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Case Report

Navigating Pitfalls in Diagnosing Verrucous Carcinoma on Histopathology

Sarandeep Singh Puri[1], Pallavi Sharma[2], Madhubala Gaur[3], Neha Goel[4], Pradeep Garg[5]

[1]Professor & Head of Department, Pathology, GS Medical College and Hospital, Pilkhuwa, Uttar Pradesh, India.
[2]Associate Professor, Pathology, GS Medical College and Hospital, Pilkhuwa, Uttar Pradesh, India.
[3]Professor & Head of Department, Surgery, GS Medical College and Hospital, Pilkhuwa, Uttar Pradesh, India.
[4]Professor, Microbiology, GS Medical College and Hospital, Pilkhuwa, Uttar Pradesh, India.
[5]Dean, GS Medical College and Hospital, Pilkhuwa, Uttar Pradesh, India.
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Corresponding Author:
Sarandeep Singh Puri, Head of Department, Pathology, GS Medical College and Hospital, Pilkhuwa (Hapur), Uttar Pradesh, India.
E-mail Id:
drsarandeep147@gmail.com
Orcid Id:
https://orcid.org/0000-0002-6523-3070
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A B S T R A C T

Histopathological diagnosis is a cornerstone in oncology, guiding treatment decisions and patient management. Clinically, the exophytic, cauliflower-like appearance of Verrucous Carcinoma (VC) often masks its malignant potential, leading to potential misdiagnosis. We report a case of VC which explores the nuances of diagnosing VC on histopathology, shedding light on the challenges and strategies for accurate identification.

Keywords: Verrucous Carcinoma (VC), Histopathology, Challenges, Misdiagnosis

Introduction

Histopathological diagnosis is a cornerstone in oncology, guiding treatment decisions and patient management. While advances in medical technology have improved accuracy, certain malignancies present diagnostic challenges due to their unique characteristics. Verrucous carcinoma (VC) is one such entity that requires scrutiny to avoid diagnostic pitfalls. It is a rare, well-differentiated variant of SCC that exhibits a locally invasive yet indolent growth pattern. It primarily affects mucosal surfaces, with oral cavity and genital areas being frequent sites of occurrence. Clinically, VC's exophytic, cauliflower-like appearance often masks its malignant potential, leading to potential misdiagnosis. We report a case of VC which explores the nuances of diagnosing VC on histopathology, shedding light on the challenges and strategies for accurate identification.[1,2]

Case Report

A 61-year-old female presented in Surgery OPD with a fungating growth over the left buccal mucosa. A biopsy was done and a tissue sample was sent for histopathology examination to the Department of Pathology, GS Medical College and Hospital, Hapur, Uttar Pradesh. Grossly two irregular grey white to grey brown soft tissue pieces measuring 1 x 0.8 x 0.5 cm were identified. Microscopic examination revealed superficial tissue comprising multiple papillary structures lined by hyperkeratotic hyperplastic stratified squamous epithelium. Mild atypia along with mitosis was seen in the cells lining the squamous epithelium. The sub-epithelial/ deeper tissue was not present to

assess the invasion in the sections examined. A diagnosis of squamous papilloma was given on the tissue examined (Figure 1). However, owing to the large size of the lesion, clinical and radiological correlation and a comprehensive sampling with deeper tissue were advised and asked to be sent for histopathological examination, following which, extensive sampling in the form of excisional biopsy along with selective supraomohyoid lymph node dissection was done and second sample was sent for histopathology. On gross examination, an irregular grey-white friable exophytic cauliflower-like growth was seen which measured 5.5 x 4 x 2 cm. Separately received in another container was a grey-brown irregular soft tissue piece measuring 6 x 5 x 2 cm. Cut surface showed a salivary gland measuring 3 x 1.5 x 1.5 cm. Five lymph nodes were also identified. Microscopic examination from the entire excised lesion revealed squamous proliferation with endophytic and exophytic components. The exophytic component shows papillomatosis, hyperkeratosis and parakeratosis. Endophytic components display pushing rete ridges invading deeply in the proximity of skeletal muscle bundles with a dense lymphoplasmacytic response at the pushing edges. The lining epithelium is well differentiated and showed mild dysplasia and brisk mitosis focally. Sections from the salivary gland and lymph nodes were free of tumours. A

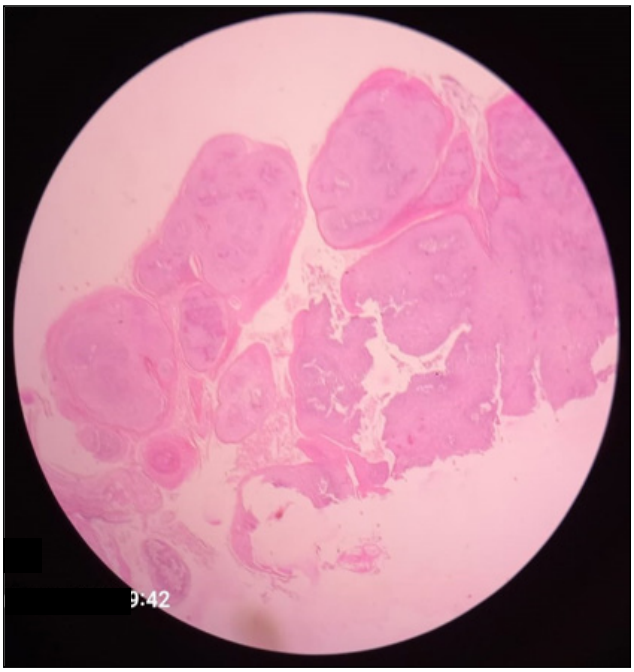

Figure 1.Superficial tissue comprising multiple papillary structures lined by hyperkeratotic hyperplastic stratified squamous epithelium. Mild atypia along with mitosis is seen in the cells lining the squamous epithelium. The sub-epithelial/ deeper tissue is not present to assess the invasion in the sections examined.

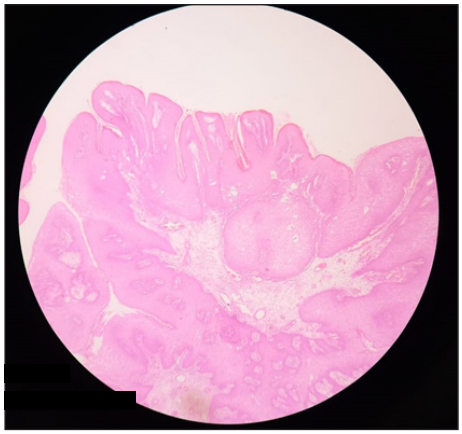

Figure 2.Squamous proliferation with endophytic and exophytic components. The exophytic component shows papillomatosis, hyperkeratosis and parakeratosis.

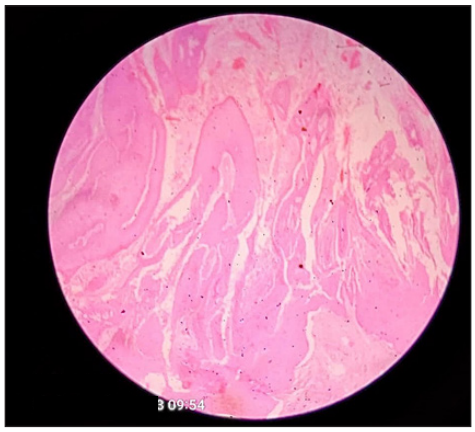

Figure 3.Endophytic components display pushing rete ridges invading deeply in the proximity of skeletal muscle bundles with a dense lymphoplasmacytic response at the pushing edges. The lining epithelium is well-differentiated and showed mild dysplasia and brisk mitosis focally.

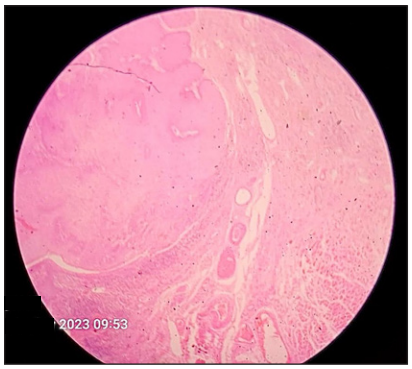

Figure 4.Endophytic components display pushing rete ridges invading deeply in the proximity of skeletal muscle bundles with a dense lymphoplasmacytic response at the pushing edges. The lining epithelium is well-differentiated and showed mild dysplasia and brisk mitosis focally.

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diagnosis of VC was made (Figures 2–4) and TNM staging was pT3NoMx.

Discussion

Verrucous carcinoma is a low-grade subtype of SCC characterised by its slow, locally invasive growth pattern and well-differentiated histology. Its predilection for mucosal surfaces, especially the oral cavity and genital region, amplifies the need for precise histopathological evaluation. Clinically, VC often mimics benign lesions due to its exophytic, cauliflower-like appearance and lack of overt malignant features. The most significant challenge in diagnosing VC is its deceptive resemblance to benign lesions. The well-differentiated nature of VC can obscure its malignant potential, leading to its misclassification as a benign hyperplastic lesion or wart. The absence of typical cytological atypia may divert attention from the possibility of malignancy. Pronounced hyperkeratosis and papillomatosis are hallmarks of VC, but they also contribute to diagnostic uncertainty. These features can be mistaken for benign hyperplastic changes or reactive processes, causing pathologists to overlook the underlying malignancy. Recognising the subtle cytological atypia amidst these hyperplastic elements is crucial for accurate diagnosis.[3,4]

Unlike conventional SCC, VC is characterised by broad pushing margins in its invasive component. This unusual growth pattern, while indicative of malignancy, can be misconstrued as a reactive process or regenerative changes, leading to an underdiagnosis of malignancy. VC often lacks the classic cytological features of malignancy, such as nuclear pleomorphism and prominent mitotic activity. This absence of overtly malignant traits may lead to VC being erroneously classified as a benign lesion, delaying appropriate management. VC shares histological features with other lesions, such as pseudoepitheliomatous hyperplasia and florid papillomatosis. This overlap complicates the differential diagnosis, potentially resulting in misclassification and inappropriate treatment. Adequate sampling is essential for accurate diagnosis. Biopsies that miss the invasive component of VC may yield a diagnosis of benign lesions. Comprehensive sampling from various areas of the lesion, especially those suspicious of invasion, is necessary to avoid diagnostic errors.[5,6]

These diagnostic pitfalls can be mitigated by clinical collaboration, i.e. effective communication between clinicians and pathologists is paramount. Clinical context, lesion location, and patient history provide valuable insights that aid in the accurate diagnosis of VC. In diagnostically challenging cases, immunohistochemical markers can provide additional information. Expression patterns of markers like p63, CK5/6, and p16 can offer insights into the malignancy's nature. When uncertainty persists, serial biopsies over time can reveal evolving features that clarify the diagnosis. This approach ensures timely diagnosis and appropriate management.[7]

Conclusion

Verrucous carcinoma's distinctive histopathological features demand meticulous evaluation to avoid diagnostic pitfalls. Collaborative efforts between clinicians and pathologists, coupled with a deep understanding of VC's unique attributes, are pivotal in achieving accurate diagnoses. By recognising the potential pitfalls and adopting comprehensive diagnostic strategies, healthcare professionals can ensure timely and appropriate management for patients affected by this intriguing malignancy. Further research in molecular markers and diagnostic techniques may enhance the accuracy of VC diagnosis and aid in refining treatment approaches.

Conflict of Interest: None

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