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Review Article **Dentistry**

Remains Cystic Enucleation with Peripheral Osteotomy Sufficient Inciting Factors, Treatment and Pathogenesis for OKCs of the Jaws: A New Appraisal

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Abstract

Odontogenic keratocysts (OKCs) are benign yet locally aggressive cystic lesions derived from the dental lamina or its remnants. Predominantly found in the mandible, OKCs often present as asymptomatic radiolucent lesions, occasionally causing symptoms such as swelling and pain. Radiographically, they appear as well-defined, unilocular or multilocular lesions with smooth borders. Microscopically, OKCs feature a thin, parakeratinized epithelium with a high mitotic index, contributing to their aggressive behavior. Treatment typically involves surgical enucleation or resection, with careful attention to ensuring complete removal to minimize recurrence. However, recurrence rates remain relatively high, ranging from 25% to 60%, necessitating close postoperative monitoring, particularly in cases associated with nevoid basal cell carcinoma syndrome. A multidisciplinary approach involving oral and maxillofacial surgeons, pathologists, and geneticists may be required, especially in cases of syndromic association. Early detection and management of recurrences are essential for optimal patient outcomes.

Keywords: Odontogenic Keratocyst, Jaw Cyst, Dental Lamina, Radiolucent, Basal Cell Carcinoma Syndrome, Surgical Enucleation, Histopathology.

INTRODUCTION

Odontogenic keratocyst (OKC), formerly known as keratocystic odontogenic tumor (KCOT), is a benign but locally aggressive cystic lesion of the jaw with distinctive histopathological features. OKCs are believed to arise from remnants of the dental lamina or primordial dental epithelium. They are considered developmental cysts rather than inflammatory in origin. First described by Philipsen in 1956, OKCs have been the subject of extensive research and debate due to their unique clinical behavior, high recurrence rates, and association with nevoid basal cell carcinoma syndrome (NBCCS), also known as Gorlin syndrome. While they can occur anywhere in the jaw, they are predominantly found in the posterior body and ascending ramus of the mandible [1].

Clinically, OKCs often present as asymptomatic lesions discovered incidentally on radiographs. However, they can manifest with symptoms such as swelling, pain, and occasionally paresthesia if they encroach on neurovascular structures. Radiographically, OKCs typically appear as well-defined, unilocular or multilocular radiolucent lesions with smooth borders. Microscopically, they are characterized by a thin, uniform, parakeratinized epithelium with a corrugated or "caterpillar-like" appearance. The management of OKCs involves surgical intervention, typically through enucleation or resection. However, due to their aggressive behavior and high recurrence rates, complete removal with adequate margins is essential to minimize the risk of recurrence.

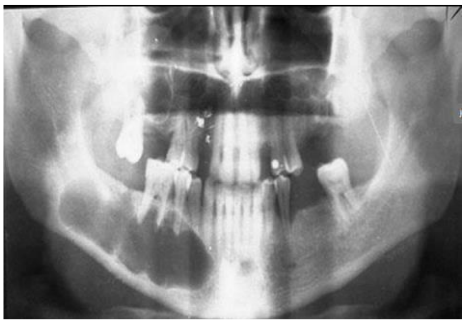
Recurrence rates vary but can range from 25% to 60%, necessitating close postoperative monitoring.

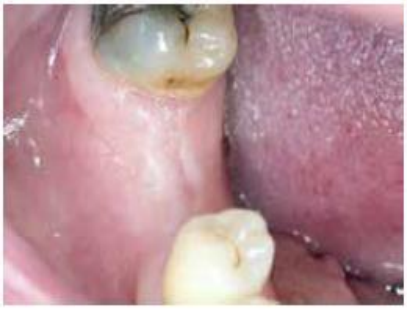
Furthermore, OKCs are often associated with NBCCS, an autosomal dominant disorder characterized by multiple basal cell carcinomas, skeletal anomalies, and various other manifestations. In patients with NBCCS, OKCs tend to occur at a younger age and have a higher propensity for recurrence. Given the complexity of OKCs and their potential syndromic associations, a multidisciplinary approach involving oral and maxillofacial surgeons, pathologists, geneticists, and dermatologists may be necessary for optimal patient care. This review aims to provide a comprehensive overview of the clinical features, histopathological characteristics, management strategies, and potential associations of odontogenic keratocysts.

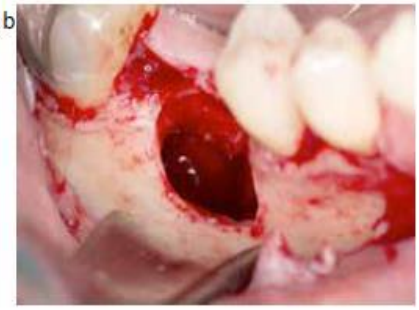
Origin: The origin of odontogenic keratocysts (OKCs) is believed to be from remnants of the dental lamina or primordial dental epithelium. The dental lamina is a band of epithelial tissue that gives rise to the enamel organs of the developing teeth. During tooth development, the dental lamina undergoes invagination to form enamel organs, which eventually give rise to the enamel-producing ameloblasts.

In some cases, remnants of the dental lamina or primordial dental epithelium may persist after tooth development is complete. It is thought that OKCs arise from these remnants, which become cystic lesions. These cysts are considered developmental rather than inflammatory in origin, as they arise from tissue remnants present during tooth development rather than as a response to inflammation or infection. The exact mechanisms underlying the development of OKCs are not fully understood, but several factors may contribute, including genetic predisposition, mutations in specific signaling pathways (such as the Hedgehog signaling pathway), and interactions between epithelial and mesenchymal tissues during development [2].

Research into the molecular and genetic mechanisms of OKCs is ongoing and may provide further insights into their origin and pathogenesis. However, the prevailing theory is that OKCs originate from remnants of the dental lamina or primordial dental epithelium, which undergo cystic transformation to form the characteristic lesions observed clinically and histologically.







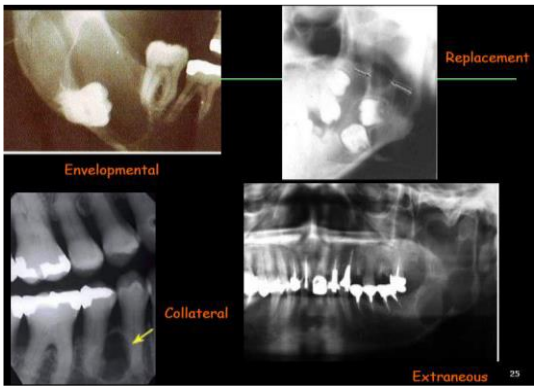
Clinical Presentation:

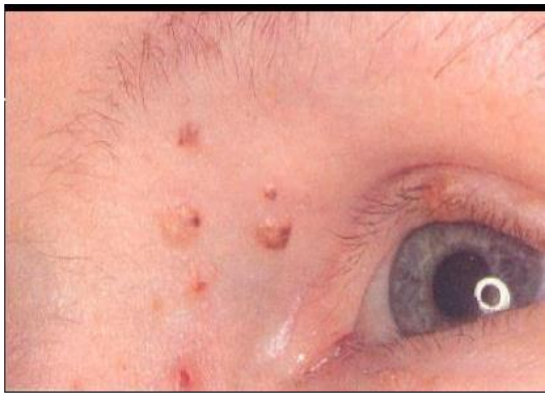
The clinical presentation of odontogenic keratocysts (OKCs) can vary widely depending on factors such as size, location, and whether they are symptomatic or asymptomatic. Here are some common clinical features associated with OKCs:

Asymptomatic Presentation: OKCs are often discovered incidentally on routine radiographs or during dental examinations, particularly if they are small and not causing any symptoms.

Swelling: Larger OKCs can cause swelling in the affected area of the jaw. The swelling may be localized and firm to palpation.

Pain: OKCs can be associated with pain, particularly if they become infected or exert pressure on surrounding structures such as teeth or nerves. The pain may be dull and persistent or sharp and intermittent.





Expansion of the Jaw: As OKCs grow, they can cause expansion of the affected jaw segment. This expansion may be noticeable clinically and can lead to facial asymmetry.

Displacement of Teeth: OKCs can cause displacement of adjacent teeth due to their expansive growth. Teeth may be pushed out of alignment or displaced into the cystic cavity.

Root Resorption: In some cases, OKCs can cause resorption of the roots of adjacent teeth, leading to tooth mobility or eventual tooth loss.

Paresthesia: In rare cases, OKCs may impinge on neurovascular structures, leading to numbness or tingling sensations (paresthesia) in the affected area of the face or oral cavity.[3]

Recurrent Infections: OKCs can become infected, leading to symptoms such as localized pain, swelling, redness, and drainage of pus (if the cyst ruptures).

Association with Nevoid Basal Cell Carcinoma Syndrome (NBCCS): In patients with NBCCS, OKCs may occur at a younger age and exhibit a more aggressive clinical course, with higher rates of recurrence.

It's important to note that OKCs can vary widely in their clinical presentation, and not all patients will experience the same symptoms. Additionally, some OKCs may remain asymptomatic and only be detected through routine radiographic imaging. Prompt evaluation and management by a dental or oral and maxillofacial specialist are essential for accurate diagnosis and appropriate treatment

Radiographic Features:

The radiographic features of odontogenic keratocysts (OKCs) can vary depending on factors such as size, location, and stage of development. However, there are several common radiographic characteristics associated with OKCs that can aid in their identification:

Radiolucency: OKCs typically appear as well-defined radiolucent lesions on radiographs. The borders of the lesion may be corticated (have a thin, radiopaque border) or non-corticated (lack a defined border).

Unilocular or Multilocular Appearance: OKCs may present as either unilocular (single-chambered) or multilocular (containing multiple compartments or "honeycomb" appearance) radiolucencies. Multilocular lesions are more common in larger OKCs or those with more advanced stages.

Smooth Margins: The margins of OKCs are usually smooth and well-defined, although they may be irregular in some cases, particularly if the lesion has undergone secondary changes such as cyst wall perforation or invasion into adjacent tissues.

Location: OKCs are often found in the posterior body and ascending ramus of the mandible, although they can occur in other locations within the jaws as well. The location of the lesion may provide additional diagnostic clues.

Associated Tooth Displacement or Resorption: OKCs can cause displacement or resorption of adjacent teeth due to their expansive growth. Teeth may appear displaced away from the lesion or exhibit root resorption on radiographs [4].

Expansion of the Jaw: As OKCs grow, they can cause expansion of the affected jaw segment, leading to a ballooning or ballooned appearance on radiographs. This expansion may be localized or involve a larger portion of the jaw.

Cortical Bone Expansion or Thinning: In cases of extensive OKC growth, the cortical bone surrounding the lesion may be expanded or thinned, leading to a "scalloped" appearance on radiographs.

Association with Impacted Teeth: OKCs may be associated with impacted or unerupted teeth, particularly in cases where the cystic lesion has developed in close proximity to tooth germ or dental follicle. Overall, radiographic imaging, including panoramic radiographs,

periapical radiographs, and cone-beam computed tomography (CBCT), plays a crucial role in the diagnosis and assessment of odontogenic keratocysts. A thorough evaluation of radiographic features, in conjunction with clinical and histopathological findings, can aid in accurate diagnosis and treatment planning for patients with OKCs.

Histopathology: Histopathologically, odontogenic keratocysts (OKCs) exhibit several distinctive features that aid in their diagnosis. Here's an overview of the histopathological characteristics typically observed in OKCs:

Epithelial Lining: The epithelial lining of OKCs is typically thin and stratified, consisting of parakeratinized or orthokeratinized squamous epithelium. Parakeratinization is more common and is characterized by the retention of nuclei in the superficial layers of the epithelium.

Surface Plicae: OKCs often display surface plicae or ridges, giving the epithelium a corrugated or "caterpillar-like" appearance under the microscope. These surface plicae are a characteristic feature of OKCs and help distinguish them from other types of cysts.

Basal Cell Palisading: Basal cell palisading is frequently observed in OKCs, where the basal cells of the epithelial lining align perpendicular to the basement membrane. This arrangement is typically seen in the parakeratinized layer but may also extend into the underlying connective tissue.[6]

Epithelial Thinning: The epithelial lining of OKCs may appear thin and attenuated in some areas, particularly in regions where the cyst wall is in close proximity to adjacent structures such as bone or soft tissue.

Epithelial Proliferation and Invagination: OKCs often exhibit epithelial proliferation and invagination into the connective tissue wall of the cyst. Epithelial islands or buds may extend into the fibrous connective tissue, contributing to the cyst's aggressive behavior and potential for recurrence.

Inflammatory Cell Infiltrate: Inflammatory cells, such as lymphocytes and plasma cells, may be present within the connective tissue wall of OKCs, particularly in cases where the cyst has become secondarily infected.

Epithelial Dysplasia: While not a universal finding, epithelial dysplasia or atypia may occasionally be observed in OKCs, particularly in cases associated with nevoid basal cell carcinoma syndrome (NBCCS) or those with aggressive clinical behavior.

Calcifications: Dystrophic calcifications or calcified deposits may be present within the epithelial lining or connective tissue stroma of OKCs, although they are less common compared to other odontogenic cysts such as calcifying odontogenic cysts.

Histopathological examination of a biopsy specimen remains the gold standard for confirming the diagnosis of OKCs. The characteristic features described above, along with clinical and radiographic findings, help distinguish OKCs from other cystic lesions of the jaws and guide appropriate management strategies.

Treatment: The treatment of odontogenic keratocysts (OKCs) typically involves surgical intervention aimed at complete removal of the cyst while minimizing the risk of recurrence. Here's an overview of the treatment options for OKCs:

Enucleation: Enucleation involves the surgical removal of the cystic lesion along with its surrounding fibrous capsule. This procedure is commonly performed for smaller OKCs with well-defined borders and minimal involvement of surrounding structures. Enucleation alone, however, carries a higher risk of recurrence compared to more aggressive treatment modalities.

Enucleation with Curettage: Enucleation combined with curettage involves not only removing the cystic lesion but also scraping the adjacent bone to remove any residual epithelial remnants. This technique aims to decrease the risk of recurrence by eliminating potential sources of regrowth. It is often used for larger or more aggressive OKCs.

Marsupialization: Marsupialization involves creating a surgical opening in the cystic lesion and suturing its lining to the oral mucosa, allowing drainage of cystic fluid and decompression of the lesion. This technique may be employed as a conservative treatment option for large or extensive OKCs, particularly when complete enucleation is not feasible initially. Following marsupialization, the cyst may be monitored and subsequently removed surgically once it has reduced in size.

Resection: Resection involves the complete surgical excision of the affected portion of the jaw containing the OKC, along with a margin of healthy tissue to ensure complete removal. This more aggressive approach is reserved for cases of extensive OKCs with involvement of vital structures, recurrence after conservative treatment, or cases associated with nevoid basal cell carcinoma syndrome (NBCCS), where the risk of recurrence is higher.

Adjuvant Therapy: Adjuvant treatments such as cryotherapy, Carnoy's solution (a chemical fixative used to destroy residual epithelial remnants), or guided bone regeneration techniques may be employed in conjunction with surgical treatment to further reduce the risk of

recurrence, particularly in cases with high-risk features or aggressive behavior.

Follow-up: Regular follow-up appointments are essential following surgical treatment of OKCs to monitor for signs of recurrence and ensure optimal healing. Radiographic imaging, such as panoramic radiographs or cone-beam computed tomography (CBCT), may be performed at follow-up visits to assess for any signs of recurrence.

The choice of treatment modality depends on various factors including the size and location of the lesion, its clinical behavior, the presence of associated symptoms, and the patient's overall health and preferences. A multidisciplinary approach involving oral and maxillofacial surgeons, pathologists, and, in cases of syndromic association, geneticists and dermatologists, may be necessary to formulate an optimal treatment plan for each individual patient.

Recurrence: Recurrence is a significant concern in the management of odontogenic keratocysts (OKCs) due to their propensity for regrowth even after seemingly successful treatment. The recurrence rates of OKCs vary depending on various factors including the treatment modality employed, the aggressiveness of the initial lesion, and the presence of underlying syndromes such as nevoid basal cell carcinoma syndrome (NBCCS). Here's a closer look at recurrence in OKCs:

Overall Recurrence Rates: Recurrence rates for OKCs have been reported to range from approximately 25% to 60%. These rates can vary widely depending on the specific study population, follow-up duration, and treatment modalities utilized.

Factors Influencing Recurrence:
Incomplete Removal: Recurrence is more likely if the cyst is not completely removed during the initial surgical procedure. Residual epithelial remnants left behind in the bone or soft tissues can serve as a nidus for regrowth.

Aggressive Behavior: OKCs with aggressive histopathological features, such as epithelial proliferation, invagination, and basal cell palisading, are more likely to recur.

Syndromic Association: OKCs associated with nevoid basal cell carcinoma syndrome (NBCCS), also known as Gorlin syndrome, tend to recur at higher rates compared to sporadic cases.

Treatment Modality: Conservative treatments such as simple enucleation have higher recurrence rates compared to more aggressive approaches such as resection with clear margins.

Size and Location: Larger OKCs and those located in anatomically challenging areas may be more difficult to completely remove, increasing the risk of recurrence.[7]

Follow-Up and Monitoring: Regular and long-term follow-up is crucial for detecting any signs of recurrence early. Follow-up typically involves clinical examination and radiographic imaging such as panoramic radiographs or cone-beam computed tomography (CBCT). Patients with OKCs should be monitored closely for several years after treatment, as recurrences can occur years after the initial intervention.

Management of Recurrence: In cases of recurrence, further surgical intervention is usually necessary. The treatment approach for recurrent OKCs may involve more aggressive surgery with wider margins to ensure complete removal. Adjuvant therapies such as cryotherapy or chemical cauterization with Carnoy's solution may also be employed to reduce the risk of further recurrence.

Overall, the management of OKCs requires a thorough understanding of the factors influencing recurrence and a multidisciplinary approach to treatment and long-term follow-up to minimize the risk of recurrence and optimize patient outcomes.

Association with Nevoid Basal Cell Carcinoma Syndrome (Gorlin Syndrome): Odontogenic keratocysts (OKCs) are notably associated with Nevoid Basal Cell Carcinoma Syndrome (NBCCS), also known as Gorlin Syndrome. This is an autosomal dominant genetic disorder characterized by a predisposition to multiple basal cell carcinomas, jaw cysts (including OKCs), skeletal anomalies, and various other developmental abnormalities. Here's a closer look at the association between OKCs and Gorlin Syndrome:

Prevalence: OKCs are one of the major diagnostic criteria for Gorlin Syndrome. Individuals with Gorlin Syndrome have a significantly increased risk of developing OKCs compared to the general population. OKCs associated with Gorlin Syndrome tend to occur at a younger age and exhibit a more aggressive clinical course, including higher rates of recurrence.

Clinical Features: In addition to multiple OKCs, individuals with Gorlin Syndrome may present with other characteristic features such as multiple basal cell carcinomas, palmar or plantar pits, skeletal anomalies (e.g., bifid ribs, macrocephaly), calcification of the falx cerebri, and various developmental anomalies.

Genetic Basis: Gorlin Syndrome is caused by mutations in the PTCH1 (patched) gene, a tumor suppressor gene located on chromosome 9q22.3-q31. PTCH1 encodes a transmembrane protein that regulates the Hedgehog signaling pathway, which plays a critical role in

embryonic development and tissue homeostasis. Loss-of-function mutations in PTCH1 lead to dysregulated Hedgehog signaling, resulting in increased cell proliferation and tumorigenesis.

Management: The management of OKCs in individuals with Gorlin Syndrome often involves early detection and surveillance for signs of cyst development. Regular clinical and radiographic examinations are recommended to monitor for the presence of new cysts or recurrence of previously treated lesions. Surgical intervention may be necessary for symptomatic or large cysts, with careful consideration given to the increased risk of recurrence in this patient population.

Counseling and Genetic Testing: Given the genetic basis of Gorlin Syndrome, genetic counseling and testing may be offered to affected individuals and their families. Identification of a pathogenic mutation in PTCH1 can confirm the diagnosis and facilitate appropriate management and surveillance strategies for at-risk individuals. In summary, the association between OKCs and Gorlin Syndrome highlights the importance of recognizing the clinical features of this syndrome and implementing appropriate management and surveillance measures to minimize the associated risks, including the development of OKCs and other neoplastic conditions.

CONCLUSION

In conclusion, odontogenic keratocysts (OKCs) represent a unique entity in the realm of oral and maxillofacial pathology, characterized by their locally aggressive behavior and propensity for recurrence. These cystic lesions arise from remnants of the dental lamina or primordial dental epithelium and are typically found in the posterior body and ascending ramus of the mandible. While OKCs can present asymptomatically, they may also manifest with swelling, pain, tooth displacement, and other clinical signs.

Histopathologically, OKCs are defined by a thin, stratified epithelial lining with parakeratinization and characteristic surface plicae, along with basal cell palisading and epithelial invagination into the connective tissue wall. Radiographically, OKCs appear as well-defined radiolucent lesions with smooth or irregular borders, often associated with tooth displacement or resorption.

Treatment of OKCs typically involves surgical intervention, ranging from enucleation to more aggressive resection, with adjuvant therapies sometimes employed to reduce the risk of recurrence. Close postoperative monitoring is essential due to the relatively high recurrence rates, particularly in cases associated with nevoid basal cell carcinoma syndrome (Gorlin Syndrome) [8].

Furthermore, the association between OKCs and Gorlin Syndrome underscores the importance of recognizing syndromic features and implementing appropriate management strategies, including genetic counseling and testing when indicated. In summary, a comprehensive understanding of the clinical, radiographic, histopathological, and syndromic aspects of OKCs is essential for accurate diagnosis, effective treatment, and optimal patient outcomes. Continued research into the molecular and genetic mechanisms underlying OKCs will further enhance our understanding of these intriguing lesions and inform future advancements in their management.

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