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Salivary Gland Tumors: A Narrative Review with Emphasis on Clinicopathological Features

HIMANI TIWARI* and PIYUSH ASNANI

Department of Oral and Maxillofacial Pathology, Faculty of Dental Sciences, Dharmsinh Desai University, Nadiad, India

Abstract

Salivary gland tumors represent a diagnostically challenging group of lesions due to their marked histological diversity, wide biological behaviour, and overlapping clinical features. These neoplasms arise from both major and minor salivary glands and encompass a broad spectrum ranging from indolent benign entities to aggressive malignant tumors with a propensity for local invasion and distant spread. Accurate diagnosis is essential, as treatment strategies and prognostic outcomes vary significantly depending on tumor type, grade, and anatomical site. This narrative review provides a structured overview of salivary gland tumors with emphasis on their clinicopathological characteristics and diagnostic considerations. The classification of salivary gland neoplasms is discussed in accordance with contemporary World Health Organization (WHO) guidelines, highlighting key benign and malignant epithelial tumors encountered in routine practice. Salient clinical presentations, histomorphological features, and patterns of biological behaviour relevant to diagnosis and management are outlined. The role of diagnostic modalities including clinical examination, imaging techniques, fine-needle aspiration cytology, and histopathological evaluation is reviewed, with particular emphasis on the strengths and limitations of each approach. Management principles and current perspectives on surgical and adjuvant treatment strategies are briefly addressed. Our knowledge of salivary gland pathology has advanced significantly in recent years, molecular diagnostic approaches are being used in an effort to find viable therapy drugs for salivary duct carcinomas. There have been descriptions of concepts like "high-grade transformation," which not only affect the macroscopic and microscopic assessment of a specimen but also have important treatment implications

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CONTACT Himani Tiwari himanicsc@gmail.com Department of Oral and Maxillofacial Pathology, Faculty of Dental Sciences, Dharmsinh Desai University, Nadiad, India

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due to the high prevalence of metastases and morbidity. Fluorescent in situ hybridization can identify some chromosomal translocations, which can improve diagnostic precision and have prognostic consequences. This review aims to serve as a concise yet comprehensive reference for dental practitioners, oral pathologists, and postgraduate students involved in the diagnosis and management of salivary gland tumors.

Introduction

Tumors of salivary gland comprise a relatively uncommon yet clinically significant group of neoplasms that originate from the secretory tissues of the major and minor salivary glands.[1] Although they account for a small proportion of head and neck tumors, their importance lies in the remarkable diversity of histological patterns and biological behaviour they exhibit, ranging from innocuous benign lesions to highly aggressive malignancies with metastatic potential. This heterogeneity poses substantial diagnostic and therapeutic challenges for clinicians and pathologists alike.[2]

The salivary gland system includes three pairs of major glands parotid, submandibular, and sublingual as well as numerous minor salivary glands dispersed throughout the oral cavity and upper aerodigestive tract. Tumors arising from these glands demonstrate considerable variation in incidence, morphology, and clinical presentation depending on the gland involved, with malignant neoplasms occurring more frequently in minor salivary glands than in major glands. Such variability necessitates a thorough understanding of site-specific tumor behaviour during clinical evaluation.[3,4]

One of the distinguishing features of salivary gland tumors is the overlap in clinical and radiological appearances among different entities. Many lesions present as slow-growing, painless masses, particularly in the early stages, which may delay diagnosis and definitive management. Accurate diagnosis requires correlation with clinical, imaging findings, cytological assessment, and histopathological examination.[2,5]

From a pathological standpoint, salivary gland tumors are notable for their complex histomorphology and cellular diversity, often displaying mixed epithelial and myoepithelial components, variable stromal backgrounds, and diverse architectural patterns. This complexity has led to the development and periodic refinement of classification systems, most notably those proposed by the World Health Organization (WHO), which provide a standardized framework for tumor categorization based on histological and biological criteria. Accurate classification is critical, as it directly influences treatment planning, prognostic assessment, and patient counseling.[6,7]

Given the diagnostic challenges and wide clinical spectrum of salivary gland tumors, a comprehensive understanding of their clinicopathological features is essential for optimal patient care. This review aims to provide an updated overview of salivary gland tumors, focusing on their classification, common benign and malignant entities, clinical presentation, diagnostic approaches, and general principles of management, thereby serving as a practical reference for dental practitioners and postgraduate students involved in head and neck pathology.

Methodology

This review carried out literature search in pubmed, Scopus and google scholar search engines from year 2001 to 2025 with key word salivary “glands” and “salivary gland tumors” and relevant article selected from this search included in this narrative review.

Areas Covered

This review covers the classification, clinicopathological features, and diagnostic approach to salivary gland tumors, with emphasis on commonly encountered benign and malignant entities. The role of clinical examination, imaging, fine-needle aspiration cytology, and histopathological assessment in diagnosis is discussed, along with general principles of management and recent perspectives in the field. The review aims to provide a concise and practical overview relevant to dental practitioners and postgraduate students.

Classification of Salivary Gland Tumors

Tumors of salivary glands constitute a highly heterogeneous group of neoplasms, making standardized classification essential for accurate diagnosis and effective clinical management. Among the various systems proposed, the World Health Organization (WHO) classification of head and neck tumors is the most widely accepted framework and provides a uniform basis for tumor categorization.[1]

The WHO classification primarily organizes salivary gland tumors according to their histogenetic origin and biological behaviour. These neoplasms are broadly divided into epithelial and non-epithelial tumors, with epithelial tumors accounting for the majority of cases encountered in routine practice. Secondary involvement of the salivary glands by metastatic tumors is recognized as a separate category due to its distinct clinical significance.[1,2]

Epithelial salivary gland tumors are further subclassified into benign and malignant entities. Benign tumors are generally well circumscribed and exhibit indolent growth patterns, whereas malignant tumors display a wide range of biological behaviour, from low-grade lesions to aggressive carcinomas with invasive and metastatic potential. Non-epithelial tumors, although uncommon, include mesenchymal and hematolymphoid neoplasms that may clinically mimic epithelial lesions. Metastatic tumors most frequently involve the parotid gland, reflecting its intraglandular lymph node content.[1-5]

Ongoing refinements in the WHO classifica-tion, incorporating histopathological, immunohisto-chemical, and molecular insights, have improved diagnostic precision and prognostic stratification. Familiarity with this classification is essential for pathologists and clinicians involved in the evaluation and management of salivary gland tumors. Table 1

Benign Salivary Gland Neoplasm

Benign neoplasms of the salivary glands represent a biologically diverse group of lesions that, despite their generally indolent clinical behaviour, demonstrate striking heterogeneity in architectural organization and cellular differentiation. These tumors most often present as localized, slowly progressive swellings and are frequently identified in the parotid gland, although a significant proportion arise from minor salivary glands within the oral cavity. From a pathological standpoint, benign salivary gland tumors require careful evaluation, as certain entities exhibit recurrence potential or overlap morphologically with low-grade malignancies.[2,3]

Table 1: Classification of tumors of Salivary glands[1]

Category	Subcategory	Tumor
Epithelial tumors	Benign tumors	Pleomorphic adenoma; Myoepithelioma Warthin tumor; Canalicular adenoma Basal cell adenoma;
Epithelial tumors	Malignant tumors	Mucoepidermoid carcinoma; Adenoid cystic carcinoma; Acinic cell carcinoma; Polymorphous adenocarcinoma
Non-epithelial tumors	—	Lymphoma; Haemangioma; Neurogenic tumors
Secondary tumors	—	Metastatic carcinomas; Directly extended from adjacent head and neck malignancies

Pleomorphic Adenoma

Pleomorphic adenoma exemplifies the morphologic complexity of benign salivary gland tumors and remains a common diagnostic consideration in salivary pathology. Microscopically, the tumor displays variable proportions of epithelial and myoepithelial cells arranged in ducts, nests, cords, or dispersed patterns within a heterogeneous

stroma. The stromal component may appear myxoid, hyalinized, or cartilaginous, often within the same lesion. Although the tumor is typically well circumscribed, subtle peripheral extensions into adjacent tissue are frequently present, explaining the risk of recurrence following limited excision. Long-standing lesions warrant particular attention due to their documented potential for malignant transformation.[2,8]

Warthin Tumor

Warthin tumor represents a distinctive benign salivary gland neoplasm with unique clinical and histological features. It arises almost exclusively in the parotid gland and may present as bilateral or multifocal lesions. Histologically, the tumor demonstrates a characteristic biphasic architecture composed of oncocytic epithelial cells forming papillary or cystic structures supported by a lymphoid stroma. This combination produces a readily recognizable pattern that facilitates diagnosis, even on limited biopsy material. The biological behaviour of Warthin tumor is typically non-aggressive, and recurrence is uncommon following complete excision.[2,9]

Basal Cell Adenoma

Basal cell adenoma being an uncommon benign epithelial tumor characterized by basaloid cell proliferation arranged in solid, trabecular, tubular, or membranous patterns. The membranous variant is of particular importance due to its tendency for multifocality and recurrence. Histologically, these tumors are composed of uniform basaloid cells with peripheral palisading and a distinct basement membrane–like material, features that assist in distinguishing them from malignant basaloid neoplasms.[2,3]

Malignant Salivary Gland Tumors

Malignant neoplasms arising in salivary glands demonstrate wide variation in clinical aggressiveness, microscopic architecture, and long-term outcome. Their behaviour is not uniform and often cannot be predicted solely on the basis of size or duration. In several instances, lesions with deceptively bland clinical appearance show infiltrative growth at the tissue level, emphasizing the limited reliability of clinical assessment in isolation.[1,4]

Histologically, malignant salivary gland tumors frequently exhibit architectural disorganization, invasive borders, and variable cytological atypia. Perineural spread, deep soft tissue infiltration, and extension beyond the apparent tumor margin are recurring themes across multiple entities. These features account for the tendency toward local recurrence and the need for meticulous pathological evaluation to guide treatment planning.

Mucoepidermoid Carcinoma

Mucoepidermoid carcinoma displays marked heterogeneity, both within and between tumors. Rather than a single uniform pattern, it is composed of different cellular populations arranged in variable proportions. The balance between mucous-producing cells, squamoid elements, and intermediate cells influences both microscopic appearance and biological behavior.[10,11] Lesions with prominent cystic architecture and minimal atypia often follow a less aggressive course, whereas tumors dominated by solid growth and cytological irregularity demonstrate increased invasive potential. Recognition of these internal differences is essential, as they directly impact prognostic assessment.[12,13]

Adenoid Cystic Carcinoma

Adenoid cystic carcinoma follows a clinical course that is often prolonged yet relentlessly progressive. Despite slow initial enlargement, the tumor demonstrates a strong tendency for neural infiltration, allowing extension well beyond the primary site. Microscopically, it shows distinctive architectural arrangements that may vary within the same lesion, contributing to diagnostic complexity in limited samples. Late recurrence and distant spread are well-recognized features, making long-term surveillance a critical component of patient management.[14]

Acinic Cell Carcinoma

Acinic cell carcinoma arises from serous acinar differentiation and most commonly involves major salivary glands. The tumor exhibits a range of architectural patterns rather than a single defining structure. While many cases behave in a relatively indolent manner, a subset demonstrates aggressive features such as infiltrative growth and recurrence. This variability highlights the importance of not assuming low biological risk based solely on tumor type.[15]

Polymorphous Adenocarcinoma

Polymorphous adenocarcinoma is characterized by architectural diversity coupled with relatively uniform

cytological features. The tumor often infiltrates surrounding tissue in a subtle manner, sometimes following neural pathways. Because of its bland cellular appearance, it may be misinterpreted as a benign process, particularly in small biopsy specimens. Accurate diagnosis depends on recognition of its infiltrative pattern rather than cytological atypia alone.[16]

Other Malignant Salivary Gland Tumors

Several additional malignant entities occur less frequently but contribute to the overall complexity of salivary gland pathology. These tumors often present with high-grade cytological features, rapid progression, and a greater likelihood of regional or distant spread. Their recognition requires careful correlation of architectural pattern, cellular morphology, and invasion characteristics to avoid misclassification.[1,2]

Clinicopathological Correlation

Correlation between clinical presentation and histopathological findings plays a central role in the accurate diagnosis of salivary gland tumors. Clinical features alone are often insufficient to predict the biological nature of these lesions, as tumors with markedly different histological profiles may present with similar external appearances. Consequently, clinicopathological correlation serves as a critical bridge between initial clinical assessment and definitive diagnosis.[2,17]

Benign salivary gland tumors typically present as slow-growing, well-localized swellings that remain asymptomatic for extended periods. The absence of pain, ulceration, or neurological deficits often contributes to delayed presentation. Histologically, these tumors usually demonstrate circumscribed growth patterns and lack overt features of tissue invasion.[6,10] However, certain benign entities may show microscopic extensions beyond their apparent margins, explaining the occasional discrepancy between clinically benign behaviour and postoperative recurrence.[17]

In contrast, malignant salivary gland tumors frequently exhibit subtle but significant clinical indicators that correlate with aggressive histological behaviour. Pain, facial nerve dysfunction, fixation to surrounding tissues, and rapid increase in size often reflect underlying invasive growth, perineural infiltration, or high-grade cellular atypia. Nevertheless, the absence of these features does not exclude malignancy, as several malignant tumors demonstrate indolent clinical progression despite infiltrative microscopic patterns.[14,16]

Anatomical location further influences clinicopathological interpretation. Tumors arising in minor salivary glands, particularly of the palate, are more likely to demonstrate malignant histology despite a relatively innocuous clinical appearance. Conversely, large parotid lesions may remain benign despite prolonged duration. This site-specific behaviour highlights the importance of integrating anatomical context into diagnostic reasoning.

Radiological findings provide additional correlation by offering insight into lesion extent, internal architecture, and relationship to adjacent structures. Well-defined margins and homogeneous internal characteristics often parallel benign histology, whereas ill-defined borders, tissue invasion, and neural canal involvement are more commonly associated with malignancy. However, imaging findings must be interpreted cautiously and in conjunction with histopathological data.[17]

Histopathological examination ultimately determines tumor classification and biological behaviour. Architectural pattern, cellular composition, presence of invasion, and interaction with surrounding tissues form the basis for definitive diagnosis. When correlated with clinical and radiological features, these findings allow accurate prognostic assessment and appropriate treatment planning.[19]

In summary, effective clinicopathological correlation requires integration of clinical presentation, anatomical site, imaging characteristics, and microscopic findings. Reliance on any single parameter may lead to misinterpretation, whereas a combined approach enhances diagnostic accuracy and guides optimal patient management.

Table 2: Comparison Between Benign and Malignant Salivary Gland Neoplasms

Feature	Benign tumors	Malignant tumors
Growth	Slow	Variable, rapid
Pain Usually	absent	May be present
Margins	Well circumscribed	Ill-defined, infiltrative
Facial nerve involvement	Rare	More common
Perineural invasion	Absent	Common in certain tumors
Metastatic potential	Absent	May be present
Prognosis	Excellent	Variable

Diagnostic Modalities

Accurate evaluation of salivary gland tumors requires a multimodal diagnostic approach, as no single investigation reliably defines tumor type or biological behaviour in isolation. Clinical assessment, imaging studies, cytological sampling, and histopathological examination each contribute complementary information that must be interpreted collectively rather than independently.[2,18]

Clinical examination serves as the initial step in evaluation and provides valuable contextual information regarding lesion duration, rate of growth, consistency, fixation, and associated symptoms.[6,10] Features such as facial nerve dysfunction, pain, ulceration, or rapid enlargement raise suspicion for malignant behaviour; however, their absence does not reliably exclude aggressive pathology. Consequently, clinical findings guide but do not determine diagnosis.[17] Table 3

Imaging techniques play a crucial role in defining lesion extent and anatomical relationships. Ultrasonography is often employed as a first-line modality for superficial lesions, allowing assessment of lesion size, internal echotexture, and vascularity. Cross-sectional imaging, particularly computed tomography and magnetic resonance imaging, provides superior delineation of deep-seated tumors, involvement of adjacent structures, and potential neural or bony extension. Imaging findings assist in surgical planning but remain limited in their ability to distinguish specific histological entities.[7]

Fine-needle aspiration cytology is broadly used as a less invasive diagnostic tool and offers valuable preoperative information. It aids in differentiating neoplastic from non-neoplastic lesions and in broadly categorizing tumors as benign or malignant. Nevertheless, cytological interpretation may be challenging due to overlapping features among salivary gland tumors and sampling limitations. FNAC results should therefore be interpreted in conjunction with clinical and radiological findings.[19]

Histopathological examination remains the definitive diagnostic modality. Evaluation of tissue architecture, cellular composition, growth pattern, and invasion characteristics forms the basis for accurate tumor classification. In certain cases, ancillary techniques such as special stains and immunohistochemistry assist in resolving diagnostic ambiguity, particularly when differentiating between morphologically similar entities or identifying specific lines of differentiation.[1,2]

Recent Diagnostic Approaches

Molecular and genetic studies are increasingly contributing to salivary gland tumor diagnostics, especially in selected cases with overlapping histological features. Chromosomal rearrangement with gene fusions are notably prevalent in salivary gland tumors and play a very crucial role in identifying specific cancer subtypes. With traditional diagnostic methods such as immunohistochemistry and fluorescence in situ hybridization , next-generation sequencing has been effectively utilized in recent years to enhance and expand our understanding of salivary gland tumors. These techniques have been employed for whole exome, transcriptome, or targeted sequencing, facilitating the precise barcoding of neoplastic samples.

Table 3: Common Salivary Gland Tumors and Site Predilection

Tumor	Common site
Pleomorphic adenoma	Parotid gland, palate
Warthin tumor	Parotid gland
Mucoepidermoid carcinoma	Parotid gland, palate
Adenoid cystic carcinoma	Minor salivary glands (palate)
Acinic cell carcinoma	Parotid gland
Polymorphous adenocarcinoma	Minor salivary glands

Management

Management of salivary gland tumors is guided by an integrated assessment of tumor type, anatomical site, biological behaviour, and extent of disease rather than by a single defining parameter. Treatment planning therefore requires close coordination between clinical evaluation, imaging findings, and histopathological interpretation. The primary objective is complete disease control while preserving function to the greatest extent possible.[2,18]

For benign salivary gland tumors, surgical excision remains the treatment of choice. The extent of surgery is determined by tumor location, size, and relationship to adjacent anatomical structures. In major salivary glands, particularly the parotid, careful surgical technique is essential to achieve complete removal while minimizing functional morbidity.[2,3] Inadequate excision may result in recurrence, especially in tumors with microscopic extensions beyond their apparent margins. Long-term follow-up is advised in selected cases due to the potential for delayed recurrence or malignant transformation.

Management of malignant salivary gland tumors is more complex and depends on tumor grade, invasiveness, and regional or distant spread. Wide surgical excision with clear margins forms the cornerstone of treatment in resectable disease. The presence of perineural invasion, deep soft tissue extension, or involvement of adjacent structures often necessitates a more aggressive surgical approach. Neck management is considered when there is clinical or radiological evidence of nodal disease or when tumor characteristics suggest a higher risk of regional metastasis.[10]

Role of Radiotherapy

Adjuvant therapy plays an important role in selected malignant cases. Postoperative radiotherapy is commonly employed to improve local control, particularly in tumors with high-grade features, close or positive margins, perineural spread, or advanced local disease. The decision to administer adjuvant treatment is individualized and based on a combination of pathological risk factors rather than tumor type alone.[2,17]

Non-surgical treatment modalities may be considered in unresectable disease, recurrent tumors not amenable to further surgery, or in patients who are poor surgical candidates. In such situations, radiotherapy may be used with palliative or disease-controlling intent. Systemic therapy is reserved for selected advanced cases and is typically considered within a multidisciplinary framework.[15]

Follow up and Prognosis

Follow-up constitutes an essential component of management for both benign and malignant salivary gland tumors. Clinical surveillance focuses on early detection of recurrence, assessment of functional outcomes, and identification of delayed complications. Malignant tumors, particularly those known for late recurrence or distant spread, require prolonged follow-up due to their unpredictable clinical course.[10,14]

In summary, management of salivary gland tumors is highly individualized and relies on thorough pathological assessment combined with careful clinical judgment. A multidisciplinary approach ensures optimal balance between disease control

and preservation of function, ultimately improving patient outcomes.

Recent Perspectives and Advances

Recently gradual advancements in the understanding and management of salivary gland tumors, primarily driven by improvements in diagnostic techniques, refinement of histopathological classification, and a better appreciation of tumor behaviour. The updated World Health Organization (WHO) classification has contributed to improved diagnostic consistency by incorporating clearer morphological criteria and recognizing distinct tumor entities based on clinicopathological features.[1,22]

Advances in imaging modalities, particularly high-resolution magnetic resonance imaging, have enhanced preoperative assessment by allowing more accurate evaluation of tumor extent, perineural spread, and involvement of adjacent structures. These developments have aided in better surgical planning and improved local disease control.[7] Similarly, refinements in fine-needle aspiration cytology and increased awareness of its limitations have improved its utility as a preoperative diagnostic tool when combined with clinical and radiological correlation.[21]

In histopathology, the adjunctive use of immuno-histochemistry has improved diagnostic accuracy in challenging cases by helping distinguish morphologically overlapping entities. Although immunohistochemical markers are not routinely required for all salivary gland tumors, their selective application has enhanced diagnostic confidence in specific scenarios.[13,18] These advances have supported more precise tumor classification and prognostication.

Therapeutic advances in salivary gland tumors remain limited; however, ongoing research into targeted therapies and novel treatment approaches has shown promise, particularly for advanced and recurrent malignancies. Despite these develop-ments, surgical excision with or without adjuvant radiotherapy continues to remain the cornerstone treatment.[15]

Next generation diagnostic tools and biological markers must be combined to provide accurate detection and dose distribution. Number of studies also pit stress on the saliva significance as major source of information on potential diagnosis and prognosis.

Molecular level studies focused on malignancy with their molecular correlations, MEC has 40-80% chance of having a CRTC1-MAML2 change and a 5% chance of having a CRTC3-MAML2 alteration.[23]

Currently, there are nearly 100 different kinds of salivary biomarkers which include metabolomics biomarkers (valine and lactic acid), protein biomarkers (p53, alpha-amylase), DNA, RNA, and microRNA-related biomarkers (p53 gene codon 63, miR-125a), and non-organic compound biomarkers like sodium, calcium. The use of salivary-based biomarkers to evaluate the risk of cancerous diseases has grown in significance. Tumors can be identified using DNA or RNA-based techniques instead of conventional methods. New methods including saliva-based identification and salivary epithelial cells are being developed to increase accurate diagnosis, and PCR identification procedures guarantee accurate measurement.[23]

Article Highlights

- Salivary gland tumors demonstrate marked biological and morphological diversity, making accurate diagnosis dependent on integrated clinicopathological assessment rather than isolated clinical features.
- Benign salivary gland tumors, although generally indolent, exhibit variable architectural patterns and may show recurrence or malignant transformation if inadequately managed.
- Malignant salivary gland tumors display wide heterogeneity in growth behaviour, invasion patterns, and long-term outcomes, often presenting diagnostic challenges due to overlapping clinical appearances.
- Histopathological evaluation remains central to tumor classification, prognostic assessment, and treatment planning, particularly in lesions with deceptively bland clinical or cytological features.
- Effective management of salivary gland tumors requires a multidisciplinary approach, balancing oncologic control with preservation of function and long-term surveillance.

Conclusion

Salivary gland neoplasm encompasses a broad range of neoplastic entities that differ markedly

in morphology, biological behaviour, and clinical outcome. Their diagnostic complexity arises not from rarity alone, but from overlapping clinical presentations and diverse histopathological patterns that challenge simplistic categorization. Accurate interpretation therefore depends on careful integration of clinical findings, imaging characteristics, and microscopic evaluation rather than reliance on any single parameter.

Benign salivary gland tumors generally demonstrate favourable outcomes when appropriately managed, yet certain entities warrant careful attention due to their potential for recurrence or malignant transformation. Malignant tumors, in contrast, exhibit variable degrees of aggressiveness, with patterns of invasion and spread that may not always correlate with initial clinical impressions. These features highlight the limitations of purely clinical assessment and reinforce the central role of histopathology in guiding management decisions.

Advances in diagnostic techniques and a deeper understanding of tumor biology have improved classification accuracy and treatment planning. Nevertheless, salivary gland pathology continues to demand a high level of diagnostic precision, particularly in limited biopsy material and tumors with deceptively bland appearances. A multidisciplinary approach remains essential to ensure optimal patient outcomes.

In conclusion, effective management of salivary gland tumors relies on a comprehensive and integrated diagnostic framework. Continued emphasis on clinicopathological correlation and meticulous pathological evaluation is crucial for accurate diagnosis, appropriate treatment selection, and long-term patient care.

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Author Contributions
- **Himani Tiwari:** Conceptualization, Analysis, Writing-Review and Editing
- **Piyush Asani:** Data collection, Methodology, Writing-Original Draft

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