-pleomorphic adenoma can occur in 2% to 15% of cases.^{47,48}

According to the American Cancer Society, the 5-year relative survival rate for localized salivary gland cancer is 95%, regional salivary gland cancer (local invasion of nearby structures and lymph nodes) is 69%, and for salivary gland cancer with distant metastases is 44%.⁴⁹ The 5-year survival rate for high-grade mucoepidermoid cancer has been reported in the range of 0% to 43%, for intermediate-grade in the range of 62% to 92%, and low-grade in the range of 92% to 100%.⁵⁰ For adenoid cystic carcinoma, although the 5-year survival rate is high (approximately 89%), the 15-year survival rate reduces significantly to about 40% due to the associated risk of perineural invasion and distant metastases.⁵¹

DIFFERENTIAL DIAGNOSIS

Odontogenic Infection

Pain and swelling in the orofacial region should raise suspicion of odontogenic infection, as it is common. The source of the infection primarily includes dental caries, pulpal and periapical disease, periodontal disease, pericoronitis, and osteomyelitis. Odontogenic infection can result in an abscess or diffuse soft-tissue bacterial infection (cellulitis), further leading to facial pain, swelling, and trismus.⁵² Potentially life-threatening conditions such as cavernous sinus thrombosis, brain abscess, airway obstruction, and mediastinitis can result from untreated odontogenic infections.⁵² Clinical examination and imaging assume a vital part in recognizing the source and determining the degree of the spread of infection and its associated complications.

The radiographic changes depend on the duration and the type of odontogenic infection as well as the immunity of the patient. The early radiographic changes in pulpal and periapical disease consist of widening of the apical periodontal ligament, disruption of lamina dura, and formation of periapical radiolucency.⁵³ If the disease

remains untreated, it can either lead to formation of apical granuloma/cyst or can result in osteomyelitis (characterized by further osteolytic changes in the bone with the formation of sequestrum) or anatomic space infection (characterized by involvement of soft tissues).⁵³ However, in odontogenic infections despite the expansion of the radiographic lesion, the epicenter would remain at the apex of the offending tooth. In the present case, the radiographic and clinical examination did not reveal any source of odontogenic infection.

Jaw Bone Tumors

Tumors arising from numerous structures in and around the TMJ, including the mandibular ramus, can cause TMD-like pain symptoms. Jaw bone tumors can also present as facial swelling depending on the growth and the extent of involvement and may be benign or malignant. Benign jaw tumors are typically slow growing and painless. The 2 most widely recognized odontogenic tumors are keratocystic odontogenic tumor (KCOT) and ameloblastoma. Both these benign tumors cause a cystic expansile mass of the jaw. Because of the locally aggressive behavior, these 2 tumors, if left untreated, could result in extraoral facial swelling. Radiographically, ameloblastoma and KCOT may present as unilocular or multilocular radiolucency predominantly in the posterior mandible and ramus.⁵⁴

Clinical signs and symptoms of malignant jaw tumors may include pain, paresthesia or anesthesia, a rapidly expanding swelling, and mobility of teeth within the field of disease.⁵⁴ The primary malignant jaw tumor, osteosarcoma of the jaw, is rare (primarily accounting for approximately 4% of all the primary malignant jaw lesions and 7% of all osteosarcomas) and commonly occurs in the fourth decade of life.⁵⁵ It may vary from a radiolucent or radiopaque lesion to a mixed lesion, or it may present as a generalized widening of periodontal ligament spaces.⁵⁴ Malignancies of the hematopoietic system such as multiple myeloma and non-Hodgkin lymphoma can also involve the jaws.^{55,56} Although multiple myeloma typically has a characteristic radiographic feature of well-defined, multiple, punched-out radiolucent lesions,⁵⁵ extranodal non-Hodgkin lymphoma may appear as poorly defined, osteolytic lesions of the jaw.⁵⁶ Distant metastasis to the jaw is rare, accounting for less than 1% of all oral cavity malignancies and generally suggests widespread dissemination of cancer.⁵⁷ The most common finding is an ill-defined radiolucency, which is typical of osteolytic metastatic breast cancer, but radiopaque changes may also be observed, as with osteoblastic tumors of metastatic prostate cancer.⁵⁷ In our patient, the presence of facial swelling along with new-onset pain raised the suspicion for a jaw tumor, but the radiographic examination did not reveal any osteolytic or osteosclerotic process, ruling out this possibility.

Sjogren Syndrome

Sjogren syndrome (SS) is an autoimmune disease characterized by lymphocytic infiltration of the secretory glands, primarily the lacrimal and salivary glands, leading to dry eyes and dry mouth, respectively.⁵⁸ However, lymphocytic infiltration and deposition of immune complexes may occur in extraglandular sites, including the skin, mucosa, lungs, kidneys, peripheral nervous system, and musculoskeletal system, making SS a systemic disease. Systemic features include fatigue (approximately 70%–80% of patients), interstitial lung disease, tubulointerstitial nephritis, neurologic symptoms, and arthritis in about 71% of patients.⁵⁸

Salivary gland enlargement is a sign of lymphoproliferation and typically presents as a facial swelling when involving the parotid glands. The risk of development of non-Hodgkin lymphoma in SS has been reported in the range of 2.7% to 9.8%.⁵⁹ Musculoskeletal involvement in SS is characterized by intermittent polyarticular arthropathy

chiefly affecting small joints.⁶⁰ The involvement of the TMJ and myofascial muscles has not been extensively assessed in patients with SS. An observational study including 72 SS patients found a 91.7% prevalence of TMD symptoms (myofascial pain, reduced range of motion, TMJ arthralgia, headache, and tinnitus) in the SS group versus the control group.⁶¹ Although facial swelling could indicate an underlying autoimmune disease such as SS involving the parotid gland, our patient did not have any clinical features of dry mouth or dry eyes, and the histopathology from the biopsy ruled it out.

Neurogenic Tumor (Schwannoma)

Schwannomas are benign neoplasms originating from the Schwann cells that sheath a nerve. Facial nerve schwannomas (FNS) are rare but, when present in the parotid gland parenchyma, can present as a painless and slow-developing mass similar to pleomorphic adenoma.^{62,63} FNS have been reported in the age range of 43 to 51 years and have been found to show no gender predilection.⁶³ Facial paralysis is a common symptom in patients with FNS, but it may not be consistently present at the time of diagnosis.⁶³

MRI with and without gadolinium contrast is the primary method of imaging for the assessment of FNS. In the parotid gland parenchyma, FNS typically presents as a well-circumscribed, avidly enhancing intra-parotid mass that is T1 isointense and T2 hyperintense to muscle.⁶² For a definitive diagnosis, a biopsy is indicated.⁶³ In our case, the imaging may be suspicious for an intraparotid, but the FNA cytology was consistent with pleomorphic adenoma.

SUMMARY

TMD represents a significant source of orofacial pain of nonodontogenic origin. When evaluating a patient with orofacial pain, clinicians should consider all the potential differential diagnoses, especially when red flags such as swelling/facial fullness or paresthesia/numbness are present. Comprehensive history taking, thorough examination, and appropriate investigation are crucial for the diagnosis and management of these conditions that can cause considerable harm if left untreated.

CLINICS CARE POINTS

- Orofacial pain can be a symptom of a myriad of head and neck pathologies; the clinician should be aware of the potential differential diagnoses.
- A thorough review of patient's history, examination, and appropriate investigation are vital to rule out pathologies that can mimic orofacial pain conditions.

DISCLOSURE

The authors do not have any disclosures. The authors do not have any conflicts of interest associated with this publication, and there has been no financial support for this work that could have influenced its outcome. This manuscript is original, has not been previously published, and is not currently under consideration by another journal.

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