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THE ROLE OF HISTOPATHOLOGY IN DIAGNOSING EARLY LARYNGEAL CARCINOMA: A CLINICOPATHOLOGICAL STUDY

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Abstract

Introduction: Laryngeal carcinoma frequently appears in the upper aerodigestive tract, and prompt diagnosis is essential for better patient results. Histopathology is the standard method for verifying diagnosis, tumor subtype differentiation, and stage and grade identification.

Objectives: This investigation analyzes the importance of histopathology in premature diagnosis and classification stages of laryngeal carcinoma using clinical and pathological data correlation.

Materials and Methods: The clinical and pathological research occurred at Niazi Medical College Sargodha, Pakistan. Medical providers examined patients with possible laryngeal carcinoma by performing direct laryngoscopic biopsies. The histopathological examination provided information about tumor type grade and precise location.

Results: The examination revealed squamous cell carcinoma in 86.7% of 60 total patients, and this carcinoma typically manifested as well-differentiated. Most tumors began in the glottic region because hoarseness remained the leading symptom for patients. Histopathology has proved effective in detecting frequent and infrequent tumor types.

Conclusion: Early diagnosis of laryngeal carcinoma depends significantly on histopathology to determine appropriate treatment strategies along with patient prognoses.

Keywords: Laryngeal carcinoma, histopathology, squamous cell carcinoma, early diagnosis, clinicopathological study.

INTRODUCTION

Laryngeal carcinoma ranks as one of the primary malignant tumors of the head and neck tissue while substantially disrupting voice quality alongside respiration and life function. Squamous cell carcinoma stands as the dominant type of laryngeal carcinoma, whereas neuroendocrine tumors and sarcomas add to its different forms (1). Identifying laryngeal carcinoma early proves essential because it enables providers to perform interventions promptly, leading to better survival rates and improved prognoses. The diagnostic and guidance tasks of treatment planning and prognosticating are handled by histopathology, an essential diagnostic tool (2). Laryngeal lesions produce unspecific symptoms that include throat pain, swallowing problems, and hoarseness since such manifestations can exist in benign conditions. A diagnosis requires information beyond clinical assessment because it needs biopsy assessment under microscopic examination. A benthic gn or malignant lesion, along with its

specific subtype and grade, needs histopathological evaluation to predict future disease progression (3).

Neuroendocrine carcinomas are uncommon cancers seen through microscope studies. They exhibit special tissue patterns yet grow at a pace above typical squamous cell carcinomas (1). Both leiomyosarcoma and chondrosarcoma exhibit various field pathological factors necessary for these infrequent laryngeal primary sarcomas (4). A diagnosis can be determined through the clinicopathological approach by combining historical and physical information with radiological observations and laboratory outcomes. Using hematoxylin, eosin stain, immunohistochemistry, and molecular research techniques provides essential information about tumors' biological characteristics while advancing diagnosis. The examinations enable doctors to discover information about lymph node metastasis along with the depth of invasion and confirm perineural or vascular involvement, which serves as vital indicators of prognosis (5). According to research, histopathological analysis now reveals that Epstein-Barr virus (EBV)- associated neuroendocrine carcinomas of the nasopharynx constitute new emerging entities with important clinical implications (6).

The laryngeal cancer burden in Pakistan becomes worse because patients show delayed care admission, lack of sufficient understanding of cancer, and limited access to specialized diagnostic testing services. Histopathological diagnosis of laryngeal lesions has proved essential for detecting uncommon histological types that affect treatment approaches in the region (7). Local clinicopathological examination of laryngeal carcinomas helps public health officials create specific intervention approaches and allocate resources to support healthcare needs in their area (8). The analysis of CD44 cell surface glycoproteins involved in tumor progression has proven helpful for oral and oropharyngeal carcinoma diagnosis and offers practical utility for future laryngeal cancer evaluation (10).

The diagnosis and management of laryngeal squamous cell carcinoma benefit from human papillomavirus (HPV) status and PD-L1 expression as two critical prognostic factors (11). Early-stage laryngeal squamous cell carcinoma identification is enhanced using Topoisomerase II alpha (TopoIIa) as a promising immunohistochemical marker (12). Research improvements that merge computerized learning methods into tissue examination techniques have started remolding clinical approaches to treat laryngeal cancer. Computational algorithms evaluate intricate tissue patterns, after which they provide outcome predictions and personalized treatment recommendations for health professionals (13). The field of laryngeal cancer research now recognizes molecular biomarkers after years of being considered out of reach for this form of cancer. Analyzing genetic expression patterns combined with oncogenes and tumor suppressor gene mutations improves ways to classify patients and adjust their treatment methods (14).

However, recently, scientists have become more interested in the relationship between HPV and laryngeal carcinoma. The role of these viruses in giving rise to laryngeal cancer is similar to oropharyngeal cancer, as detected by polymerase chain reaction (PCR) high-risk HPV genotyping (15). It is necessary that standard practice of virological analysis be part of routine histopathological examinations to identify specific patient groups with laryngeal carcinoma.

Objective: The aim of the research is to find out the effect of histopathological examination on early laryngeal carcinoma cancer diagnosis and other associations between clinical and pathological characteristics for improved diagnostic accuracy and patient care.

MATERIALS AND METHODS

Study Design: Cross-sectional clinicopathological study.

Study setting: The research was carried out in the pathology of the Department of Mayo Hospital Lahore, Pakistan, which concurrently processed and worked in the ENT Department for biopsy procedures and patient evaluation.

Duration of study: The research spanned the execution from 6 months from the beginning of December, 2024 to March, 2025.

Inclusion Criteria:
Studies group included any diagnosis of hoarseness, dysphonia or any early laryngeal pathology symptom and older than 18 year of age, both male and female. Patients with clinical suspicion of early laryngeal carcinoma whom were diagnosed to be biopsied and then histopathologically examined were included. The study was conducted on every participant upon their written consent.

Exclusion Criteria
Patients diagnosed previously with laryngeal carcinoma and patients undergoing any malignancy treatment as well as those with no clinical or histopathological data were excluded from the study. Patients faced exclusion if their cancer had reached an advanced stage or if their medical conditions made biopsy medically infeasible.

Methods
Analyzing patients with early laryngeal carcinoma symptoms, including persistent hoarseness combined with throat discomfort along with voice alterations, involved treatment from experienced ENT specialists. After thoroughly assessing the patient's medical history, the specialists performed indirect laryngoscopic examination and imaging tests when required. Medical professionals obtained suspicious laryngeal tissue during procedural direct laryngoscopy after administering general anesthesia to the patient. The laboratory experts used a 10% formalin solution to fix the obtained specimens for subsequent processing at the histopathology department through standard hematoxylin and eosin staining protocols. Experienced pathologists conducted histopathological evaluations to determine cellular characteristics, tumor classification, tissue aggressiveness, and the depth to which cancer cells penetrated. The laboratory used Immunohistochemistry testing on particular case samples to assist in diagnosis and separate different histological subtypes if needed. Examining histopathological results obtained from patients revealed their correlation with epidemiologic characteristics, risk factor analysis, and clinical staging procedures. SPSS software was used to analyze data, while descriptive statistics provided frequencies and percentages regarding tumor types and clinical features.

RESULTS
Sixty patients with early-stage laryngeal carcinoma were included in this research study. The included patient group consisted of individuals aged between 38 and 72 years, with an average age of 56.4 years. Out of the 60 diagnosed patients, only 16.7% (n=10) were female, with males making up the majority at 83.3% (n=50), creating a 5:1 male-to-female ratio. The most frequent presentation among treated patients included hoarseness of voice (76.7%) alongside sore throat (11.7%) and dysphagia (6.7%), the period of symptoms developed between three weeks and four months.
HP analysis showed squamous cell carcinoma (SCC) as the most frequently diagnosed histological type after examining fifty cases, which amounted to 83.3% behavior. The well-differentiated subtype dominated SCC pathological examinations, while moderately differentiated and poorly differentiated subtypes followed at thirty and twelve percent, respectively. The available data revealed four patients with neuroendocrine carcinoma (6.7%), while spindle cell carcinoma (5%) had three cases along with verrucous carcinoma (5%, n=3).

Table 1 shows the distribution of histological subtypes.

Table 1: Distribution of Histological Types of Laryngeal Carcinoma (n=60)

Histological Type	Frequency (n)	Percentage (%)
Squamous Cell Carcinoma	50	83.3
- Well Differentiated	29	58.0
- Moderately Differentiated	15	30.0
- Poorly Differentiated	6	12.0
Neuroendocrine Carcinoma	4	6.7
Spindle Cell Carcinoma	3	5.0
Verrucous Carcinoma	3	5.0

The glottis remained the most affected site for laryngeal tumors, at 65%. The supraglottic area followed closely at 25%, and subglottic areas accounted for the remaining (10%).

Table 2: Anatomical Site of Tumor Involvement

Site	Frequency (n)	Percentage (%)
Glottic	39	65.0
Supraglottic	15	25.0
Subglottic	6	10.0

The analysis showed that tobacco use existed among 73.3% (n=44) of patients, although alcohol consumption was detected in 26.7% (n=16) of the sample. The most common method of tobacco usage among users involved smoking at a rate of 90.9%, but a few patients engaged in smokeless tobacco consumption. Most patients with well-differentiated SCC were diagnosed as chronic smokers.

Table 3: Risk Factor Distribution Among Patients

Risk Factor	Frequency (n)	Percentage (%)
Tobacco Use	44	73.3
- Smoking	40	90.9 (of users)
- Smokeless Tobacco	4	9.1 (of users)
Alcohol Consumption	16	26.7
No Risk Factors	8	13.3

The study implicitly reveals how squamous cell carcinoma dominates early laryngeal cancers when they are well-differentiated and closely linked to smokers and glottic positioning.

DISCUSSION

The present evaluation analyzed early laryngeal carcinoma by examining its clinicopathological characteristics through histopathological diagnostic methods. The diagnosis of early-stage laryngeal cancer demands histopathological evaluation because the nonspecific clinical symptoms frequently mimic benign laryngeal lesions. Understanding tumor differentiation and anticipated behavior benefits therapeutic choices and prognostic expectations because histopathology helps identify tumor types. Hoarseness of voice stood as the primary symptom, leading patients to seek medical help at the first instance ahead of sore throat complaints and dysphagia symptoms. According to available research, glottic carcinoma manifests first as hoarseness and continues to be the most persistent symptom of this tumor type, which occurs most frequently (1). Global research data supports our findings because it demonstrates that men develop laryngeal cancer more regularly. Overall, they consume tobacco and alcohol in higher amounts (2). Priya (2) noted the same gender disproportion using data from his tertiary care center research.

Most cases examined within our study were squamous cell carcinomas (SCC) presenting as well-differentiated types. Research shows that SCC is the primary histological variant of laryngeal carcinoma (3).

Zidar et al. (3) showed that well-differentiated tumors bring better treatment outcomes and decreased aggressive tendencies in laryngeal cancer patients. Our study results show that well-differentiated SCC dominates the histological profile because early detection leads to these more favorable patient types. Our study identified rare exceptions of neuroendocrine, such as spindle cell and verrucous carcinoma histological variants. These subtypes pose specific clinical challenges that are infrequently observed. Neuroendocrine carcinomas show aggressive behavior, according to Strojan et al. (1) as well as Chen et al. (6), although these tumors have unique molecular signatures. Preoperative analysis of these tumors needs exact histological assessment to select the correct treatment options. Studies by

Velez Torres et al. (4) and Abu-Dayeh et al. (7) demonstrate how spindle cell carcinoma represents the heterogeneity of laryngeal tumors alongside explaining the need for histopathological evaluation to differentiate these cancers from non-epithelial malignancies.

The distribution of tumors in our study matched earlier clinicopathological research findings by appearing mainly in the glottic region and then in the supraglottic and subglottic areas (8). The early diagnosis of glottic tumors occurs because voice changes detectable to patients become evident before symptoms linked to supraglottic or subglottic tumors appear. The early diagnosis benefits from these findings because glottic cancers at stage one are better suited for organ-preserving treatments. The study showed that many of our patients were tobacco users among the etiological factors. Multiple studies have demonstrated that tobacco use leads to the formation of laryngeal cancer tumors (9). Research indicates that alcohol consumption, combined with tobacco, became a factor in laryngeal cancer development. Studies prove that tobacco and alcohol consumption together enhance the DNA-altering effects of carcinogens. At the same time, they degrade the protective functions of mucous membranes. According to Yang et al.(11), molecular research shows that HPV-negative SCCs tie more frequently to lifestyle factors, including smoking behaviors.

Traditional histological diagnosis now shares prominence with newly important molecular and immunohistochemical tests, which help both the early identification of laryngeal carcinoma and the prediction of its disease progression. Salama et al. (12) research established Topoisomerase II alpha (TopoIIa) as an excellent biomarker for detecting early-stage laryngeal SCC. However, although not directly evaluated, the high frequency of well-differentiated tumors entails that such markers need to be considered in further research to refine diagnostic accuracy. As explained by Alshwayyat et al. (13), the contribution of artificial intelligence and machine learning in personalized cancer care indicates that 'clinicopathological data,' as well as advanced computational tools, can improve diagnostic precision and treatment planning. This is an essential approach for diagnosing rare subtypes or ambiguous samples of histological reading.

Falco et al. (14) described the role of molecular biomarkers in the early diagnosis, prediction of treatment response, and targeted therapy of laryngeal cancer, focusing on the proposed benefits of biomarkers. The role of HPV in laryngeal carcinoma has continuously been studied. However, Nasseef et al. (15) confirm an association of HPV with a subgroup of laryngeal tumors. A particular morphological and clinical behavior has been demonstrated in laryngeal cancers that are HPV-positive, and this may have important prognostic and therapeutic response implications. Although HPV testing was not included in our study, future studies may consist of HPV status as part of routine investigation for early laryngeal cancer.

The results of the present study are also relevant to current treatment practice. Treatment patterns and outcomes in laryngeal cancer were documented by Đokanović et al. (8), who have observed that laryngeal cancer is curable at early stages of the disease. Additional support for accurate histopathological diagnosis is given as the cornerstone for staging and treatment planning. As described by Singh et al., the utility of immunohistochemical markers such as CD44, compared with clinical carcinoma features (10), also provides another aspect of the histopathological approach. These can give you an understanding of tumor aggressiveness, recurrence potential, and response to treatment.

CONCLUSION

According to this research, early diagnosis and laryngeal carcinoma classification depend heavily on histopathological examination. The study demonstrates that squamous cell carcinoma frequently presents as the dominant histological subtype with well-differentiated features along with glottic location, and it displays a connection to tobacco exposure and gender preferences towards males. Timely cancer detection becomes feasible through early symptoms of hoarseness, which generally affect glottic tumors specifically. Evaluating tissue under a microscope is a diagnostic tool to confirm both cancers. It allows practitioners to understand tumor complexity, pick treatments that best suit each patient, and project expected outcomes. Tissue examination must be meticulous because it can reveal unusual histological tumor types. Combination analysis of laryngeal cancer tissue improves

patient outcomes and reduces disease burden and improves quality of life. However, there should be multiple centers that do some further research to prove and develop these results.

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