5

Differential Diagnosis of Pains and Radiolucencies of Nonpulpal Origin

BRADLEY ELI, NASSER SAID-AL-NAIEF, AND MAHMOUD TORABINEJAD

CHAPTER OUTLINE

LEARNING OBJECTIVES

After reading this chapter, the student should be able to:

1. Identify the personal and societal effect that orofacial pain conditions can have.
2. Understand the classification systems for common orofacial disorders that can cause tooth pain.
3. Understand both extracranial and intracranial conditions that can refer pain to the teeth.
4. Identify and manage confusing dental causes of tooth pain.
5. Identify and manage muscles, joint, neurovascular causes of tooth pain.
6. Understand head and neck structures that refer pain to the teeth.
7. Understand temporomandibular disorders (TMD) that can cause pain in the jaw, head, and neck.
8. Identify the radiographic features of normal anatomic structures and developmental entities and understand the clues on differentiating these entities from true pathologies of the maxillofacial region.
9. Identify the clinicopathologic and radiographic features of incisive canal cyst.
10. List the odontogenic and nonodontogenic tumors and cysts that involve the maxillofacial region.
11. Understand the key differentiating points when examining the odontogenic and nonodontogenic tumors and cysts that involve the maxillofacial region.
12. List different types of benign fibro-osseous lesions of the jaw and identify the clinicopathologic features of each.
13. Identify the clinicopathologic and radiographic features and etiopathogenesis of surgical ciliated cyst, traumatic bone cyst (TBC), and focal osteoporotic bone marrow defect, with a brief description of the histologic feature of each.
14. List and identify the clinicopathologic features of selective benign and malignant bone tumors.
15. Identify the spectrum of hematolymphoid disorders as well as plasma cell disorders and Langerhan cell disease (LCD).

Introduction

Several conditions of nonendodontic origin simulate clinical and the radiographic appearances of pulpal and/or periapical lesions. Determining the cause of these conditions is a critical first step in diagnosis and treatment planning. Without an accurate diagnosis, treatment is unlikely to be effective. Initially, the clinician must determine whether the cause of the problem is odontogenic (pulpal or periodontal) or nonodontogenic. Because of the similarities of clinical and radiographic appearance of many of these conditions, dentists must perform clinical tests in a systematic manner to arrive at an accurate diagnosis and avoid critical

mistakes. Pulp vitality tests are the most important aids in differentiating most of these conditions. To avoid misdiagnosis and performing wrong treatment, all relevant patient history, clinical signs and symptoms, vitality tests, and radiographic examinations should be utilized. The purpose of this chapter is differentiating and treating (1) pains of nonpulpal origin from those of pulpal and or/periodontal origin, and (2) radiolucencies of nonpulpal origin from those of pulpal origin.

Pains of Nonpulpal Origin

Toothache of Nonpulpal Origin

Nonodontogenic pain can be extremely distressing to the patient and baffling to the clinician. For patients, this can result in years of misdiagnosis, mismanagement, and overtreatment, thus risking the development of chronic pain pathology. To further complicate the problem, patients will jump from one provider to another as treatment failures continue to mount. A history of unsuccessful treatment by numerous providers is a red flag for the endodontist to expand the differential diagnosis to include pain of a nonodontogenic origin. In this group of patients taking the time to complete a comprehensive history will avoid unneeded diagnostic tests and misdirected treatment.

All pain disorders have a negative effect on the patient and those around them. This is especially true when it comes to painful conditions in the facial region. These disorders have an especially high level of concern because this region is the center for both verbal and nonverbal communication as well as nourishment.

The face is also highly innervated by both sensory and special sensory nerves. The motor and special motor nerves respond to this afferent information. This cross talk of malfunctioning nerves can make specific diagnosis elusive for the provider and at the same time making the patient frantic for an explanation.

This combination is the perfect environment for unnecessary or unsupported treatment resulting in more failure and despair. Using a linear model of cause and treatment is not always successful. To address this issue further, the research diagnostic criteria of Dworkin and Leveche considered the psychosocial side of pain and that both physical conditions and psychologic conditions contribute to the suffering, pain behavior, and disability associated with a person's pain experience.[1]

Dentists are often the first clinicians involved in diagnosis and treatment of these conditions.[2,3]

To be successful in treating these patients, it is important to have a clear understanding of the many different ways in which the patient may experience nonodontogenic pain and how to avoid unnecessary treatment. In the dental field, the most useful pain consultants are (1) orofacial pain trained dentists, (2) endodontists, and (3) oral maxillofacial surgeons. These professionals are a resource for medically trained pain management providers as well as dentists. Referral to one of these specialists is preferable to sending a patient to an urgent care facility or an emergency room.

Incidence of Orofacial Pain

The frequency of continuing pain after endodontic treatment has been reported at 5%. Of these patients, 62% were found to be a pain of nonodontogenic origin.[4] The frequency of persistent pain after orthograde root canal treatment in one study subsequently identified as nonodontogenic pain was 53%. In this study myofascial pain was determined to be the source.[5] Another study found that 44% of patients with persistent pain had previously received endodontic treatment or tooth extractions in an attempt to resolve their pain.[6] Moreover, 23.5% of patients with headaches reported tooth pain referral as well.[7] The importance of comprehensive examination of the muscles in the head and neck is emphasized in a study that reported pain referral patterns to the teeth in 138 of 230 patients.[8]

In a survey of 827 randomly selected individuals from a general population group, 10% reported pain in the head, face, or neck.[9] Another group surveyed 1016 members of an HMO and found that 12% reported facial pain within the preceding 6 months and 26% reported headache.[10] Lipton et al. surveyed 45,711 households and found 22% had at least one of 5 types of orofacial pain in the preceding 6 months. Most common orofacial pains were toothache at 12.2%, temporomandibular (TM) joint pain at 5.3%, and face/cheek pain in 1.4%.[11]

To better understand disorders of the orofacial region, a study was undertaken titled "Orofacial Pain: Prospective Evaluation and Risk Assessment (OPPERA)."[12] This study provided improved insight into the number of people affected by pain in the orofacial region. Epidemiologic surveys in the United States, Canada, and the United Kingdom report the frequency of orofacial pain in the general adult population as ranging from 14% to 40%.

Basic Terminology in the Understanding and Diagnosis of Pain

Pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.[13,14] Orofacial pain refers to oral pain, dental pain, and pain in the face above the neck, anterior to the ears, and below the orbitomeatal line.

Common Terms

Algesia – Any pain experience after a stimulus
Allodynia – Painful response to a nonpainful stimulus
Dysesthesia – An abnormal sensation that is unpleasant
Hyperalgesia – An increased pain response to a noxious stimulus
Hypoalgesia – A diminished pain response to a noxious stimulus
Hypoesthesia – A decreased sensitivity to stimulation similar to anesthesia
Neuroma – A mass of peripheral neurons formed by a healing damaged nerve
Neuropathic Pain – Aberrant sensation produced by a malfunctioning nerve
Nociception – Perception of pain arising from tissue damage or injury
Pain Threshold – The lowest level of stimulation perceived as painful
Pain Tolerance – The highest level of pain a subject is prepared (or able) to tolerate
Sensitization – The increased excitability of nerve terminals or neurons produced by trauma or inflammation of peripheral tissues

Diagnostic Process for Nondental Orofacial Pain

Due to the complexity of orofacial pain, many authors suggest classification or grouping of functional systems as the most direct method to evaluate these orofacial pain problems.[2,3,14] Effective diagnosis and treatment of these disorders require a working knowledge of functional neuroanatomy, peripheral nervous

system (PNS) and central nervous system (CNS) pathways, descending pain-modulating systems, and their related structures. CNS changes may underlie persistent pain. The patient's emotional response to continuing pain is another factor that should be considered in the diagnostic process. To be an effective care provider, the clinician must have a solid understanding of the various categories in which persistent orofacial pain can be classified.

It is important to remember that directing and providing the most appropriate care may involve multiple clinicians. By taking a thorough medical history and carefully processing clinical characteristics, the clinician can begin to identify the unique characteristics of extracranial, intracranial, musculoskeletal, vascular, neurologic, and psychological symptoms. This assessment provides the most direct path to diagnosis, referral, or treatment.[2,3,5,16]

When a thorough assessment is completed, the clinician can confidently reassure the patient that his or her symptom will be appropriately managed. This proficiency is another critically important skill for the specialist to develop. Without confidence in the treatment provider, the patient's anxiety and worry can interfere with the diagnostic process and resulting care.

Localization of the Pain

1. Eyes, ears, nose, throat, sinuses, tongue, teeth, and glands are head and neck structures that may be a source of pain. The quality of pain in a region involving such a broad range of structures can range from mild aching to excruciating pain. As previously mentioned, the most common cause of pain in the orofacial region is dental pathology.
2. A diligent search for dental pathology should begin early and continue throughout diagnosis and treatment.
3. Pain of dental origin will often awaken a patient from sleep or prevent sleep. Patients may regard sleep disturbance as noncritical medical information.[2,3] Sleep disturbance is an important part of the differential diagnosis. It is important to ask very specific questions about the effect of pain on sleep patterns.
4. Pain of the pulpal tissues or periodontium is often very acute and easily localized on examination or by patient report. Affected teeth are typically painful to palpation or percussion. Use of percussion testing is extremely helpful in the diagnostic process.
5. Any tooth-related pain should be evaluated radiographically to exclude dental disease. Most computed tomography (CT) imaging and radiology reporting from a medical center do not provide an adequate evaluation of the dental structures. If imaging is completed, a dental provider should access the images and review them personally.
6. With nonodontogenic pain, the maxillary sinus and teeth are the areas that are most commonly affected by disease. Typical descriptors of sinus disease are "constant," "aching," "pressure," and "fullness." Pain will often include the teeth or ear. Fever, congestion, and/or discharge may also be present. Head position or movement can often exacerbate this symptomatology.[2,3]

Confusing Dental Pathology

Periodontal Ligament Pain

Caused by repetitive strain to the dental periodontal ligaments through clenching, gross occlusal prematurities, or trauma to the teeth, this type of pain is characterized by deep somatic musculoskeletal pain. Periodontal ligament pain is generally a dull, aching pain in and around the teeth and can affect multiple teeth. Inflammatory fluid accumulation from a periodontitis or an apical abscess may cause displacement of the tooth in its socket, with a resulting acute malocclusion and pain (Fig. 5.1). The most common sign is tenderness of the teeth to percussion in the absence of pulpitis or periapical/periodontal abscess. Treatment consists of using a splint to protect the teeth, reducing oral habits, and encouraging healing. The use of a transitional splint can help in diagnosing and treating these conditions.

• **Fig. 5.1** Periodontal ligament pain is cause by inflammatory and fluid accumulation from either a periodontitis or an apical abscess. (Redrawn after Fricton J, Kroening R, Hathaway K: *TMJ and craniofacial pain: diagnosis and management*, St. Louis, 1988, Medico Dental Media International, Inc.)

Intracranial and Headache Pain

Although uncommon, neoplasm, hematoma, hemorrhage, edema, aneurysm, and infection of the CNS can result in facial pain. Space-occupying lesions are often associated with progressive pain complaints and associated neurologic deficit or signs. Patient descriptors, including the "worst" or "first," have been identified as specifically pathognomonic of more serious conditions.[2,3,15,16] These conditions can progress quickly and lead to permanent disability or even death. Prompt identification and referral for neurology consultation can be critical to successful diagnosis. The SNOOP acronym can be helpful to determine level of concern, as follows:

Systemic symptoms or disease: fever, weight loss, human immunodeficiency virus (HIV), systemic cancer
Neurologic signs or symptoms: confusion, clumsiness, weakness, aphasia, vision change
Onset sudden: thunderclap, progressive, positional
Onset after age 40 years: vascular (temporal arteritis), tumor, infection
Pattern change: any new or changed headache pattern or quality or increase in frequency or intensity

Some of the most difficult primary headache diagnoses involve the orofacial region. It is important to remember that headache disorders can and do occur anywhere in the trigeminal distribution and can be difficult to differentiate from disease. For example, midface migraine and sinus disease can look and act very similar in many ways to dental pathology. Careful history-taking is critical to diagnostic accuracy and treatment effectiveness. Recurrence and duration can often be helpful in differentiation of primary headache. In addition, with the introduction of the specific drug class triptans, a medication trial can help clarify the diagnosis.

Temporomandibular Disorders

Musculoskeletal conditions are the major cause of nonodontogenic pain in the orofacial region. Included in this group are cervical spine and temporomandibular joint disorders (TMD). Oral and facial pain may be the result of TMD, myofascial disorders, or systemic rheumatologic, collagen, or cervical spine disease. TMD refers to pain and dysfunction specific to the TM joint that frequently involves mandibular movement disorders. Palpation of the region is usually associated with exacerbations of pain, and functional pain is common.

The TM joint is made up of three major structures: the condyle, the disk, and the skull. The TM joint is a complex joint, capable of both rotational and translational movements. Rapid displacement of the joint can result in pressures that disrupt the disk–condyle relationship, resulting in lack of coordinated movement. On examination, this disorder can be identified as clicking or popping in the joint. Less subtle noises, such as crepitation, can occur with degenerative disease of the region and must be considered in the diagnostic process.

Mechanical disturbance of this joint is often associated with inflammatory events that often respond to antiinflammatory treatment.[2,15,16] Noise in the TM joint that presents without pain, catching, locking, or sudden and notable change in bite position is often simply a finding that requires no more than identification. Because of the TM joint's location in relation to the ear, patients' concerns about joint noise must be addressed and explained as present and being considered in the diagnostic process to avoid unnecessary treatment focused on the TM joint.

Trauma is thought to be the main cause of dysfunction in the region. Microtrauma resulting from tooth grinding or jaw clenching, or macrotrauma resulting from external forces such as a MVA or facial effect has been discussed in the literature as the etiology of such disorders.[2,3,15-17] Jaw joint and muscle strain and sprain (JAMSS) is another potential precedent to TMD and facial pain. Trauma may occur during dental treatment. Hyperextension of the mouth for extended time periods and excessive force placed on the jaw during a procedure or after local anesthetic injections may cause injury. More than 50% of patients with TMD associate initial onset of this problem with this type of trauma.[18]

Psychological Disturbances

Psychological disturbances have also been proposed as a cause of tooth pain. However, even though practitioners know factors such as stress, muscle tension, anxiety, and depression can contribute to an enhanced experience of pain, psychological factors have not been established as a cause of toothaches of nondental origin. Psychological disturbances are considered more of a contributing factor to periodontal ligament strain and muscle pain but not tooth pain. Psychological illness with reported pain complaints is common. Psychological illness requires the inclusionary criteria present for any other disease and should not be assumed. Once identified, treatment plans should be developed and presented as clearly and succinctly as those of the other pain etiologies discussed.

It is important to remember that many of the currently described pain disorders were, as recently as the 1990s, considered to be psychological illnesses. Therefore care should be exercised when allowing this diagnosis to be made by exclusion.[2,3] It is also important to remember that with extended time, multiple treatment failures, and constant pain, patients who present with depression, fear, and feelings of hopelessness and helplessness are actually showing signs of a "normal" response to a chronic condition.

Types of Pain

Musculoskeletal Pain

Myofascial pain is the most common muscle pain disorder of the orofacial region. Muscle splinting, muscle spasm, and myositis are the most common acute conditions and, based on duration, may precede myofascial pain in etiology.[17] Factors associated with aggravation of muscle pain include prolonged muscle tension, poor posture, parafunction, trauma, sleep disturbance, viral infection, metabolic disturbance, and specific joint pathology.[17] The most common examination finding associated with muscle problems involves pain with palpation, movement anomalies, and referred pain. Knowing the common referral patterns for the head and neck muscles will save hours of confounding findings and prevent failed treatments. The text by Travell and Simons is the best resource for information about this disorder.[17]

Joint Disorders

Joint disorders have been identified as a major cause of nondental pain in the orofacial region and are considered to be a subclassification of musculoskeletal disorders.[19]

Neurovascular Pain

Migraines, cluster headaches, and hemicrania continua are types of headaches that result from changes in the nerves and blood vessels of the head. In some cases, through referral patterns of the trigeminal nerve, these headaches can also be felt in the teeth, causing toothaches. The pain can be spontaneous, severe, and throbbing, and it can have periods of remission. Treatment is directed at the cause of the headache and often includes behavioral therapy and medications.

Neuropathic Pain

Neurologic or neuropathic pain is the result of abnormality in nociceptors. These receptors are activated by stimuli that threaten or damage the body's integrity. They respond to mechanical, thermal, and chemical stimuli. Both peripheral and central locations and mechanisms may be involved.

Decreased inhibition and/or increased peripheral activity result in two basic types of pain: paroxysmal and continuous neuralgias.[2,20,21]

Paroxysmal neuralgias are described as intense, sharp, stabbing, electric-like pains, usually of unilateral presentation involving a specific nerve.

The intensity of the pain is described as "the worst pain known to man." This type of pain can occur in short or extended-duration volleys.[20,21] Although the intensity of these types of pain is extreme, they do not often awaken the sleeping patient, which helps differentiate this pain from pulpal or periodontal pain.

Trigeminal neuralgia affects the fifth cranial nerve. It is usually unilateral and is more common in women over the age of 50.

Etiology includes idiopathic, demyelination, or vascular malformations.[2,3] Additional etiology theory includes pathologic (bone) cavities at the site of previous tooth extraction, periodontal lesions, and previous endodontic therapy.[3]

Because of the similarity between the symptoms of trigeminal neuralgia and dental etiology, it is common for patients to have consulted with an endodontist. The endodontic specialists must become very familiar with the unique features and provide the evaluation "to eliminate" toothache as the etiology.

The majority of patients describe the classic high-intensity, triggerable pain in association with such activities as eating and talking. Even simple things, such as a cold breeze, can trigger a pain episode.[20,21]

In addition to the paroxysmal nature of classic trigeminal neuralgia, a pretrigeminal neuralgia has also been described by Fromm.[22] This type of pain is of note due to its more constant, dull aching characteristics and is often described by patients as feeling "like a toothache." To further confound the pain provider, most neuralgias are disabled for 4 to 8 weeks by dental procedures such as endodontic treatment and oral surgery. When the pain returns, it is "transferred" to the next tooth in the same arch, which is then incorrectly treated. Patients can often undergo multiple endodontic procedures chasing this disorder.

Glossopharyngeal neuralgia and nervous intermedius neuralgia are more rare than trigeminal neuralgia and involve branches of the glossopharyngeal and vagus nerves.[20,21] Symptoms of pain often include the ear, throat, tonsillar pillar, and submandibular regions. Triggering mechanisms, including chewing, talking, and swallowing, are often the hallmark. Aggressive imaging of the region is recommended because of the high likelihood of regional lesion or pathology associated with this disorder.[3]

Deafferentation Syndromes

Partial or total loss of nerve supply to a region can result in a painful condition. This disorder can be a direct result of traumatic injury, surgery, or a breakdown of the neural structures.

Deafferentation-type pain is thought to involve the sympathetic nervous system, as blockade of this system may often eliminate or reduce the complaints of the patient. Characteristic descriptors used with this type of pain seem most commonly to include the words "burning," "stinging," "itching," and "crawling." Pain is not always present immediately at the time of injury or trauma and may be the result of a breakdown of the central inhibition.

Atypical Odontalgia

This term is used to describe a persistent, painful condition in the oral cavity that cannot be readily attributed to a known cause. The International Headache Society defines atypical odontalgia (AO) as a subgroup of persistent idiopathic facial pain that does not have the characteristic cranial neuralgias and is not attributed to another disorder."[23]

Phantom tooth pain, atypical facial neuralgia, and idiopathic toothache are terms that are used synonymously with AO.

Differential diagnosis includes these four findings:

- Duration longer than 4 months
- Normal radiographic examination
- No clinical observable cause
- Description as a toothache or tooth site pain

Words often used to describe this pain are "diffuse," "burning," "stabbing," or "throbbing."

It is generally thought that AO is a subset of neuropathic pain, i.e., "pain arising as a direct consequence of any lesion or disease affecting the somatosensory system."[24] In this instance, it is thought to result from injury to sensory fibers supplying the extirpated pulp or extracted tooth.

Dental procedures, testing, and diagnostic block of the somatic system are rarely conclusive. Confirmation is associated with positive sympathetic nerve block.[2,3,16]

Neuromas and Neuritis

Neuromas are a growth or tumor of nerve tissue and are often associated with trauma or a direct section of nerve tissue. Stimulation of the region is consistent for diagnostic purposes; however, treatment can be elusive due to recurrence. Neuritis as a systemic inflammatory response is often associated with herpes zoster viral infection. Aggressive and early identification and treatment can often decrease or eliminate the constant sequelae of a zoster episode.[20,21]

Referred Pain

Cervical Spine Pain

Disruption in spine position, structure, and movement can often refer pain into the orofacial region. Careful assessment, history, and clinical examination, including the cervical spine, are paramount to correct identification of etiology and exclusion of referred pain phenomena.[3,16,17]

These disorders can generally be subdivided into muscles or those from the cervical spine. These structures commonly refer to the face and should not be overlooked in cases wherein a diagnostic question exists.[25]

Pain Arising from Vascular Structures

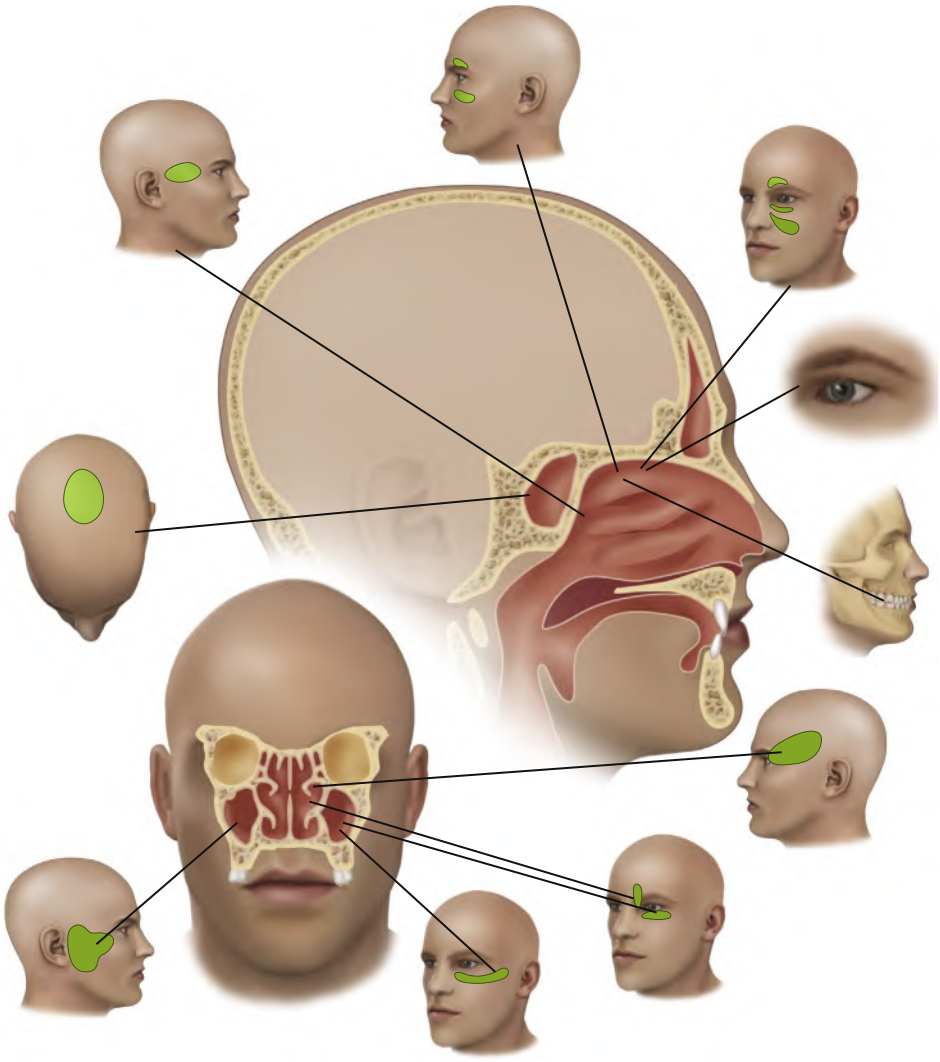
Carotidynia and temporal arteritis are two such disorders that can present with pain in and around the teeth, jaws, and related structures. Palpation localized to their specific anatomic locations assist in the diagnostic process.[2,3,15,16]

Cardiac Toothache

Heart problems such as angina pectoris or acute myocardial infarction refer pain to the shoulder, arm, and even to the jaw. We know that these conditions can refer pain to teeth as well. Sometimes cardiac toothache is associated with chest pain, but occasionally it is not. When a toothache has a cardiac origin, it usually increases with exercise and decreases with medication specifically prescribed for the heart (such as nitroglycerin tablets). Treatment is directed to the underlying heart problem usually after a dentist has evaluated the tooth.

Sinus/Nasal Toothache

Problems in the maxillary sinuses and/or paranasal mucosa can refer pain to the upper teeth. The pain is usually felt in several teeth as dull aching or throbbing. Sometimes it is associated with pressure under the eyes, and it can increase with lowering the head (which puts pressure over the sinuses), coughing, or sneezing. Tests performed on the teeth, such as cold, chewing, and percussion, can increase the pain from sinus origin. A history of an upper respiratory infection, nasal congestion, or sinus problem should lead to suspicion of a "sinus toothache." Diagnostic tests such as visual nasal examination, sinus x-rays, or magnetic resonance imaging (MRI) will reveal this condition. Also, application of topical anesthesia to the offending area should eliminate the pain. Treatment with antihistamines, decongestants, and antibiotics will help (Fig. 5.2).



• **Fig. 5.2** Sinuses and Associated Structures. (Redrawn after Fricton J, Kroening R, Hathaway K: *TMJ and craniofacial pain: diagnosis and management*, St. Louis, 1988, Medico Dental Media International, Inc.)

Neoplasias and Other Lesions in the Head

Some tumors, aneurysms, and other intracranial disorders can cause pain in the mouth or teeth. The tooth symptoms are generally accompanied by other nerves malfunctioning or by systemic symptoms, such as weight loss, fatigue, and so on. These accompanying symptoms suggest more than a localized tooth problem is occurring. Tumors can also appear in the areas near the nerves of the teeth, which may cause the teeth to be loose or displaced. Proper imaging of the face, jaw, and head is important to evaluate for these problems. Although possible, these problems are very rare, and treatment needs to be directed to the specific problem.

Salivary Gland Dysfunction

Patients with salivary gland dysfunction can experience dental pain through different mechanisms. Pain may occur through referred pain from the glands to the teeth. It may also occur through compromising the health of the teeth and supporting structures and by the absence of the protective saliva. In such cases, a comprehensive evaluation of the salivary glands is needed (Fig. 5.3).

Treatment

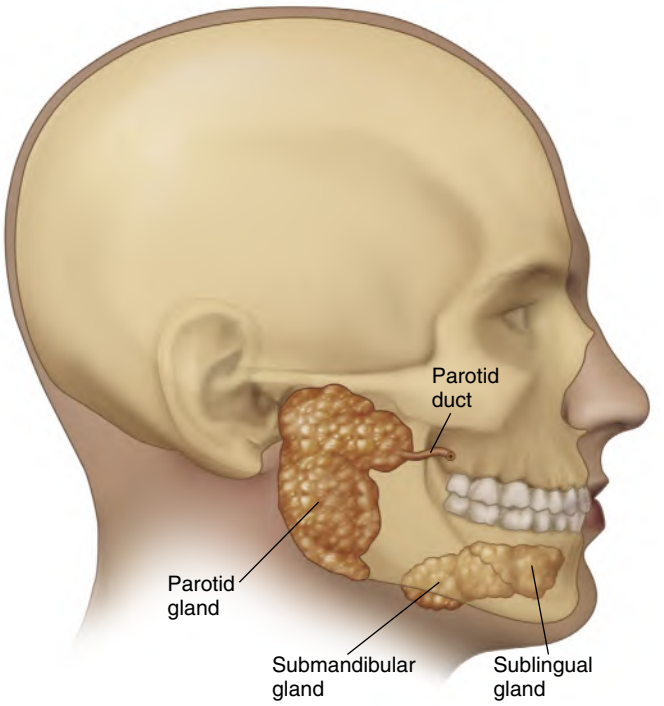
Over the past three decades, significant progress has been made in understanding the pathophysiology of painful conditions.[26]

Treatment of painful conditions of the orofacial region involves identification of the specific illness and correction of the site. If there is no current curative understanding, a management strategy is employed, with the focus being on improving quality of life and decreasing unnecessary treatment and resulting suffering.

Management of painful conditions attempts to employ the most efficient medications and treatments with little or no negative experience, side effect, or misuse potential. This goal can be quite elusive and is the subject of another chapter in this book.

Radiolucencies of Nonpulpal Origin

The radiolucencies that simulate clinical and radiographic appearances of pulpal and/or periapical lesions include normal anatomic structures and developmental entities, odontogenic and nonodontogenic cysts and tumors, osseous pathology, as well as hematolymphoid conditions, malignancies, and related disorders.



• **Fig. 5.3** Salivary Glands. (Redrawn after Fricton J, Kroening R, Hathaway K: *TMJ and craniofacial pain: diagnosis and management*, St. Louis, 1988, Medico Dental Media International, Inc.)

• BOX 5.1 Study Questions

1. Orofacial pain is present in what percent of the population:
   a. 5% to 9%
   b. 10% to 14%
   c. 15% to 40%
   d. More than 50%
2. Pain tolerance is best described by:
   a. The minimum amount of pain a person can perceive
   b. The average amount of discomfort a person reports
   c. The maximum a person will allow
   d. The maximum amount of energy a nerve can generate
3. Oral splints can be helpful in the diagnostic process of toothache:
   a. Only when a TM joint dysfunction is present
   b. When bruxism may be present
   c. When the patient has a history of "TMJ"
   d. When endodontic testing is resulting in inconsistent results
4. Clicking in the TM joint should be suspected:
   a. As always a contributing factor in endodontic diagnosis
   b. As present before endodontic therapy
   c. As likely the primary cause of toothache
   d. If directly associated with the onset of a person's chief complaint
5. "Classic" trigeminal neuralgia
   a. Involves V1
   b. Involves V2
   c. Involves V3
   d. All of the above
6. What does SNOOP refer to?
   a. Concerns regarding family members, opinions on what is wrong
   b. An animal-based contagious disorder
   c. A method to remember key risk factors in diagnosis
   d. Syndrome unrelated to the diagnostic process of facial pain

Normal Anatomic Structures and Developmental Entities

Several normal anatomic landmarks and developmental entities may be confused with true pathologic conditions.

The Mental Foramen

Clinical Features

This foramen bilaterally transmits the sensory and motor fibers of the mental nerve.

Radiographic Features

Despite the fact that the location and appearance of the mental foramen is well-characterized and described as asymmetric unilocular radiolucency between the roots of the premolar teeth, many variations in its position and number have been reported[27] and are best viewed on cone beam computed tomography (CBCT) imaging. Accessory foramina can sometimes appear as multiple, small, well-demarcated, or semi–well-defined radiolucencies, close to and/or juxtaposed to the mental foramen proper.[27,28] The foramen, which is typically located below the apices of the first and second premolars, may occasionally be confused with periapical pathology. Clinicians must use judgment during radiographic evaluation and account for age-related variation in the location of the foramen with respect to the width and height of the alveolar ridge and potential changes in respect to the ridge height (Fig. 5.4, *A* and *B*).

Histology

Histologic confirmation is not required, but it would demonstrate mature neural tissue with perineural sheath, representing the mental nerve. Tooth vitality testing and changing the angulation of radiographs can help in differentiating between the foramen and periapical lesions of pulpal origin.

Nasopalatine Duct Cyst

Also referred to as "incisive canal cyst" (Fig. 5.5), nasopalatine duct cyst (NPDC) is the most common developmental cyst of the maxillofacial region. It constitutes approximately 60% of all nonodontogenic cysts of this region and is derived from nasopalatine ductal epithelial lining remnants.

Clinical Features

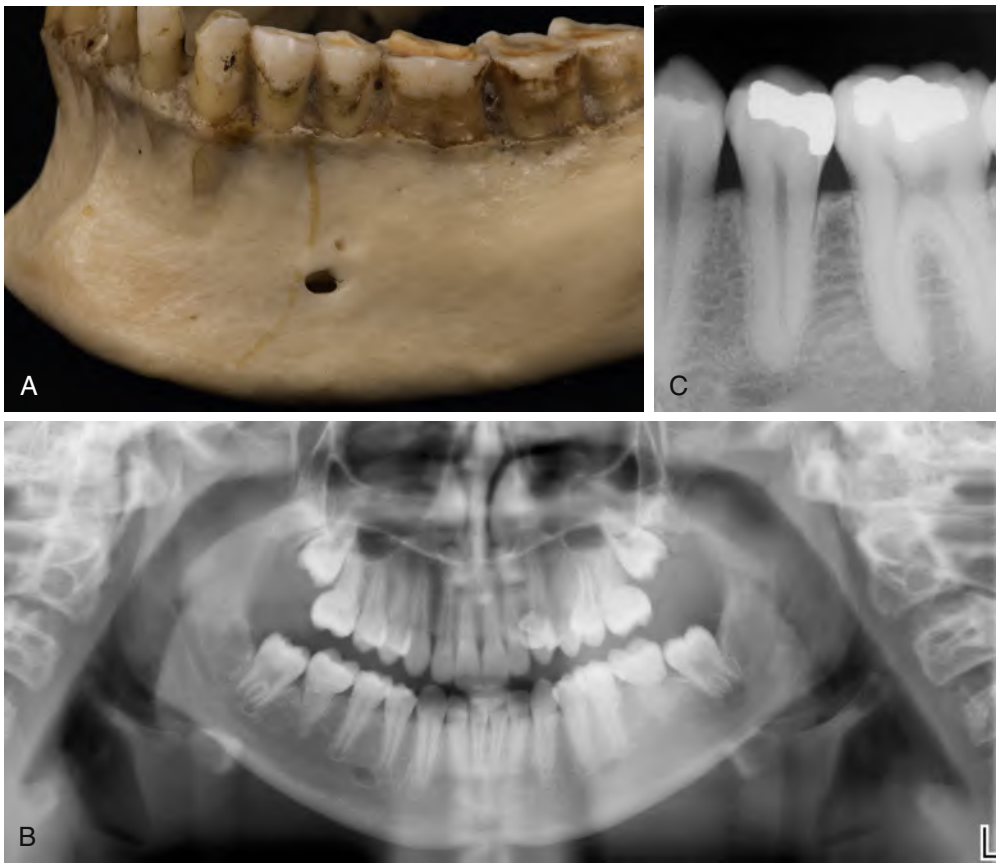
The NPDC may be totally asymptomatic or may produce anterior maxillary palatal swelling, and occasionally a salty taste originating from the anterior palatal region may be experienced.

Radiographic Features

A well-circumscribed, round or heart-shaped radiolucency, identified slightly higher than the interradicular region of vital maxillary central incisors with intact lamina dura, is considered diagnostic of this cyst, which may be also potentially confused with periapical pathology of pulpal origin including a periapical cyst.[29-31]

Histology

Histomorphologic examination should easily distinguish NPDC from a periapical cyst. NPDC typically demonstrates a cystic cavity lined by pseudostratified columnar respiratory-type epithelium, an inflammatory cell infiltrate of variable intensity, and minor salivary gland lobules, compared with a



• **Fig. 5.4** **A**, A cadaver mandible, showing the typical location of the mental foramen between the roots of the mandibular premolars. **B**, The typical radiographic presentation of the mental foramen as a well demarcated radiolucency in the interradicular region of the mandibular premolars. **C**, The mental foramen appearing in close relationship to the mandibular second premolar, mimicking periapical pathosis. (**A** and **C**, Courtesy Dr. Dwight Rice, Loma Linda University; **B**, Courtesy Dr. Ying Wu, OHSU.)

• **Fig. 5.5** Radiographic presentation of nasopalatine duct cyst, demonstrating a heart shaped radiolucency, situated above the roots of viable maxillary central incisors *(yellow arrow)*. The mental foramen could also be seen in the interproximal region of the mandible premolar teeth *(white arrow)*.

radicular cyst, which typically shows nonkeratinized stratified squamous epithelium that is intensely inflamed, hyperplastic, and edematous, and that often contains cholesterol clefts within the cyst wall.[29] A thorough pulp testing, confirming vitality status of the maxillary central incisors, should delineate NPDC from periapical pathosis. Changing the horizontal angulation of a periapical radiograph may further help differentiate NPDC from a radicular cyst, which, compared with NPDC, typically tends to maintain its position around the apex of the maxillary central incisor.

Incisive Foramen

Generally, the identification of an ill-defined 0.6-cm to 0.8-cm radiolucency in the interradicular area of maxillary central incisors should suggest the diagnosis of a normal but widened incisive foramen. The least-invasive technique to differentiate between a NPDC, radicular cyst, and an enlarged incisive foramen is a fine-needle aspiration and examination of the contents of the foramen.[31,32]

Stafne Defect

Stafne defect (SD), also called *Stafne bone cavity* and *static bone defect*, is a rare, asymptomatic developmental mandibular concavity.

Clinical Features

The condition is asymptomatic and is discovered during routine dental examination. It is overwhelmingly prevalent among males. A connection between the lower border of the lesion and inferior border of the mandible exists. This connection and lack of cortical bone leads to the herniation of the submandibular gland into the concavity that is often seen and best viewed on CBCT images.

Radiographic Features

Radiographic features present as a unilateral, homogeneous, well-circumscribed, unilocular radiolucency in the posterior part of the mandibular body, more commonly than in the anterior and ramus areas, below the inferior alveolar canal (Fig. 5.6). Documentation of stability in size with time is characteristic of this entity.

Histology

Fine-needle aspiration of the concavity may demonstrate salivary tissue within or may yield nothing. The stable size and pathognomonic radiographic presentation below the inferior alveolar canal can readily exclude other pathologies, including a residual cyst and aneurysmal bone cyst (ABC), among others.[33,34] Performing tooth vitality tests should also aid in differentiating between SD and true aforementioned pathologies.

Odontogenic and Nonodontogenic Cyst, Tumors, and Related Entities

Several odontogenic and nonodontogenic cysts and tumors can be included under this category of lesions. These include ameloblastoma (Am), calcifying odontogenic cyst (COC), calcifying epithelial odontogenic tumor (CEOT), odontogenic keratocyst (OKC), odontoma, ameloblastic fibro-odontoma (Amfo), ameloblastic fibroma (Amf), dentigerous cyst (DC), odontogenic myxoma, and adenomatoid odontogenic tumor (AOT).[34-39]

• **Fig. 5.6** Stafne bone defect appearing as a well-demarcated radiolucency below the inferior alveolar canal.

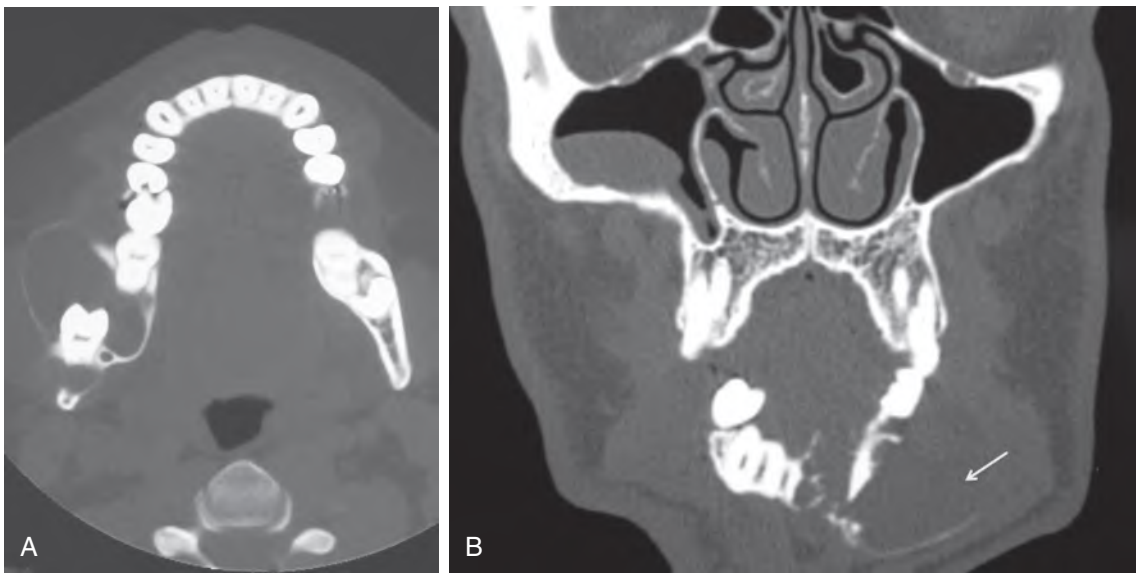
Ameloblastoma

Clinical Features

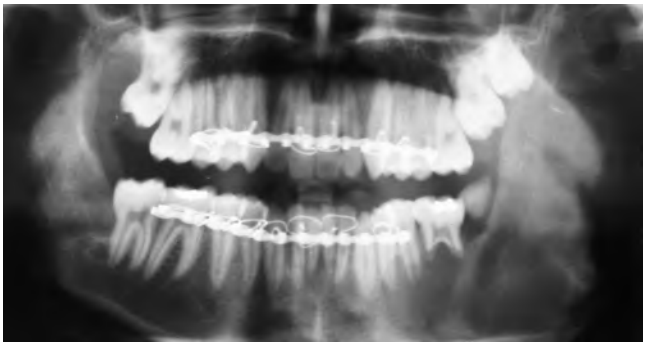
Am is the most common odontogenic tumor (aside from odontoma). It most commonly involves the posterior mandibular body and ramus regions, more than other gnathic areas, as an expansile asymptomatic mass with a potential for buccal and lingual cortical, as well as teeth root resorption. Am occurs in patients of a wide age range, from the third to seventh decades, with a mean age of 40 years old.

Radiographic Features and Differential Diagnosis

The majority of cases present as large, expansile, multilocular radiolucencies, more than unilocular radiolucencies, but may also present as a pericoronal, interradicular, or even a periapical lesion, mimicking radiolucencies of pulpal origin.[34-38] Differentiating Am from the latter from periapical pathology, which can be readily achieved by thorough tooth vitality testing and histologic examination, is of special significance, taking in consideration the locally aggressive nature of the tumor. The identification of a multilocular radiolucency in middle-aged patients, which involves the posterior mandibular area more than it does the maxilla or other gnathic regions, includes three entities in addition to the differential list: Am (Figs. 5.7 and 5.8), OKC, and odontogenic myxoma, whereas the detection of radiographic evidence of radiopacity within the same age spectrum favors CEOT and in a younger age favors the differential diagnosis of COC and Amfo.[40-44] Helpful clues in the diagnosis of odontogenic myxoma are the identification of fine bony trabeculation and septae that transect the radiolucency. Am characteristically does not demonstrate any evidence of hard tissue formation, histologically or radiographically reflecting the development of the tumor from the odontogenic epithelium of developing enamel organ before the processes of induction and cell differentiation taking place.



• **Fig. 5.7** **A**, A sagittal view of computed tomography (CT) scan demonstrating a large pericoronal radiolucency associated with impacted tooth #32. This was enucleated and demonstrated histologically dentigerous cyst. **B**, A large expansile radiolucency in the left mandibular body of a 45-year-old female, causing significant bone destruction, buccal cortical expansion and perforation. Biopsy revealed ameloblastoma. (Case courtesy Dr. Rui Fernandez, Jacksonville, FL.)



• **Fig. 5.8** A large multilocular radiolucency causing significant bone destruction in left mandibular angle and rams of a 50-year-old female. Biopsy showed ameloblastoma.

Histology

Am is characterized by islands, follicles, and cords of odontogenic epithelium showing reverse peripheral palisaded columnar cells and enclosing stellate reticulum-like tissue. The unicystic Am appears confined to cystic lining detected around an impacted tooth, compared with solid tumors where they show a diffuse infiltrative pattern. Variable histomormorphologic patterns have been reported, albeit with no significant prognostic differences. Nevertheless, in the desmoplastic type, a dense collagenous tissue background supports the ameloblastomatous islands, where the tumor displays a mixed radiolucent and opaque pattern and therefore is seldom diagnosed as Am but is rather easily confused for other osseous pathology. In CEOT, a monotonous benign epithelial tissue is seen, accompanied by concentric-type calcification (Liesegang rings) and also characteristically shows amyloid deposition, whereas in COC, ghost cells, many of which calcify, are characteristically seen. Odontogenic myxoma shows mildly vascular, loose, myxoid tissue that is gelatinous in nature due to high hyaluronic acid content and supports stellate-shaped nuclei with tapered ends.[38]

Dentigerous Cyst and Pericoronal Radiolucencies

Clinical Features

DC is the most common inflammatory odontogenic cyst of the gnathic region, and it may present with limited expansion but occasionally may also be associated with marked swelling, tooth displacement, and discomfort. The cyst occurs in a wide age range but most likely to be encountered in middle-aged adults and virtually around any impacted tooth, most specifically around impacted third molars.

Radiographic Features and Differential Diagnosis

DC appears as pericoronal radiolucency around any impacted teeth but is more commonly seen in association with impacted mandibular third molar teeth more often than with others. The differential diagnosis of pericoronal radiolucency in a middle identification of pericoronal radiolucency in adolescent- to middle-aged patients should include the differential diagnosis of DC, unicystic Am, OKC, and myxoma, whereas the detection of radiopacity in the same age range may favor CEOT. In comparison, similar lesions detected in young and adolescent patients may represent COC, Amf, and Amfo. AOT is another rare odontogenic tumor to be included in the differential of pericoronal radiolucencies when radiopacities are detected within. However, this tumor uniquely involves the anterior maxillary canine region more than other regions and is also typically seen in teenagers, 19 years old and under, with a slight female predilection. Thorough vitality teeth testing, coupled with a representative biopsy of the tumors discussed, should readily distinguish the aforementioned entities from periapical pathology of odontogenic origin.

Histology

A biopsy of a DC typically presents as a cystic cavity lined by hyperplastic inflamed and edematous stratified squamous epithelium, which often demonstrates variable histologic patterns, including the presence of cilia, mucous cell prosoplasia, and apocrine-type changes. Further, an inflamed cyst with bleeding may also depict cholesterol clefts with accompanying multinucleated foreign-body-type giant cell reaction. AOT demonstrates benign odontogenic epithelium, arranged in ducts and spherules and may or may not contain amyloid, and is diagnostic for AOT.[38] Occasionally, an apical displacement of DC or even an adenomatoid odontogenic tumor may also mimic periapical pathosis, and therefore vitality testing, in addition to a representative biopsy showing the histomorphologic features of DC and AOT, should confirm the diagnosis and exclude any periapical pathology present, avoiding any unnecessary root canal therapy and/or tooth extractions.

Differential Diagnosis of a Soft Tissue Mass, With or Without Opacity Obstructing the Eruption of a Permanent Tooth

In addition to what has been described in the previous section, the detection of a soft or mixed soft and hard tissue mass that is obstructing the eruption of a permanent tooth would most likely represent one of three entities, namely, an odontoma, Amf, or an Amfo.[34,37,38]

Odontoma

This tumor is considered the most common odontogenic tumor overall, despite the fact that some favor classifying the lesion as a hamartoma rather than a tumor.

Clinical Features

The majority of the cases are discovered incidentally during the investigation of lack of permanent tooth eruption, but rarely, jaw expansion has been also reported.

Radiographic Features

An odontoma may simulate miniature teeth or dense solid radiopaque pattern favoring compound and complex odontoma subtypes, respectively.

Histology

Odontomas basically recapitulate tooth formation, showing enamel, dentin, and cementum and odontogenic epithelial fragments arranged in teethlike figuration haphazardly, defining the compound and complex subtypes respectively.

Ameloblastic Fibroma

Clinical Features

Amf is typically detected in the posterior mandible discovered incidentally during the investigation of lack of the eruption of a permanent tooth in patients 20 years of age and under.

Radiographic Features
Almost half of the cases are associated with unerupted tooth; however, lesions may also demonstrate unilocular or multilocular well-defined radiolucent pattern.

Histology
Amf demonstrates cellular mesenchymal tissue-type proliferation with high resemblance to dental papilla tissue, supporting ameloblastic epithelium with inconspicuous stellate-reticulum component and also typically shows compressed and slender tumor islands.

Ameloblastic Fibro-odontoma

Clinical Features
This tumor is also most likely detected during the investigation of a soft and hard tissue mass that is preventing the eruption of a permanent tooth; however, similar to what has been described earlier, lesions may also cause painless expansion of the jaw.

Radiographic Features
The lesion most likely appears as a soft and hard tissue density overlying an impacted tooth, but it may also appear as a unilocular or a multilocular radiolucency with radiopacity within.

Histology
An identical feature to those described in Amf would be encountered in Amfo, albeit with the addition of an odontoma component, as described earlier,[34,37,38] although the aforementioned tumors are not easily confused with periapical pathosis and do not cause a challenge and diagnosis, especially after histologic confirmation and confirmation of the vitality status of the teeth should readily exclude the possibility of periapical pathology, especially when the soft tissue mass is apically or laterally displaced.

Odontogenic Keratocyst

Clinical Features
OKC is a rare, benign, locally aggressive developmental cyst that is more commonly encountered in the posterior mandibular body and ramus regions in adolescent and middle-aged adults, although it has also rarely been reported in wider age ranges. The cyst is also well-known for its high incidence of postsurgical recurrences.

Radiographic Features
OKC most commonly presents as a multilocular, pear-shaped, interradicular radiolucency, pericoronal radiolucency, or rarely as a periapical lesion associated with vital teeth, which is essential in distinguishing the lesion from periapical pathology, especially when taking into consideration its locally aggressive and destructive growth potential.

Histology
OKC demonstrates a stratified, squamous epithelium of uniform thickness, with a wavy parakeratinized surface, palisaded basal layer, and devoid of rete ridges. The latter feature is often associated with detachment of the cystic epithelium from the underlying connective tissue wall, which may significantly contribute to the recurrence to the characteristic high-recurrence potential. The differential diagnosis of an interradicular radiolucency of the jaw, identified within the context of tested and confirmed vital teeth, should include lateral periodontal cyst, Am, squamous odontogenic tumor (SOT), as well as OKC, among few other entities. It is also essential to differentiate a lateral radicular cyst, which occurs as a result of the lateral canal transmitting inflammation and bacteria to the periodontal ligament, from a true lateral periodontal cyst and OKCs, primarily to initiate appropriate treatment, as well as to avoid unnecessary endodontic treatment. An accurate pulp testing of vitality status should help the clinician exclude that possibility with confidence.

Squamous Odontogenic Tumor

Clinical Features
SOT is a benign, locally infiltrative odontogenic tumor, which arises within the periodontal ligament with a well-known familial transmission, and also shows equal tendency for maxillary and mandibular involvement. It is regarded by many to be a hamartomatous-type growth, rather than a true neoplasm because of its histologic features. The tumor may be asymptomatic or may produce mild painful gingival swelling.

Radiographic Features
SOT may appear as an interradicular radiolucency that pushes the roots of teeth apart or as a well- or an ill-defined radiolucency with or without sclerotic borders.

Histology
SOT demonstrates benign monotonous squamous epithelium that lacks atypia or abnormal morphology and may even produce keratinization, analogous to normal native epithelial tissue.[34,35,39]

Surgical Ciliated Cyst

Clinical Features
This is a true cyst of the maxillary sinus that develops iatrogenically secondary to surgical intervention with involvement of the sinus floor (Fig. 5.9).

Radiographic Features
The most common presentation is that of a well-demarcated unilocular radiolucency present in the sinus and is considered fairly nonspecific and should be excluded from other pathologies, including a residual cyst pushed into the sinus lining.

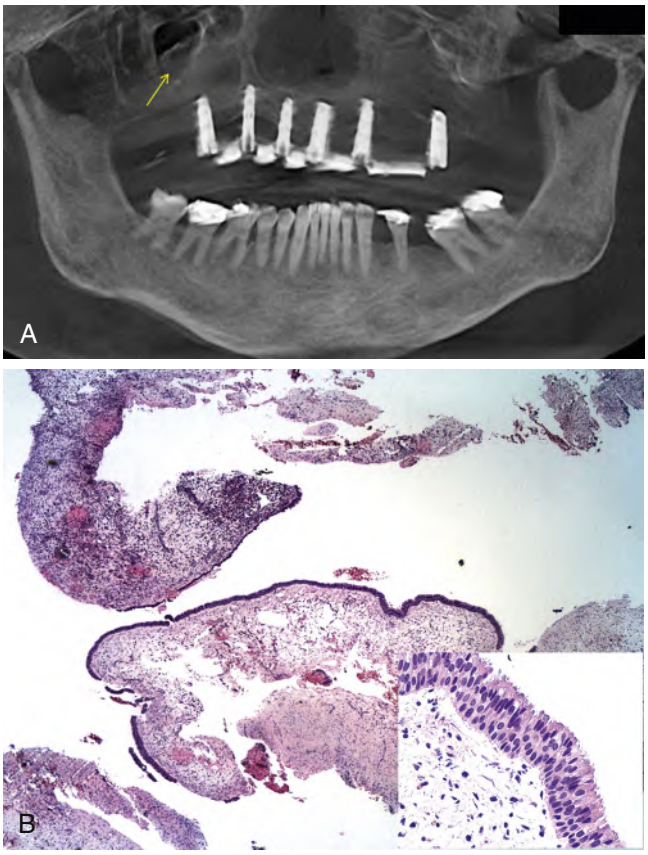
Histology
A cystic cavity lined by respiratory-type epithelium with the cystic wall contiguous with Schneiderian membrane is required to establish the diagnosis and exclude other sinonasal pathology, including those of pulpal origin; however, history of surgical intervention, coupled with the confirmation of vitality tests of the teeth in the region, and histomorphological confirmation can help arrive at the correct diagnosis.[40]

Other nonodontogenic entities, such as traumatic bone cyst (TBC), ABC, and central giant cell lesion (central giant cell granuloma [CGCG]), may be also included in this category of lesions.

Traumatic Bone Cyst

Clinical Features
TBC is a pseudocyst. The cyst is most likely discovered incidentally during radiographic examination of the patient's dentition during the second decade of life.

Radiographic Features
The presentation of an interradicular unilocular radiolucency, showing scalloping between the roots of teeth with the



• **Fig. 5.9** Surgical Ciliated Cyst of the Maxillary Sinus. **A**, A Panto-mogram generated from the cone beam computed tomography (CBCT) study, depicting a well-demarcated radiolucency detected within the R. maxillary sinuses *(yellow arrow)*. **B**, Histologic examination confirmed the diagnosis of surgical ciliated cyst, showing a cystic cavity, lined by respiratory type epithelium and inflamed Schneiderian membrane (hematoxylin and eosin stain, ×20, inset ×40.)

confirmation of the presence of an empty cavity upon surgical exploration is diagnostic and at the same time therapeutic for solitary bone cyst (also known as TBC or hemorrhagic bone cyst).[41] Complete bone repair is expected after surgical manipulation.[40,42]

Histology

Histology, TBC is usually noncontributory. Exploratory surgical manipulation reveals fragments of bony trabeculae, hemorrhage, and/or potential fragments of collagenous soft tissue.

Focal Osteoporotic Bone Marrow Defect

Clinical Features

This defect is a rare, reactive, nonneoplastic condition of the jaw, primarily affecting the posterior mandibular alveolar ridge and is discovered during routine dental examination in middle-aged females more than in others. It is often seen in the area of an extraction or surgical manipulation.

Radiographic Features

This defect most likely presents as an ill-defined radiolucency of variable dimensions, typically present above the inferior alveolar canal, and most often presents with fine lines/trabeculae within the radiolucency.

• **Fig. 5.10** Displaying a well-demarcated radiolucency located in the interradicular region of the posterior mandibular teeth. Histomorphological examination was consistent with aneurysmal bone cyst. (Courtesy Dr. Edwin Leung, Portland, OR.)

Histology

Although histology is very typical and diagnostic, showing red marrow elements, namely megakaryocytes and nucleated red blood cells (RBC), among other elements, histology is required for making the accurate diagnosis, especially because radiographic presentation may overlap with other odontogenic lesions such as Am, CGCG, ABC, as well as metastatic tumors. Further, it should be also distinguished from lesions of endodontic origin, and this clarification could be achieved tentatively with accurate teeth vitality testing and further confirmed with histologic examination.

ABC

Clinical Features

ABC of the maxillofacial region constitutes approximately 2% of all cases involving jaw bones. ABC may be self-limiting or may demonstrate an aggressive behavior with a tendency for marked expansion and post enucleation and curettage local recurrence[43] (Figs. 5.10 and 5.11). The etiopathogenesis of ABC is controversial and may be attributed to trauma, or nonneoplastic reactive malformation, with possible genetic predisposition, namely chromosome translocation t(16;17)(q22;p.13) abnormality.[43]

Radiographic Features

Variable presentations may be encountered, ranging from the well-demarcated unilocular radiolucency to a more common presentation as an expansile multilocular radiolucency that may also present with a lateral ballooning extension and extrusion from the alveolar ridge.

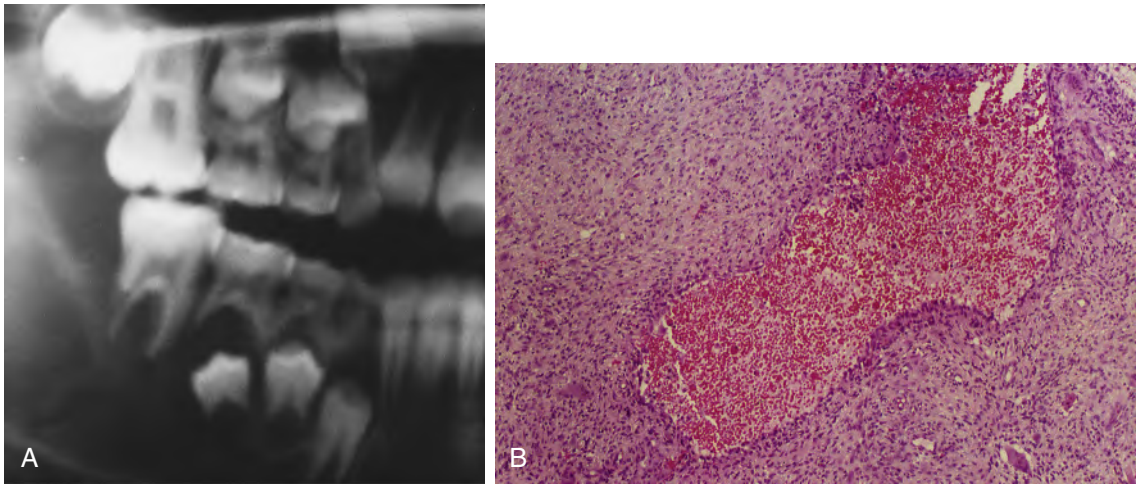
Histology

ABC demonstrates large blood-filled spaces, lacking true endothelial lining and often showing multinucleated giant cells in the vicinity of the blood-filled spaces.

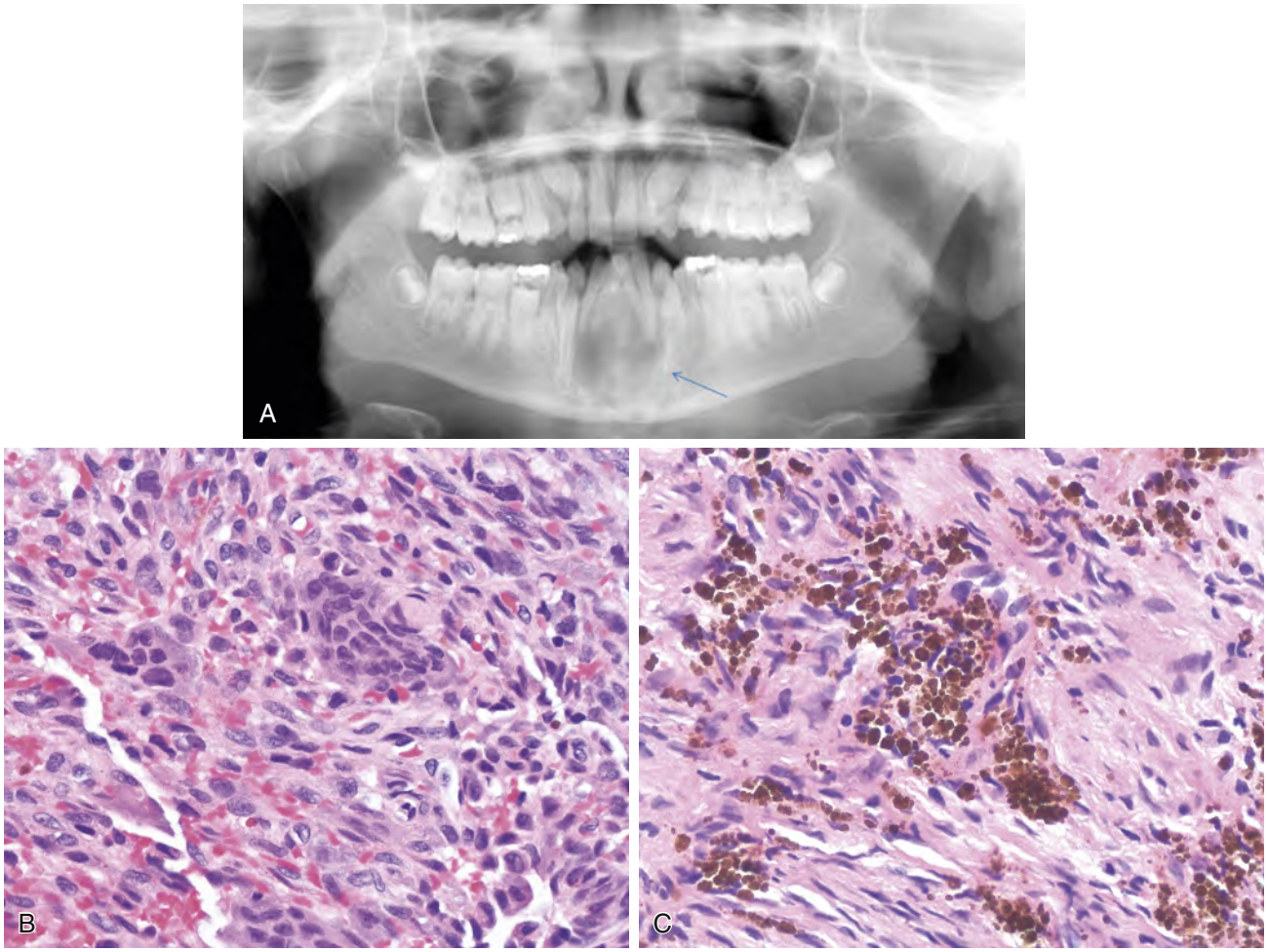
Central Giant Cell Lesion

Clinical Features

CGCG (Figs. 5.12 and 5.13) is a reactive nonneoplastic entity that is somewhat unique to the gnathic–jaw region and tends to involve younger individuals, with a mean age of approximately 25 years old and with predilection for mandibular occurrence.



• **Fig. 5.11** **A**, Demonstrates a large multilocular radiolucency, occupying the entire mandibular ramus. **B,** Histomorphologic examination demonstrated large blood filled pseudocystic spaces, characteristically lacking endothelial lining, diagnostic of aneurysmal bone cyst. (Hematoxylin and eosin stain, original magnification ×20.)



• **Fig. 5.12** **A**, A large expansile radiolucency of the anterior mandible in a 14-year-old male. **B,** Biopsy confirmed the diagnosis of recurrent central giant cell granuloma (CGCG), which was previously enucleated from the same region several months prior. **B**, The lesion demonstrated multinucleated osteoclasts type giant cells supported by a well vascularized cellular stroma. **C**, Hemorrhage with abundant hemosiderin pigment deposition is also evident (**A** and **B,** hematoxylin and eosin stain, original magnification ×40). (**A,** Courtesy Dr. Petrisor, OHSU.)

Radiographic Features

The most common radiologic presentation of central giant cell granuloma is a multilocular radiolucency; however, it may also be unilocular or may be also rarely seen in a periapical location, which may also constitute a diagnostic and management dilemma.[45] However, accurate pulpal status evaluation, coupled with thorough histomorphologic evaluation, should confidently distinguish CGCG and ABC from periapical radiolucencies of pulpal origin.

• **Fig. 5.13** Demonstrating large expansile radiolucency involving the maxillary sinus and left maxilla with considerable facial expansion. Biopsy revealed central giant cell granuloma (CGCG). (Courtesy Dr. Roman Carlos, Guatemala.)

Histology

Histologically, CGCG shows a highly vascularized collagenous stroma that is loaded with monotonous multinucleated osteoclast type giant cells observed. Fine-needle aspiration showing blood with hemosiderin pigmentation is highly suggestive of the diagnosis of ABC or CGCG but most significantly excludes other intraosseous true vascular lesions—specifically, high flow hemangiomas and arteriovenous malformation.[46]

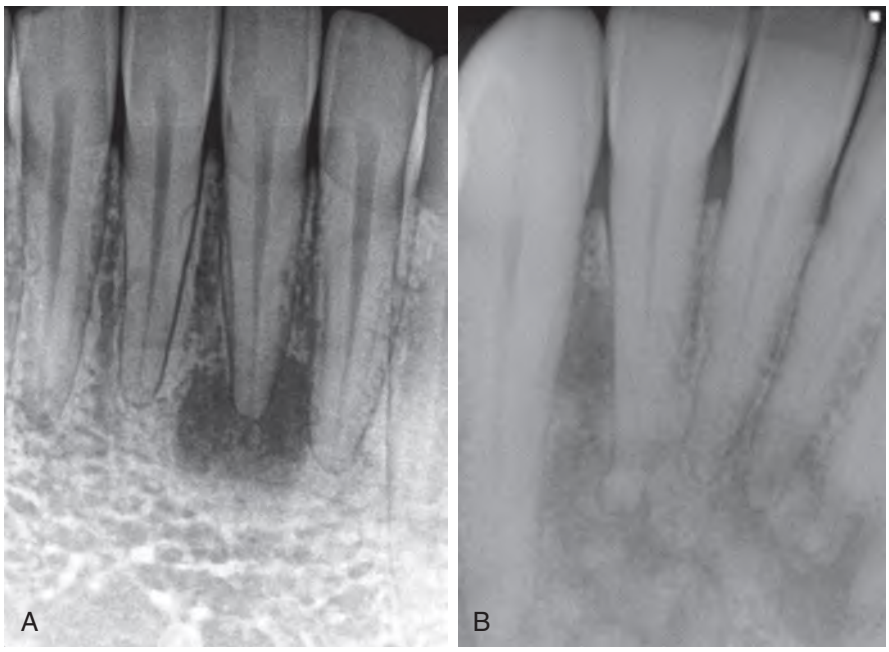
Osseous Pathology

Bone pathology often presents with diverse radiographic manifestations, which in turn translate to a large list of entities to be included in the differential diagnosis with significant overlap in clinical and radiographic presentation.

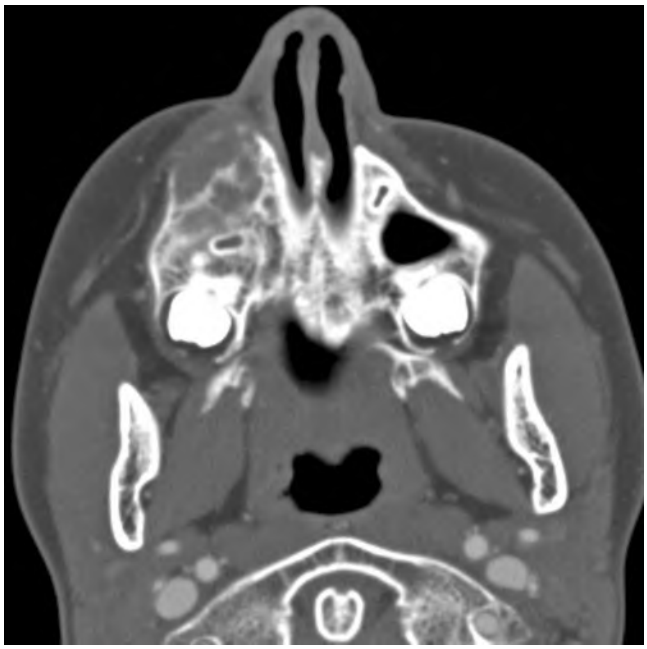
Benign Fibro-osseous Lesions of the Maxillofacial and Gnathic Region

Clinical Features

Benign fibro-osseous lesions of the maxillofacial and gnathic region (BFOL) is a classic example of such diverse entities. They can be separated into one of three categories: (1) fibrous dysplasia (FD), which is considered by some to be a developmental type with neoplastic potential and by others to be a neoplastic condition from the very beginning, based on the identification of the *GNAS* gene mutation in these lesions and is characterized by a diffuse, ill-defined expansion of bone in younger individuals during adolescent years and constitutes less than 10% of all benign bone tumors; (2) ossifying fibroma (also known as *cementifying and ossifying fibroma*, or *CCOF*) (Fig. 5.14), which is a benign neoplastic



• **Fig. 5.14** **A**, A periapical radiograph which reveals the presence of an evolving periapical cementoosseous dysplasia, seen in association with vital mandibular central incisors. **B**, A mixed stage of periapical cemento-osseous dysplasia, with evidence of radiopacity, evolving at the edges of the radiolucent periapical lesion. (Courtesy Dr. Ying Wu, OHSU.)



• **Fig. 5.15** Sagittal computed tomography (CT) scan demonstrating a large expansile mixed, radiolucent and radiopaque mass effacing the right maxillary sinus. Biopsy demonstrated central cementifying and ossifying fibroma. (Courtesy Dr. Patrick Louis, UAB.)

condition that is unique to the maxillofacial region. CCOF occurs in patients who are approximately10 years older than those seen with FD. It is also more common in females and also shows prevalence toward the posterior mandible; and (3) cemento-osseous dysplasias, representing a group of reactive nonneoplastic conditions. The last category, cemento-osseous dysplasia, is of special interest here because it is exclusive to the gnathic area and exists as focal cemento-osseous dysplasia, florid cemento-osseous dysplasia, and periapical cemento-osseous dysplasia, where the latter is of special significance because it could be easily confused with periapical pathology of endodontic origin.

Radiographic Features

FD typically presents as an ill-defined mixed radiolucent or radiolucent/radiopaque lesion which displays a ground-glass radiographic pattern which also demonstrates obliteration of the periodontal ligament spaces. In comparison, CCOF characteristically shows a well-defined radiolucent or a radiolucent/radiopaque mass that is also described to be easily shelled-out in one piece by the surgeon during its removal. Osseous dysplasia, on the other hand, presents initially with well-defined radiolucencies of the apical portion of vital mandibular central incisors with gradual production of radiopacities at the edges of the radiolucencies (Fig. 5.15). Furthermore, it typically involves the periapical region of vital mandibular central incisors and may therefore be mistaken for periapical pathology if pulpal vitality testing is not conducted, which leads to unnecessary endodontic treatment.[38,47-49] One exception to the well-demarcated routine presentation of CCOF is observed in the "juvenile cementifying-ossifying fibroma" subtype, which tends to be less well-demarcated radiographically, more aggressive clinically, and having higher tendency for local recurrence and a more cellular osteoblastic rimming with osteoid production on microscopic examination, which may be alarming to the untrained observer.[34,49]

Osteoblastoma

Clinical Features

Osteoblastoma (OB) is another rare benign bone tumor with known predilection for the maxillofacial and head and neck bones, especially the mandible.

Radiographic Features

OB may appear either as a well-defined or an ill-defined radiolucency, with or without radiopaque pattern, depending on the time the lesion is discovered. It may also rarely mimic lesions of endodontic origin but confirmation of the vital status of the adjacent teeth should easily delineate the lesion from periapical pathology.[50]

Histology

OB demonstrates osteoid and woven-bone production that also typically exhibits well-formed prominent and plump osteoblastic rimming, supported by dense well-vascularized fibrocollagenous background.[51]

Although rare, selective malignant entities may also be included here, specifically gnathic osteogenic and chondrogenic sarcomas.

Osteogenic Sarcoma

Clinical Features

Osteogenic sarcoma (OS) of the gnathic region accounts for 7% to 13% of all osteosarcomas with equal distribution between the maxilla and mandible. The tumor is slightly more commonly seen in males during the third and fourth decades of life. A painful swelling is typically seen and is often accompanied by paresthesia, loosening of teeth, as well as nasal obstruction and epistaxis in maxillary tumors.

Radiographic Features

OS is radiographically characterized by large destructive "moth-eaten" lytic or opaque lesions, accompanied by widening of the periodontal ligaments around the teeth in the involved region and a distinct sunray pattern, which is directly attributed to osteoblastic activity that is also often observed on the surfaces of these tumors.

Histology

Malignant osteoid, cartilage and/or fibrous tissue, or a combination of all of the aforementioned tissues may be detected. The bone is typically laid down in a lacelike pattern within this tumor.

Chondrogenic Sarcoma

Significant overlap in the clinical features and radiographic features between chondrogenic sarcoma (CS) and OS may be seen; however, CS of the maxillofacial and gnathic region is far rarer compared with OS. Additionally, pain is more characteristic of OS, whereas bone expansion, which may or may not be symptomatic, favors chondrosarcoma.

Radiographic Features

To reiterate, overlap in radiographic presentation of OS and CS may be seen, where both lesions can demonstrate widening of the periodontal ligament (PDL), spiky roots resorption, and lytic "moth-eaten" and destructive lesions. Further, chondrosarcoma may occasionally present as a multilocular lesion and thus would be potentially mistaken for an odontogenic tumor or cyst, or even other primary intraosseous pathology. Additionally, both entities may also rarely present as radiolucencies in the apical regions and

thus may be also mistaken for periapical pathology. The presence of pain may further direct the clinician toward the diagnosis of periapical pathology of pulpal origin; however, accurate pulpal vitality assessment confirming vitality status of the teeth, coupled with histomorphologic examination confirmation of malignancies, can help the clinician reach an accurate diagnosis.

Histology

Lesions show malignant cartilaginous tissue with variation in histomorphology, including mesenchymal chondrosarcoma that demonstrates a small round cell tumor component within.

Ewing's Sarcoma

Ewing's sarcoma (ES) is a rare tumor of neuroectodermal origin that is considered rare in the head and neck region. Jaw involvement is extremely rare, less than 3% of cases seen involving this region; however, mandibular involvement is more common in comparison with involvement of maxilla. The tumor also shows prevalence for children and young adult Caucasian males.[45,52-54]

Clinical Features

The tumor typically exhibits an aggressive rapidly expanding and painful mass with high probability of metastasis, which is often discovered at the time of diagnosis.

Radiographic Features

The tumor exhibits a large destructive lytic lesion with buccal and/or lingual cortical erosion. Less commonly, lesions may also appear as a multilocular radiolucency and also have a tendency to periosteal reaction (onion skinning radiographic pattern). Although rare, reports of ES mimicking periapical pathology, including odontogenic infections, are also well-documented; however, a thorough vitality testing of the teeth coupled with representative histomorphologic confirmation should help clinicians arrive at the right diagnosis. Additionally, tumors involving the maxillary sinus and alveolar process may initially present with tooth pain and may even devitalize teeth, which results in undesirable delay in establishing the accurate diagnosis, as well as unnecessary endodontic treatment.[45] However, histomorphologic confirmation, the confirmation of tooth histology, and vitality status may allow clinicians to confidently exclude periapical pathosis. [45,52-54,]

Histology

ES demonstrates a cellular proliferation of small, round, blue cell with a well-demarcated nuclear contour and inconspicuous cytoplasm. A brisk mitotic activity and hyperproliferative index are often seen. The tumor cells demonstrate positive staining with vimentin, and desmin and a distinct membranous staining with anti-CD99. Other immunohistochemistry stains may also be performed to exclude other small round cell tumors including lymphoma. Chromosomal analysis, demonstrating t(11;22) gene rearrangement performed by FISH (fluorescence in situ hybridization) is also considered confirmatory and diagnostic.

Hematolymphoid Conditions, Malignancies, and Related Disorders

The involvement of the head and neck region with metabolic and neoplastic hematolymphoid conditions is well established.

Sickle Cell Anemia

Sickle cell anemia (SCA) is the most common inherited hemoglobinopathy worldwide, characterized by the production of abnormal hemoglobin (HgS),

Clinical Features

Patients characteristically have anemia, RBC deformity, and hemolysis; they also experience pain, including bone pain and necrosis, among other complications.

Radiographic Manifestations

SCA typically produces widening of the marrow spaces with course trabecular bone pattern, which may also be mistaken for periapical pathology, accentuated by the presence of pulpal necrosis that arises secondarily in these patients.[45,47-54,55-57] Detailed medical, social, and family history, as well as thorough laboratory and genetic workup, should definitely exclude lesions of endodontic origin.

Lymphoma

Lymphoma is a malignancy of the immune system cells, which could be roughly divided into Hodgkin's lymphoma, malignancy derived from B-cell lineage and non-Hodgkin's types, and those with T-, B-, or plasmablastic cell lineages. Approximately 40% of the non-Hodgkin's lymphomas are encountered in extranodal sites, and of these, approximately 2% to 3% involve the oral cavity and the gnathic bones with jaw bones representing the most common location of osseous lymphomas in the craniofacial skeleton.[58-61]

Clinical Features

Jaw involvement with this potentially aggressive and even deadly malignancy typically presents with marked bone destruction and expansion.

Radiographic Features

The majority of the cases present as large radiolucent lesions with significant bone resorption and destruction and are often accompanied by cervical lymphadenopathy; however, it may also rarely mimic periapical pathology.[60,61]

Histology

Although the majority of cases represent large B-cell lymphoma, the whole spectrum of hematolymphoid malignancies, including those of B-cell, T-cell, and plasmablastic cell lineage, may be seen. A diffuse atypical lymphoid infiltrate showing brisk mitotic activity and a variable amount of cytoplasm, depending on the tumor subtype and phenotype, may be observed. Subclassifying lymphomas requires a battery of immunohistochemistry staining in addition to other studies such as chromosomal analysis, flow cytometry, and others. Thorough vitality teeth testing, coupled with histomorphologic confirmation and immunohistochemistry staining, would aid in reaching an accurate diagnosis with definitive disease phenotyping.

Langerhan Cell Disease

Clinical Features

The vast majority of Langerhan cell disease (LCD) patients do not exceed 20 years of age, and the disease can be separated, in descending-age predilection, into three categories: eosinophilic

granuloma (localized bone involvement); Hand–Schüller–Christian disease, characterized by the triad of exophthalmos, diabetes, and bone lesions of LCD; and Letterer–Siwe syndrome, characterized by cutaneous involvement with the disease.

Radiographic Features

Jaw involvement often presents with distinguished radiographic manifestations, displaying punched-out radiolucencies in the jaw, skull, and other bones, that lack sclerotic borders and may show the so-called "teeth floating in air" phenomenon mimicking an advanced periodontal disease.

Histology

LCD is characterized by an admixture of histiocytes that often exhibit grooved nuclei, a prominent number of eosinophils, and a distinct population of reactive plasma cells in the supporting connective tissue background. Positive immune-histochemical staining for anti S-100 protein, CD1a/Langerin are considered diagnostic and confirmatory of the diagnosis.[62] Although rare, LCD may also mimic periapical pathosis, and therefore a thorough tooth vitality testing in addition to histologic sampling showing features described previously may be required to confirm the diagnosis.

Multiple Myeloma

Multiple myeloma (MM) is an aggressive neoplasm of plasma cell origin characterized by proliferation of histologically atypical plasma cells that also characteristically display monoclonal plasma cell infiltrate.

Clinical Features

The disease is most often seen in adults, with age ranges between the sixth and seventh decades of life. It is also characterized by bone pain, most likely experienced in the spine, but could be also experienced with any bone involved, including the jaws. Additionally, patients with advanced disease may also suffer from bone fractures and repeated episodes of osteomyelitis.

Radiographic Features

In comparison with LCD, the identification of punched-out radiolucencies in the jaw or skull, which also may be accompanied by large lytic and destructive lesions of the jaw with a spiky pattern of teeth root resorption in older patients (age range is sixth to seventh decades),[34,62] is considered diagnostic of MM.[63-65] Generally, plasma cell dyscrasia may present as solitary jaw or sinus lesions or disseminated disease, and in the former, monoclonal and polyclonal plasma cell infiltrate may be detected.

Histology

A thorough histomorphologic examination, depicting an atypical plasma cell infiltrate, coupled with the immunohistochemistry assessment for kappa and lambda clonality studies should be confirmatory of the diagnosis. Rarely, the lytic lesions of MM may also mimic periapical pathosis, which may be further complicated by the fact that these lesions have been also found to devitalize teeth in long-term disease and which may further delay the diagnosis and lead to unnecessary endodontic treatment. However, the identification of malignant monoclonal plasma cell population in large painful lytic lesions of the jaw, spine, or skull is characteristic of MM. Additionally, patients also typically present with hypercalcemia and markedly elevated levels of monoclonal immunoglobulins (Bence Jones protein) and may also demonstrate the deposition of amyloid protein in the involved bones. The aforementioned features may collectively distinguish MM from periapical pathology of endodontic origin.[63-65] Despite the aggressive therapeutic regimens applied in its management, and the fact that up to 60% of patients may experience remission, the disease remains incurable, with a guarded prognosis and an overall median survival rate ranging from 13 to 31 months, depending on the overall underlying health status of the patient.[65]

Acknowledgment

The author acknowledges the help of Mrs. Carmelita Metz and Mrs. Debbi Schwarm administrative assistants, Oregon Health and Sciences University (OHSU), School of Dentistry for the help and support in the preparation of the manuscript.

• BOX 5.2 Study Questions

7. The mental foramen is typically situated between the first and second mandibular molars.
   a. True
   b. False
8. Nasopalatine duct cyst (NPDC) typically presents as heart-shaped radiolucency between the maxillary central incisors.
   a. True
   b. False
9. Am recapitulates the process of odontogenesis before epithelial/mesenchymal induction.
   a. True
   b. False
10. Which of the following is true regarding malignant myeloma (MM)?
    a. It is a disease of childhood.
    b. It is histologically characterized by eosinophils and histiocytes.
    c. Serologically, patients demonstrate high immunoglobulin production.
11. The majority of jaw lymphomas are of the large B-cell type.
    a. True
    b. False
12. What is the most common radiographic presentation of sickle cell anemia (SCA) in the mandible?
    a. Widened marrow spaces
    b. Sunray pattern
    c. Punched out radiolucencies
13. Which of the following does not typically present as a multilocular radiolucency?
    a. Ameloblastoma (Am)
    b. Odontogenic keratocyst (OKC)
    c. Traumatic bone cyst
14. Which of the following entities proves to be devoid of any content upon surgical exploration?
    a. Traumatic bone cyst (TBC)
    b. Odontogenic keratocyst (OKC)
    c. Surgical ciliated cyst
15. Of the following entities, which has a well-known familial transmission?
    a. Ameloblastoma (Am)
    b. Ameloblastic fibroma (Amf)
    c. Squamous odontogenic tumor (SOT)
16. All of the following are true regarding the radiographic features of Langerhan cell histiocytosis except one. Which is the exception?
    a. Often presents with teeth hanging in air pattern
    b. Often presents with punched-out radiolucencies
    c. Often present as multiple radiopaque jaw masses

ANSWERS

Answer Box 5

1 c. 15% to 40%
2 c. The maximum a person will allow
3 d. When endodontic testing is resulting in inconsistent results
4 d. If directly associated with the onset of a person's chief complaint
5 d. All of the above
6 c. A method to remember key risk factors in diagnosis
7 b. False
8 a. True
9 a. True
10 c. Serologically, patients demonstrate high immunoglobulin production.
11 a. True
12 a. Widened marrow spaces
13 c. Traumatic bone cyst
14 a. TBC.
15 c. SOT
16 c. Often present as multiple radiopaque jaw masses

References

1. Dworkin SF, LeResche L: Research diagnostic criteria for temporomandibular disorders: review, criteria, examinations and specifications, critique, *J Craniomandib Disord* 6:301–355. 1992.
2. Okeson JP, editor: *Orofacial pain: guidelines for assessment, classification, and management.* Carol Stream, IL, 1996, Quintessence.
3. Bell WE: *Orofacial pains: classification, diagnosis, management,* ed 4, Chicago, 1989, Year Book Medical Publishers.
4. Vena DA, Collie D, Wu H, et al: Prevalence of persistent pain 3 to 5 years post primary root canal therapy and its impact on oral health-related quality of life: PEARL network findings, *J Endod* 40(12):1917–1921, 2014.
5. Nixdorf DR, Law AS, John MT, et al: Differential diagnosis for persistent pain after root canal treatment: a study in the national dental practice-based research network, *J Endod* 41(4):457–463, 2015.
6. Linn J, Trantor I, Teo N, et al: The differential diagnosis of toothache from other orofacial pains in clinical practice, *Aust Dent J* 52(1 Suppl):S100–104, 2007.
7. Molina OF, Huber Simião BR, Yukio Hassumi M, et al: Headaches and pain referred to the teeth: frequency and potential neurophysiologic mechanisms, *Rev Sul-Brasileira Odontol (RSBO)* 12(2):151–159, 2015.
8. Wright EF: Referred craniofacial pain patterns in patients with temporomandibular disorder, *J Am Dent Assoc* 131(9):1307–1315, 2000.
9. Brattberg G, Thorslund M, Wikman A: The prevalence of pain in a general population. The results of a postal survey in a county of Sweden, *Pain* 37:215–222, 1989.
10. Von Koorff M, Dworkin SF, LeResche L, Kruger A: An epidemiologic comparison of pain complaints, *Pain* 32:173–183, 1988.
11. Lipton JA, Ship JA, Larach-Robinson D: Estimated prevalence and distribution of reported orofacial pain in the United States, *J Am Dent Assoc* 124:115–121, 1993.
12. Maixner W, Diatchenko L, Dubner R, et al: Orofacial pain prospective evaluation and risk assessment study – The OPPERA Study, *J Pain* 12(11 Suppl): T4–T11, 2011.
13. Merskey H, Bogduk N, editors: *Classification of chronic pain: descriptions of chronic pain syndrome and definitions of pain terms,* Seattle, 1994, IASP Press, pp 59–76.
14. de Leeuw R, Klasser G: *Orofacial pain guidelines for assessment, diagnosis and management,* ed 5, Quintessence, 2013.
15. Pertes RA, Heir GM: Temporomandibular disorders and orofacial pain, *Dent Clin North Am* 35:123–140, 1991.
16. Pertes RA, Gross SG, editors: *Clinical management of temporomandibular disorders and orofacial pain,* Carol Stream, IL, 1995, Quintessence.
17. Travell JG, Simon DG: *Myofascial pain and dysfunction: the trigger point manual,* Baltimore, 1999, Williams & Wilkins.
18. Fricton J, Eli B, Gupta A, Johnson N. Preventing chronic pain after acute jaw sprain or strain. *J Am Dent Assoc,* 147(12):979–986, 2016.
19. Okeson JP: Pains of muscle origin. In *Bell's orofacial pains,* ed 6, Chicago, 2005, Quintessence, pp. 287–328.
20. Long D: Contemporary diagnosis and management of pain, ed 2, Newtown, PA, 2001, Handbooks in Health Care.
21. Chapman CR, Syrjala KL: Measurement of pain. In Bonica JJ, editor: *The management of pain* (vol 1). ed 2, Philadelphia, 1990, Lea & Febiger, pp. 580–594.
22. Fromm GH, Graff-Radford SB, Terrence CF, Sweet WH: Pre-trigeminal neuralgia, *Neurology*, 40(10):1493–1495, 1990.
23. IHS Headache classification committee of the International Headache Society. *Classification and diagnosis criteria for headache disorders, cranial neuralgias and facial pain,* ed 2, *Cephalgia* (Suppl 1):1–160, 2004.
24. Treede, RD, et al: Neuropathic pain: redefinition and a grading system for clinical and research purposes, *Neurology* 70(18):1630–1635, 2008.
25. Piovesan EJ, Kowacs PA, Tatsui CE, et al: Referred pain after painful stimulation of the greater occipital nerve in humans: evidence of convergence of cervical afferences on trigeminal nuclei, *Cephalgia* 21:107–109, 2001.
26. American Pain Society Quality Assurance Standards for Relief of Acute Pain and Cancer Pain. In *Proceedings of the 6th World Congress on Pain*, New York, 1991, Elsevier.
27. Goyushov S, Tözüm MD, Tözüm TF: Accessory mental/buccal foramina: case report and review of literature, *Implant Dent* 26(5):796–801, 2017.
28. Rahpeyma A, Khajehahmadi S: Accessory mental foramen and maxillofacial surgery, *J Craniofac Surg* 1–2, 2017 (Volume publish ahead of print).
29. Barros CCDS, Santos HBP, Cavalcante IL, et al: Clinical and histopathological features of nasopalatine duct cyst: a 47-year retrospective study and review of current concepts, *J Craniomaxillofac Surg* 46:264–268, 2018.
30. Chapman MN, Nadgir RN, Akman AS, et al: Periapical lucency around the tooth: radiologic evaluation and differential diagnosis, *Radiographics* 33:15–32, 2013.
31. Abrams AM, Howell FV, Bullock WK: Nasopalatine cysts, *Oral Surg Oral Med Oral Pathol* 16:306–332, 1963.
32. Allard RH, van der Kwast WA, van der Waal I: Nasopalatine duct cyst. Review of the literature and report of 22 cases, *Int J Oral Surg* 10:447–461, 1981.
33. Assaf AT, Solaty M, Zrnc TA, et al: Prevalence of Stafne's bone cavity—retrospective analysis of 14,005 panoramic views, *In Vivo* 28:1159–1164, 2014.
34. Wright KR, Rice DD, Luo, Z: Chapter 1: Anatomical zones in endodontic surgery. In Torabinejad M, Rubinstein R, editors: *The art and science of contemporary surgical endodontics*, Philadelphia, 2016, Quintessence, pp. 1–17.
35. WHO: *World Health Organization classification of head and neck tumours,* ed 4, Lyon, 2017, IARC Press.
36. Dhanuthai K, Chantarangsu S, Rojanawatsirivej S, et al: Ameloblastoma: a multicentric study, *Oral Surg Oral Med Oral Pathol Oral Radiol* 13(6):782–788, 2012.
37. Zouhary KJ, Said-Al-Naief N, Waite PD: Ameloblastic fibro-odontoma: expansile mixed radiolucent lesion in the posterior maxilla: a case report, *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 106(4):15–21, 2008.
38. Said-Al-Naief N: Odontogenic tumors for general pathologists, *Review Adv Exp Med Biol* 563:148–164, 2005.
39. Chrcanovic BR, Gomez RS: Squamous odontogenic tumor and squamous odontogenic tumor-like proliferations in odontogenic cysts: an updated analysis of 170 cases reported in the literature, *J Craniomaxillofac Surg* 26(17):3045–3059, 2017.

40. Yamamoto S, Maeda K, Kouchi I, et al: Surgical ciliated cyst following maxillary sinus floor augmentation: a case report, *J Oral Implantol* 43:360–336, 2017.
41. Surej Kumar LK, Kurien N, Thaha KA: Traumatic bone cyst of mandible, *J Maxillofac Oral Surg* 14(2):466–469, 2015.
42. Hs CB, Rai BD, Nair MA, Astekar MS: Simple bone cyst of mandible mimicking periapical cyst, *Clin Pract* 2(3):59, 2012.
43. Urs AB, Augustine J, Chawla H, Aneurysmal bone cyst of the jaws: clinico-pathological study, *J Maxillofac Oral Surg* 13(4):458–463, 2014.
44. Regezi JA: Odontogenic cysts, odontogenic tumors, fibro-osseous and giant cell lesions of the jaws, *Mod Pathol* 15(3):331–341, 2002.
45. Bornstein MM, von Arx T, Altermatt HJ: Loss of pulp sensitivity and pain as the first symptoms of a Ewing's sarcoma in the right maxillary sinus and alveolar process: report of a case, *J Endod* 34(12):1549–1553, 2008.
46. Mohammedi H, Said-al-Naief N, Hafez LB: Arteriovenous malformation of the mandible: report of a case with a note on the differential diagnosis, *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 84(3):286–289, 1997.
47. Kontogiannis TG, Tosios KI, Kerezoudis NP, et al: Periapical lesions are not always a sequelae of pulpal necrosis: a retrospective study of 1521 biopsies, *Int Endod J* 48(1):68–73, 2015.
48. Daviet-Noual V, Ejeil AL, Gossiome C, et al: Differentiating early stage florid osseous dysplasia from periapical endodontic lesions: a radiological-based diagnostic algorithm, *BMC Oral Health* 17(1):161, 2017.
49. Spatafore CM, Griffin Jr JA, Keyes GG, et al: Periapical biopsy report: an analysis over a 10-year period, *J Endod* 16(5):239–241, 1990.
50. Ribera MJ: Osteoblastoma in the anterior maxilla mimicking periapical pathosis of odontogenic origin, *J Endod* 22(3):142–146, 1996.
51. Burić N, Jovanović G, Tijanić M: Endosteal (central) osteochondroma of the mandibular body, *Oral Surg Oral Med Oral Pathol Oral Radiol* 115(4):e20–22, 2013.
52. Bhadage CJ, Vaishampayan S, Kolhe S, Umarji H: Osteosarcoma of the mandible mimicking an odontogenic abscess: a case report and review of the literature, *Dent Update* 40(3):216–218 & 221, 2013.
53. Yamamoto-Silva FP, Silva BSF, Batista AC, et al: Chondroblastic osteosarcoma mimicking periapical abscess, *J Appl Oral Sci* 25(4):455–461, 2017.
54. Bueno MR, De Carvalhosa AA, De Souza Castro PH, et al: Mesenchymal chondrosarcoma mimicking apical periodontitis, *J Endod* 34(11):1415–1419, 2008.
55. Neville B, Damm DD, Allen C, Chi, A: *Oral and maxillofacial pathology,* ed 4, St. Louis, 2015, Elsevier.
56. Souza S, de Carvalho H, Costa C, Thomaz E: Association of sickle cell hemoglobinopathies with dental and jaw bone abnormalities, *Oral Dis* 20(3):393–403, 2018.
57. Andrews CH, England MC Jr, Kemp WB: Sickle cell anemia: an etiological factor in pulpal necrosis, *J Endod* 9(6):249–252, 1983.
58. Koivisto T, Bowles WR, Magajna WA, Rohrer M: Malignant lymphoma in maxilla with cystic involvement: a case report, *J Endod* 39(7):935–938, 2013.
59. Paes FM, Kalkanis DG, Sideras PA, et al: FDG PET/CT of extranodal involvement in non-Hodgkin lymphoma and Hodgkin disease, *Radiographics* 30:269–291, 2010.
60. Pereira DL, Fernandes DT, Santos-Silva AR, et al: Intraosseous non-Hodgkin lymphoma mimicking a periapical lesion, *J Endod* 10:1738–1742, 2015.
61. Wong GB, Spadafora S, Barbon N, Caputo M: Primary extranodal B-cell non-Hodgkin lymphoma mimicking an endodontic lesion: report of 2 cases, *J Can Dent Assoc* 79:d93, 2013.
62. Pinkus GS, Lones MA, Matsumura F, et al: Langerhans cell histiocytosis immunohistochemical expression of fascin, a dendritic cell marker, *Am J Clin Pathol* 118(3):335–343, 2002.
63. Dhanrajani PJ, Abdulkarim SA: Multiple myeloma presenting as a periapical lesion in the mandible, *Indian J Dent Res* 8(2):58–61, 1997.
64. Witt C, Borges AC, Klein K, Neumann HJ: Radiographic manifestations of multiple myeloma in the mandible: a retrospective study of 77 patients, *J Oral Maxillofac Surg* 55(5):450–453, 1997.
65. Tamura H, Zhonghua X, Ye X, Za Z: Immunopathogenesis and immunotherapy of multiple myeloma, *Int J Hematol* 107(3):27–285, 2018.

Video 5.0: Endodontic–Periodontic Introduction
Video 5.1: Periodontal Defects of Pulpal Origin
Video 5.2: Periodontal Defects of Periodontic Origin