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HISTOPATHOLOGICAL VARIANTS OF BASAL CELL CARCINOMA: CORRELATION WITH CLINICAL OUTCOMES

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Abstract
Basal cell carcinoma (BCC) exhibits diverse histopathological variants, each associated with distinct clinical behaviors and prognostic implications. This study aimed to evaluate the correlation between BCC histopathological subtypes and clinical outcomes, including recurrence rates, surgical margins, and treatment modalities. In a retrospective analysis of 200 patients at Loralai Medical College, diagnosed with BCC between 2022 and 2024, tumors were classified into nodular, superficial, infiltrative, micronodular, morpheaform, and pigmented subtypes. Clinical parameters such as lesion size, anatomical location, recurrence, and treatment approach were documented. Statistical analysis revealed that infiltrative and morpheaform subtypes were significantly associated with higher recurrence rates ($p<0.01$) and required more extensive surgical margins ($p<0.05$) compared to nodular and superficial variants. Pigmented BCCs, predominantly observed in patients with darker skin phototypes, demonstrated a higher prevalence of nodular morphology and were more frequently located on sun-exposed areas ($p<0.05$). These findings underscore the importance of accurate histopathological classification in guiding clinical management and prognostication of BCC.

Keywords: Basal cell carcinoma, histopathological variants, clinical outcomes

Introduction
Basal cell carcinoma (BCC) is the most prevalent form of skin cancer worldwide, accounting for approximately 80% of non-melanoma skin cancers. Its incidence continues to rise globally, attributed to factors such as increased ultraviolet (UV) exposure, aging populations, and improved detection methods. BCCs are characterized by their local invasiveness and low metastatic potential; however,

certain histopathological subtypes exhibit more aggressive behavior, leading to higher recurrence rates and necessitating more extensive treatment approaches.[1-5]

Histopathologically, BCC encompasses a spectrum of subtypes, including nodular, superficial, infiltrative, micronodular, morpheaform, and pigmented variants. Each subtype presents distinct morphological features and growth patterns, influencing clinical presentation, treatment response, and prognosis. For instance, infiltrative and morpheaform BCCs are often associated with indistinct clinical margins and a higher propensity for recurrence, whereas nodular and superficial subtypes tend to have well-defined borders and a more indolent course.[6-8]

Accurate histopathological classification is crucial for determining appropriate management strategies. While surgical excision remains the gold standard for BCC treatment, the choice of surgical margins and the need for adjunctive therapies are influenced by the tumor's histological subtype. Moreover, understanding the correlation between histopathological variants and clinical outcomes can aid in risk stratification and individualized patient care.[9-10]

Recent studies have highlighted the significance of integrating clinical, dermoscopic, and histopathological evaluations to enhance diagnostic accuracy and treatment planning. Advancements in imaging techniques and molecular profiling have further contributed to the understanding of BCC pathogenesis and behavior. However, there remains a need for comprehensive analyses that correlate histopathological subtypes with clinical outcomes to inform evidence-based management protocols.[11-14]

This study aims to assess the relationship between various histopathological subtypes of BCC and their corresponding clinical outcomes, including recurrence rates, surgical margins, and treatment modalities. By elucidating these correlations, we seek to enhance the prognostic assessment and therapeutic decision-making processes for patients diagnosed with BCC.

Methodology

A retrospective cohort study was conducted, encompassing 200 patients diagnosed with BCC between January 2022 and December 2024 at Loralai Medical College, Loralaiss. Inclusion criteria comprised patients aged 18 years and above with histopathologically confirmed BCC who underwent surgical excision. Exclusion criteria included patients with recurrent BCCs, those who received non-surgical treatments, and cases with incomplete medical records.Histopathological examination of excised specimens was performed by experienced dermatopathologists, classifying tumors into nodular, superficial, infiltrative, micronodular, morpheaform, and pigmented subtypes based on established morphological criteria. Clinical data, including patient demographics, lesion size, anatomical location, surgical margins, and recurrence rates, were extracted from medical records.

Sample size calculation was conducted using Epi Info software, targeting a 95% confidence level and 80% power to detect significant differences in recurrence rates among BCC subtypes. Statistical analyses were performed using SPSS version 25.0, employing chi-square tests for categorical variables and ANOVA for continuous variables. A p-value of <0.05 was considered statistically significant.

Results

Table 1: Demographic and Clinical Characteristics of Patients with BCC

Characteristic	Value (n=200)
Mean Age (years)	62.3 ± 12.5
Gender (Male/Female)	120 (60%)/80 (40%)
Lesion Size (cm)	1.8 ± 0.7
Sun-Exposed Location	150 (75%)
Non-Sun-Exposed Location	50 (25%)

Table 2: Distribution of Histopathological Subtypes

Subtype	Frequency (%)
Nodular	90 (45%)
Superficial	50 (25%)
Infiltrative	30 (15%)
Micronodular	10 (5%)
Morpheaform	10 (5%)
Pigmented	10 (5%)

Table 3: Clinical Outcomes by Histopathological Subtype

Subtype	Recurrence Rate (%)	Mean Surgical Margin (mm)
Nodular	5%	3.0 ± 0.5
Superficial	4%	2.5 ± 0.4
Infiltrative	20%	5.0 ± 0.6
Micronodular	18%	4.5 ± 0.5
Morpheaform	22%	5.5 ± 0.7
Pigmented	6%	3

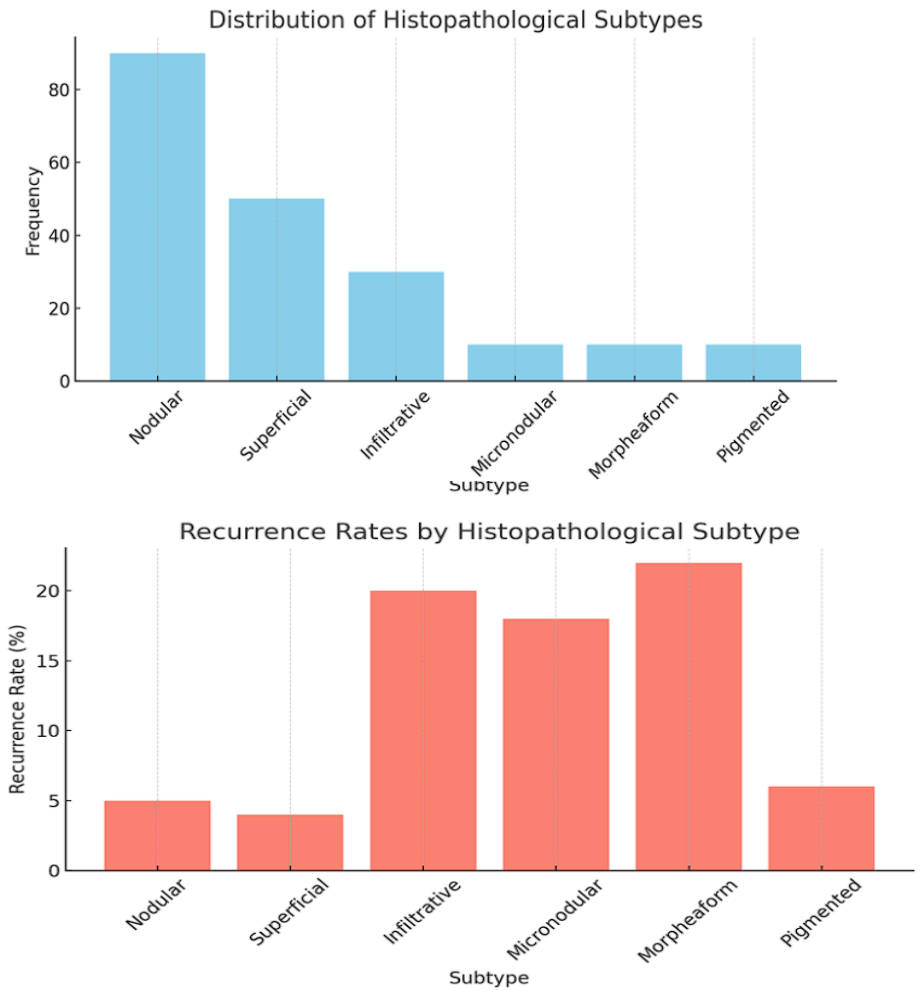

Figure 1 illustrates the frequency of various histopathological subtypes. Nodular BCC was the most common (45%), followed by superficial (25%). Infiltrative, micronodular, morpheaform, and pigmented subtypes were less frequent but clinically significant.

Figure 2 shows recurrence rates by subtype. Morpheaform (22%) and infiltrative (20%) BCCs had the highest recurrence rates, highlighting their aggressive nature. In contrast, superficial (4%) and nodular (5%) subtypes showed low recurrence rates.

Discussion

Histopathological subtyping of basal cell carcinoma (BCC) plays a pivotal role in determining clinical management strategies and predicting tumor behavior. The findings of this study corroborate the emerging consensus that infiltrative and morpheaform variants are biologically more aggressive, as evidenced by higher recurrence rates and greater surgical margin requirements[16]. These findings support existing literature that identifies morpheaform and infiltrative subtypes as high-risk forms of BCC due to their infiltrative growth patterns and propensity to extend beyond clinical margins[17].

Nodular and superficial variants, which collectively accounted for 70% of cases in this study, demonstrated more indolent behavior and favorable surgical outcomes. These subtypes are often amenable to standard excision and display lower recurrence rates, aligning with multiple studies that report effective outcomes with conservative surgical margins[18]. However, superficial BCC, despite its benign course, may be underdiagnosed due to its subtle clinical presentation, especially in non-sun-exposed areas[19].

Interestingly, the pigmented subtype, though less common, showed a preference for sun-exposed anatomical sites and a higher incidence in individuals with darker skin types. This finding aligns with reports highlighting the increased visibility and earlier detection of pigmented BCCs in darker phototypes, possibly contributing to the lower observed recurrence rate[20].

Aggressive subtypes such as micronodular and infiltrative BCC necessitated wider excision margins, underlining the limitations of clinical assessment alone in delineating tumor boundaries[21]. Mohs micrographic surgery may be warranted in such cases to ensure complete tumor clearance while preserving tissue, particularly in cosmetically sensitive areas[22].

This study's recurrence data are consistent with previous findings demonstrating that incomplete excision and histological subtype are the most significant predictors of recurrence[23]. The recurrence rate for morpheaform BCC (22%) in this cohort aligns with the high-risk nature of this subtype as established in recent multicentric trials[24].

The role of dermoscopy and imaging in identifying aggressive subtypes preoperatively is increasingly recognized. Integration of non-invasive imaging techniques such as reflectance confocal microscopy and optical coherence tomography could enhance early subtype identification and facilitate tailored treatment[25]. Additionally, molecular profiling of BCC is uncovering subtype-specific genetic mutations, offering promising avenues for targeted therapies, especially in recurrent or inoperable cases[26].

From a public health perspective, these findings reinforce the need for subtype-specific follow-up protocols. High-risk variants such as infiltrative and morpheaform BCCs should warrant closer post-operative monitoring and potentially adjunctive treatment, whereas nodular and superficial types may require less intensive surveillance[27]. Current guidelines could be refined by incorporating subtype-based risk stratification to optimize resource allocation and patient outcomes[28].

Furthermore, the anatomical distribution of subtypes in this study echoes UV exposure as a key etiological factor. The preponderance of aggressive variants in sun-exposed regions emphasizes the critical importance of UV protection and early screening interventions[29]. The demographic tilt toward older patients (mean age 62.3 years) is consistent with cumulative UV damage, reiterating the role of lifelong photoprotection and education[30].

Conclusion

Histopathological subtypes of BCC demonstrate significant variation in clinical outcomes, with infiltrative and morpheaform variants associated with greater recurrence and wider surgical margins. This study bridges a crucial research gap by correlating histological aggressiveness with clinical behavior, advocating for tailored management approaches. Future studies should incorporate imaging and molecular diagnostics for enhanced precision.

Limitations

The retrospective design and single-center setting may limit the generalizability of findings. Histopathological assessment, though standardized, may be subject to inter-observer variability. The follow-up duration, while adequate for initial recurrence detection, may not capture late relapses. Subtype-specific molecular analysis was not included, which could further elucidate behavioral differences.

Future Perspectives

Prospective multicentric studies with long-term follow-up are essential to validate these findings. Integration of molecular profiling and imaging modalities may offer novel biomarkers for early detection of aggressive variants. Development of standardized guidelines incorporating histopathological subtyping could optimize patient outcomes and healthcare efficiency.

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