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Original article

Analysis of Immune System Responses in Lymph Nodes and The Pattern of Malignant Tumor Cell Infiltration in Oral Squamous Cell Carcinoma

Asmaa Algharyani*, Marwa Maghrabi

Department of Oral and Maxillofacial Pathology, Faculty of Dentistry, Tripoli University, Tripoli, Libya.
Email. *asm_1981mmm@yahoo.com*

Abstract
The host immune response to malignant tumor cells was evaluated indirectly by the immunomorphological patterns observed in the lymph nodes. (LNs), which function as indicators of the patient's immunological status and may either facilitate or hinder the localization of tumor cells during a metastatic event. This study sought to evaluate the immunomorphological patterns of LNs in head and neck cancer and to correlate these patterns with the histological grading of OSCC. An additional evaluation was conducted to determine the pattern of tumor cell infiltration in lymph node metastases. The current investigation was conducted on seventy archival paraffin blocks of oral squamous cell carcinoma (OSCC), comprising twenty-five well-differentiated squamous cell carcinoma (WDSCC), twenty-four moderately differentiated squamous cell carcinoma (MDSCC), and twenty-one poorly differentiated squamous cell carcinoma (PDSCC). One hundred thirty-nine lymph nodes were collected from seventy cases of OSCC, which were classified into four distinct patterns. From seventy cases of OSCC, 139 lymph nodes were harvested. The prevailing pattern of lymph node reactivity was lymphocyte predominance (54.7%), followed by germinal center predominance (41%). Furthermore, while analyzing the immunomorphological patterns of LNs and the invasion patterns of neoplastic cells in metastatic lymph nodes, the islands/sheets pattern of tumor cells exhibited a high lymphocyte predominance, whereas the total replacement of neoplastic cells was mainly observed in nodes with germinal center predominance. The immunomorphological patterns of regional lymph nodes in OSCCs appear to be a crucial prognostic predictor. The cell-mediated immune response, characterized by lymphocyte predominance and sinus histiocytosis, restricts metastasis, while the humoral response, marked by germinal center predominance, promotes metastasis.
Keywords. Tumor Invasion Pattern, Immunomorphological Patterns, Lymph Node Metastasis, Different Grades of OSCC.

Introduction

Cancers of the head and neck (HNCs) rank as the sixth most prevalent cancer globally, exhibiting a steadily rising total incidence, with an anticipated annual increase over the coming decade. Oral Squamous Cell Carcinoma (OSCC) is the predominant malignant tumor among head and neck cancers (HNC). The prognosis is affected by various factors, including patient characteristics (age, sex, etc.) and tumor properties (size, location, histology, host immune response, and metastasis). The development of lymph node metastases is considered the most significant factor influencing the prognosis of individuals with OSCC [1,2].

In recent years, increasing attention has been directed toward the host immune response and its defense mechanisms against tumor progression. Lymph nodes reflect the patient's immunological status and may either promote or inhibit the homing and establishment of tumor cells during metastatic spread. The host immune response is discerned by analyzing diverse immunoreactive patterns within the lymph node. The World Health Organization (WHO) suggested a standardized reporting method for the morphological properties of lymph nodes concerning immunological function, utilized to delineate the immunomorphological patterns of lymph nodes. Furthermore, the immunologic reactivity of a regional lymph node can be delineated by examining its microscopic morphology [3].

The evaluation of immunomorphological patterns in lymph nodes will clarify the host-tumor immunological relationship and offer further insights into patient prognosis by facilitating the early identification of cancers that show a propensity for metastasis. This study concentrates on changes in morphology in lymph nodes by recognizing, evaluating, and connecting various patterns in metastatic lymph nodes with the histological grading of oral squamous cell carcinoma and the tumor cell invasion patterns inside the lymph nodes.

Methods

In this study, seventy archival formalin-fixed and paraffin-embedded tissue blocks of oral squamous cell carcinoma with confirmed lymph node metastases were included. The cases were histologically classified into three groups according to Broders' classification: twenty-five well-differentiated, twenty-four moderately differentiated, and twenty-one poorly differentiated OSCCs. From these seventy cases, 139 metastatic lymph nodes were obtained. All tissue specimens were obtained from the archival blocks maintained in the General Pathology Department at the Tripoli University Hospital. After being fixed in 10% formalin, the lymph node tumors from every OSCC case were processed and prepared into paraffin blocks. Following that, standard Hematoxylin and Eosin techniques were used to produce slices that were 4 µm thick and then to stain them.

Following the guidelines provided by Tsakraklides et al., four separate morphological patterns were identified in each metastatic lymph node: lymphocytic predominance (Figures 1, 2), germinal center predominance (Figure 3), sinus

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histiocytosis (Figure 4), and lymphocytic depletion. Meanwhile, the lymph node tumor cell invasion pattern was categorized as either island/sheets (Figure 5), strands/cords (Figure 6), or total replacement.
Data were entered into the computer and analyzed using the IBM SPSS software package version 30.0 (Armonk, NY: IBM Corp.). Qualitative data were described using numbers and percentages. The statistical association was evaluated using the Pearson Chi-Square test of independence, with results considered statistically significant at a P-value less than 0.05. Qualitative data are described using frequencies and percentages.

Results

Twenty-five of the seventy OSCC cases had WDSCC, twenty-four had MDSCC, and twenty-one had PDSCC. 139 lymph nodes from 70 OSCC cases were collected for this investigation. Lymphocyte predominance was the most common pattern of lymph node reactivity at 54.7% (n=76) (Figure 1&2), followed by germinal center predominance at 41% (n=57) (Figure 3), sinus histiocytosis at 4.3% (n=6) (Figure 4), and lymphocytic depletion at 0% (n=0). illustrates the demographic data [Table 1]. Fifty lymph nodes were extracted from 25 cases of WD OSCC; among these, 64% (n=32) exhibited a lymphocytic predominance pattern, 32% (n=16) presented a germinal center predominance pattern, 4% (n=2) presented a sinus histiocytosis pattern, and 0% (n=0) exhibited a lymphocytic depletion pattern. Forty lymph nodes were obtained from twenty-four cases of MD OSCC; among these, 70% (n=28) exhibited a lymphocytic predominance pattern, 22.5% (n=9) displayed a germinal center predominance pattern, 7.5% (n=3) presented a sinus histiocytosis pattern, and 0% (n=0) revealed a lymphocytic depletion pattern. In twenty-one cases of PD OSCC, 49 lymph nodes were examined; of which, 32.7% (n=16) had a lymphocytic predominance pattern, 65.3% (n=32) exhibited a germinal center predominance pattern, 2% (n=1) showed a sinus histiocytosis pattern, and 0% (n=0) demonstrated lymphocytic depletion.
The current study revealed a higher prevalence of the LP pattern in WDSCC and MDSCC, with percentages of 64% and 70%, respectively. Conversely, the GCP pattern was most prominent in poorly differentiated squamous cell carcinoma, at 65.3%, while the SH pattern exhibited the lowest occurrence in poorly differentiated SCC. A highly significant statistical association was observed between lymph node immunoreactivity patterns and tumor differentiation grade (Table 1; Graph 1). Regarding the studied groups, the least frequent pattern of total replacement invasion in our study was observed in all cases of well- and moderately differentiated SCC. At the same time, the highest frequency was recorded in PDSCC. However, the islands/sheets pattern of tumor cells was highest in well- and moderately differentiated OSCC. Statistical analysis revealed a highly significant correlation between the tumor differentiation grade and the pattern of cancer cell invasion (Table 2), Graph 2). Moreover, in the comparative analysis of immuno-morphological patterns and the invasion patterns of neoplastic cells in metastatic LNs, the islands/sheets configuration of tumor cells exhibited a higher prevalence in lymphocyte predominance (Figure 5), whereas the total replacement was more obvious in the germinal center. Statistical analysis using the Chi-Square test showed a highly significant correlation between the lymph node immunoreactive patterns and the pattern of invasion (Table 3, Graph 3).

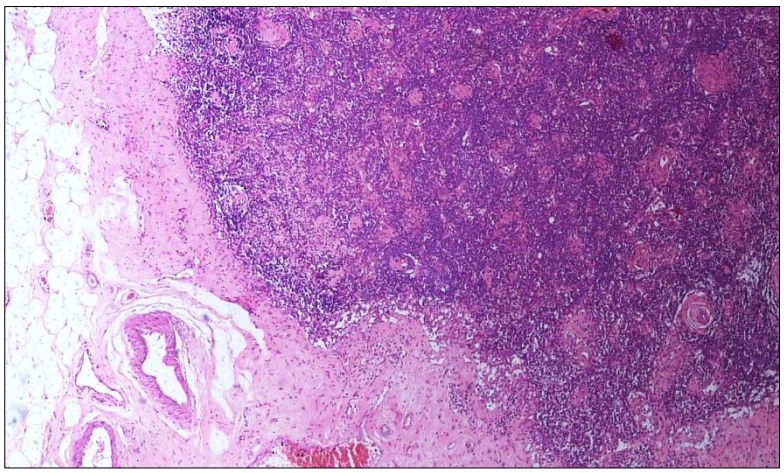

Figure 1. Photomicrograph exhibiting a prominent lymphocyte pattern (H and E section, ×10 magnification).

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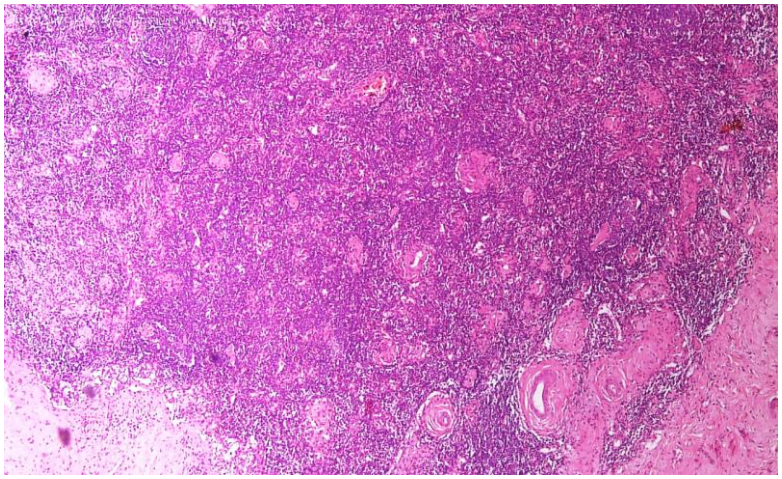

Figure 2. Another photomicrograph showing a lymphocyte-predominant pattern (H and E section,×100 magnification)

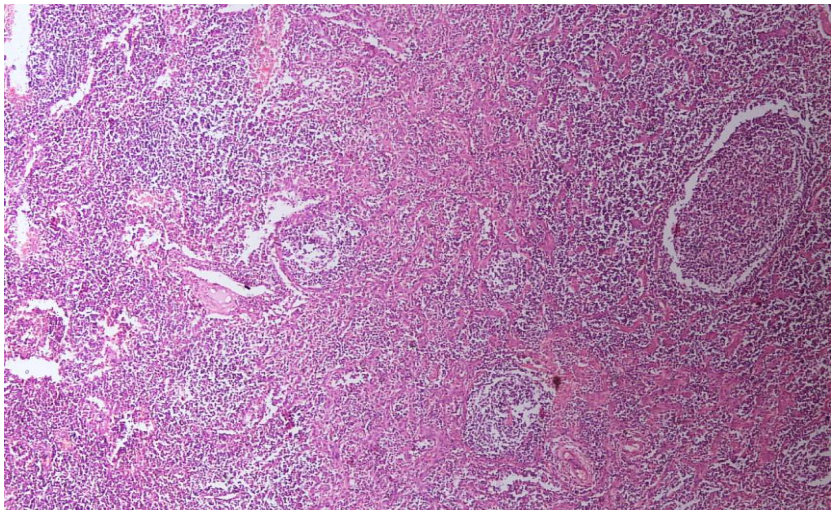

Figure 3. Photomicrograph demonstrating a germinal center-predominant pattern (H and E section, ×100 magnification)

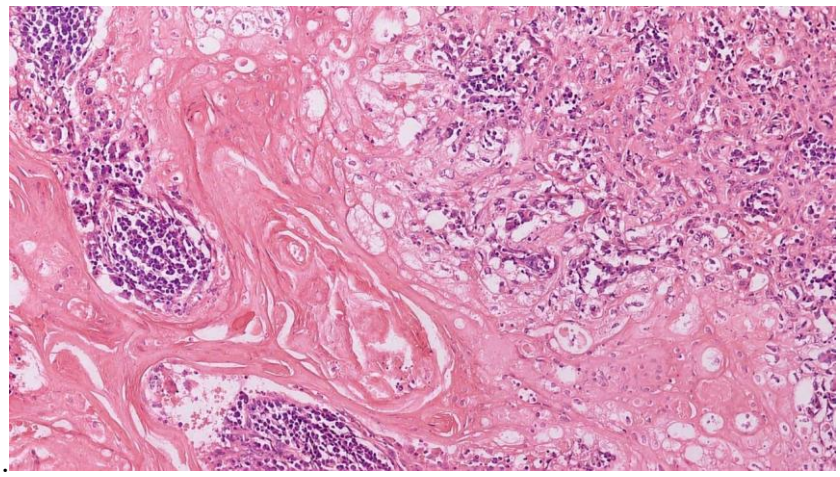

Figure 4. Photomicrograph showing sinus histiocytosis (H and E section, ×200 magnification).

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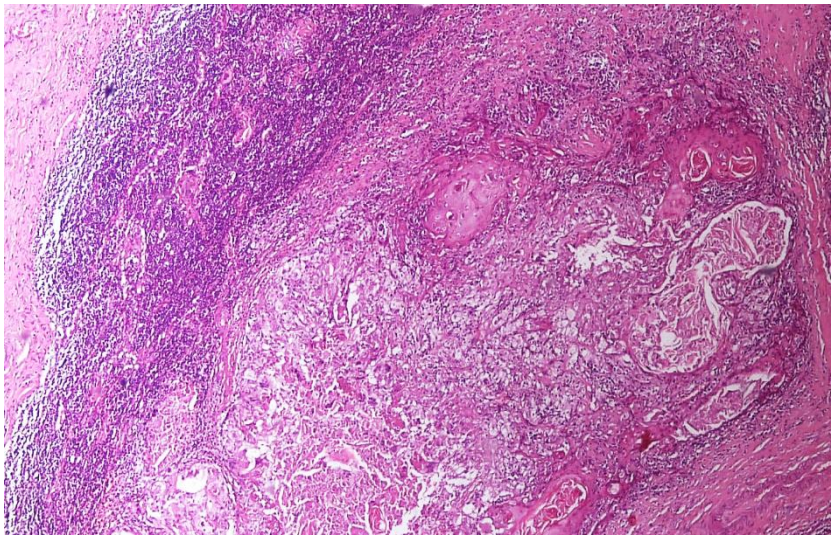

Figure 5. Photomicrograph illustrating tumor cell invasion in the form of islands within the LNs (H and E section, ×100 magnification)

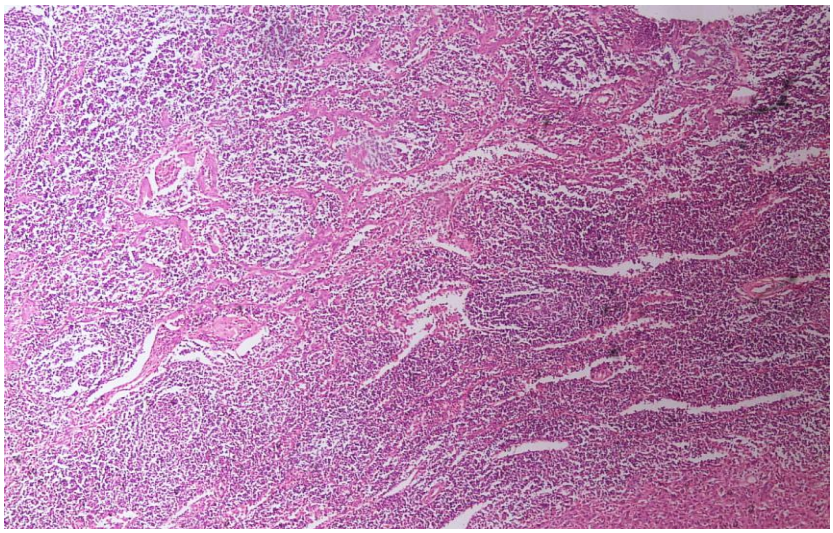

Figure 6. Photomicrograph showing tumor cell invasion in the form of cords within LNs (H and E section, 100X magnification)

Table 1. Comparison between immuno-morphological patterns of metastatic LNs and grading of the OSCC

Grading	Number of metastatic LNs	Immunological pattern of LN				p-value
		LP	GCP	SH	LD	
Well-differentiated (n= 25 cases)	50 (36%)	32(64%)	16(32%)	2(4%)	0(0)	**P<0.01**
Moderately differentiated (n= 24 cases)	40 (28.8%)	28(70%)	9(22.5%)	3(7.5%)	0(0)	
Poorly differentiated (n= 21cases)	49 (35.2%)	16(32.7%)	32(65.3)	1(2%)	0(0)	
Total 70(100%)	139 (100%)	76 (54.7%)	57 (41%)	6 (4.3%)	0(0)	

(X^2); 19.78, P<0.01: highly significant. LP (lymphocyte predominance), GCP (germinal center predominance), sinus histiocytosis (SH), and LD (lymphocytic depletion).

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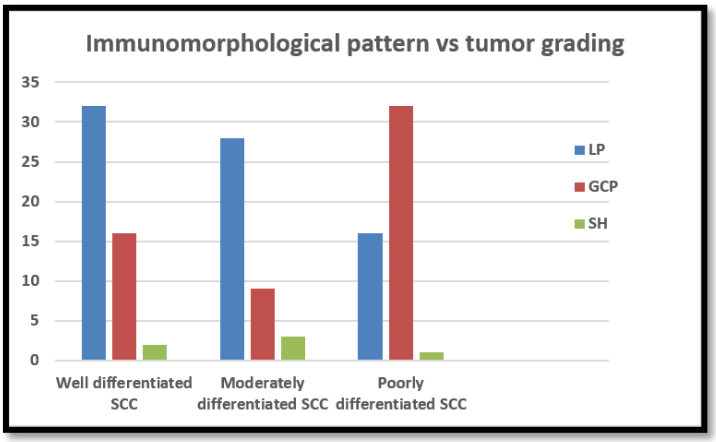
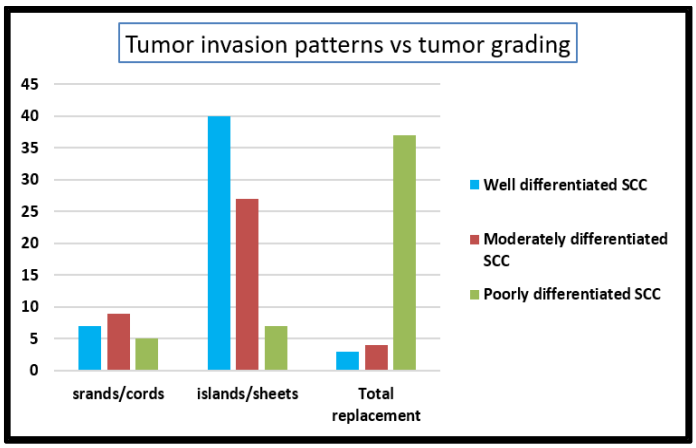


Graph 1. Immunomorphological patterns and tumor grading of OSCC

Table 2. Correlation between grading of the tumor and the tumor cells' invasion pattern in metastatic LNs

Grading of OSCC	Pattern of the tumor cells' invasion in LN			p-value
	Strands/cords	Islands/sheets	Total replacement	
Well-diff (LN= 50)	7(14%)	40 (80%)	3 (6%)	(P<0.01)
Moderately-diff (LN= 40)	9(22.5%)	27 (67.5%)	4 (10%)	
Poorly-diff (LN= 49)	5(10.2%)	7 (14.3%)	37 (75.5%)	
Total LN=139 (100%)	21 (15.1%)	74 (53.2%)	44 (31.7%)	

(X^2); 70.58, P<0.01: highly significant.



Graph 2. Tumor invasion patterns and tumor grading of OSCC

Table 3. Correlation between immuno-morphological patterns and the tumor cells invasion pattern in metastatic LNs

Immuno-morphological patterns	Pattern of invasion of neoplastic cells			p-value
	Strands/cords	Islands/sheets	Total replacement	
LP (n=76)	9 (11.8%)	60 (79%)	7 (9.2%)	(P<0.01)
GCP (n=57)	10 (17.5%)	13 (22.8%)	34 (59.6%)	
SH (n= 6)	2 (33.3%)	1 (16.7%)	3 (50%)	
LD (n=0)	0(0%)	0(0%)	0(0%)	
Total LN=139 (100%)	21 (15.1%)	74 (53.2%)	44 (31.7%)	

(X^2); 53.4, P<0.01: highly significant.

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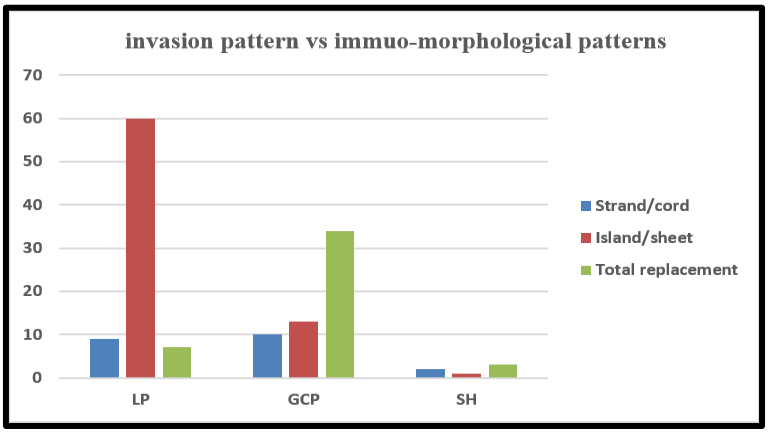

Graph 3. Tumor invasion patterns and immuno-morphological patterns

Discussion

The squamous cell carcinoma of the head and neck (HNSCC) remains a considerable global health concern. According to the latest GLOBOCAN estimates, an estimated 20.6 million new cancer cases were diagnosed, and 9.8 million deaths occurred worldwide in 2024, highlighting the persistent and growing global burden of the disease [6]. This is mainly attributable to the heightened incidence of loco-regional recurrence and later to distant metastases. The prevalence of regional lymph node metastases in head and neck cancer is significant and serves as a crucial factor in overall clinical outcome [7].

Regional lymph nodes in OSCC are essential organs that significantly enhance the immune response to neoplastic cells. Complex interactions of immune defenses between lymphoid populations and tumor-presented antigens, which ultimately influence the histological patterns observed within the nodes [8]. The immunomorphological reactivity revealed in the 139 analyzed lymph nodes in our study coincides with the fundamental principles outlined by Berlinger et al. [9]. Our findings indicated that lymphocyte predominance was the predominant pattern of reactivity in the lymph nodes. This finding was in alignment with the classic concepts established by Tsakraklides et al. [10], who emphasized that T-cell-mediated proliferation in regional nodes serves as a protective barrier hindering early tumor dissemination. Furthermore, a similar trend was noted by several researchers, including Jadeja et al. [11], Yadav et al. [12], Kalyani et al. [13], Suchitra et al. [14], and Balla et al. [15], who also found that lymphocyte predominance was the most frequent pattern in lymph nodes

In the meantime, germinal center dominance was the second most common pattern in our analysis with 41%(n=57). GCP is indicative of active antigenic stimulation as described by Makesh Raj et al. [16]. The result was consistent with the findings by Bhatlawande et al. [17], who indicated that regional lymph nodes in head and neck malignancies exhibit changes in architectural dominance influenced by the tumor microenvironment and the expression level of tumor antigens. In relation to the histological grades of OSCC, the current investigation showed a significant difference regarding the immunomorphological characteristics of metastatic lymph nodes. While germinal center predominance lymph nodes were seen in PDSCC, the lymphocyte predominance pattern was most prevalent in WDSCC and MDSCC. These observations agreed with the data published by Balla et al. [15] and Raj et al. [16]. This can be elucidated by the observation that lymph nodes exhibiting a lymphocytic predominance pattern may signify an active cell-mediated immune response that might help delay distant metastases.

On the other hand, germinal centers in lymph nodes denote a humoral response to antigenic stimuli, which involves plasma cells and antibody production, and this might assist distant metastasis. The mechanism via which humoral immunity facilitates nodal invasion remains unidentified. A humoral immune response may facilitate the tumor to disseminate through the lymph nodes by hindering or impairing the cytotoxic function of T-lymphocytes and histiocytes [16]. A noticeable pattern of germinal centers was also seen in patients who developed cancer recurrence, indicating invasion of the cancer cells in the nodes and a worse prognosis. Yadav et al. observed that patients exhibiting a GCP pattern had twice the incidence of cervical lymph node metastases compared to patients with a lymphocyte predominance, which was a statistically significant finding. On the other hand, the SH pattern was the least prevalent in poorly differentiated OSCC compared to WDSCC and MDSCC. In instances of sinus histiocytosis, the prevalence of macrophages and histiocytes does not denote a specific type of immune response. The accumulation of macrophages in sinus histiocytosis was oriented against the tumor and regarded as the initial morphological response of the host immune system to the tumor. These results were analogous to those attained by Mady et al. Regarding the neoplastic pattern of tumor cells in metastatic deposits in lymph nodes with respect to grading in our study, the highest frequency pattern of total replacement invasion was observed in cases of poorly differentiated OSCC, which supports the hypothesis that germinal center predominance promotes metastasis. These findings were aligned with the research conducted by Jadeja et al. [11] and Balla et al. [15].

Conclusion

Various head and neck disorders may have distinct histologic immunoreactive patterns in the lymph nodes. These specific patterns reflect both the underlying pathology and the patient's immune response, which can be useful for planning therapy

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and predicting clinical outcomes. Thus, the analysis and integration of different lymph node patterns in the reporting of neck dissection cases may aid physicians in formulating treatment strategies and evaluating prognosis in OSCC.

Conflicts of Interest

No conflicts of interest exist.

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References

1. Li Y, Wu Y, Li X, Lin Y, Chen Y, Yang H, et al. Clinical and molecular characterizations of HNSCC patients with occult lymph node metastasis. Sci Rep. 2025;15:25263.
2. Johnson DE, Burtness B, Leemans CR, Lui VWY, Bauman JE, Grandis JR. Head and neck squamous cell carcinoma. Nat Rev Dis Primers. 2020;6(1):92.
3. Prema S. Morphological assessment of lymph nodes draining carcinoma. MGM J Med Sci. 2016;3:192-7.
4. Okura M. Lymph node metastasis. In: Pandalai SG, editor. Recent research developments in cancer. Vol. 4. Trivandrum: Transworld Research Network; 2002. p. 331-7.
5. Saldanha P. Morphological assessment of lymph nodes draining carcinoma. MGM J Med Sci. 2016;3:190-7.
6. Sung H, Filho AM, Laversanne M, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2024: GLOBOCAN estimates of incidence and mortality worldwide for 34 cancers in 186 countries. CA Cancer J Clin. 2026.
7. Mady HR, Darwish ZE, Ramadan OR, Abdel-bary AM. Immuno-morphological patterns of lymph nodes draining oral squamous cell carcinoma. Alex Dent J. 2019;44(3):93-8.
8. Contaldo M, Di Napoli A, Pannone G, Franco R, Ionna F, Feola A, et al. Prognostic implications of node metastatic features in OSCC: a retrospective study on 121 neck dissections. Oncol Rep. 2013;30(6):2697-704.
9. Berlinger NT, Tsakraklides V, Pollak K, Adams GL, Yang M, Good RA. Immunologic assessment of regional lymph nodes in malignant tumors of the head and neck. Am J Surg. 1976;132(4):476-83.
10. Tsakraklides V, Anastassiades OT, Kersey JH. Prognostic significance of regional lymph node histology in uterine cervical cancer. Cancer. 1973;31(4):860-8.
11. Jadeja N, Parikh N, Nandini C. Assessment of immunomorphological patterns in metastatic and non-metastatic lymph nodes of oral squamous cell carcinoma patients. Adv Hum Biol. 2023;13(3):261-6.
12. Yadav ST, Madhu Shankari GS, Chatura K, Dhanuja RJ, Rashmi M. Immunomorphological assessment of regional lymph nodes for predicting metastases in oral squamous cell carcinoma. Indian J Dent Res. 2012;23(6):1212.
13. Kalyani T, Yadav Y, Rai AL, Shetty D, Kaul N. Immunohistochemical evaluation of tumor angiogenesis and architectural changes in regional lymph nodes of oral squamous cell carcinoma (OSCC). Int J Health Sci. 2022;6(S9):1621-32.
14. Suchitra G, Puranik RS, Vanaki SS, Prasad BG, Malgaonkar NI. Immunoreactivity of excised lymph nodes in neck dissections of squamous cell carcinoma of oral cavity. J Oral Maxillofac Pathol. 2015;19(2):128-33.
15. Balla H, Uppala D, Majumdar S, Kotina S, Kodati S, Namana M. Evaluation of immunomorphological patterns of cervical lymph nodes in oral squamous cell carcinoma. J Oral Maxillofac Pathol. 2020;24(2):285-92.
16. Raj LSM, Boaz K, Natarajan S. Prognostic significance of lymph node pattern in oral squamous cell carcinoma (OSCC). J Clin Diagn Res. 2014;8(1):232-5.
17. Bhatlawande HC, Kale AD, Desai KM, Hallikerimath S, Belaldavar C, Mane D, et al. Role of immunoreactive patterns of lymph nodes in neck dissection cases of oral squamous cell carcinoma: A clinical and histopathological study. J Korean Assoc Oral Maxillofac Surg. 2019;45(5):267-75.

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