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A Rare Case of Amelanotic Mucosal Malignant Melanoma of the Penis: First of Its Kind Case Report from India

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Abstract

Amelanotic mucosal malignant melanoma of the penis is extremely rare. To our knowledge, this is the first case from India. In the present case report, we have discussed the diagnostic challenges, treatment, and prognosis related with this rare condition. A 55-year-old male presented with a 2-month history of a nonhealing penile ulcer. This duration reflects delayed presentation, as the diagnosis was only confirmed following comprehensive diagnostic workup, including imaging and immunohistochemistry. Partial penectomy with 2 cm margin with sentinel lymph node biopsy was performed. The postoperative period was uneventful. Currently, the patient is on close follow-up. In exceptionally rare cases like this, lack of melanin pigmented lesions may delay the diagnosis and management process. In such scenarios, knowledge related to this rare condition will promptly help the clinicians in early diagnosis, which will be a key for effective treatment and better prognosis of the patient.

Keywords
- amelanotic
- mucosal
- malignant melanoma
- penis
- case report

Introduction

Representing less than 5% of all skin cancers, melanoma is the leading cause of death among skin cancer patients.[1] The most frequently observed type is cutaneous melanoma, with other potential sites for melanocyte migration including the mucosal areas, meninges, and uveal tract.[2]

Melanomas located in the genital region are exceedingly uncommon, representing only 0.1 to 0.2% of all melanoma cases and less than 1.4% of primary malignant lesions of the penis.[3] Among these genital melanomas, 31% are classified as scrotal melanomas, while 69% are identified as penile melanomas.[4] The latter can be further divided into cutaneous melanomas, which develop from the foreskin or penile skin, and mucosal melanomas, which originate from the urethra, glans penis, meatus, crown, and the internal aspect of the foreskin.[5] Common sites for penile melanomas include the urethral meatus (8%), penile shaft (9%), foreskin (28%), and glans penis (55%).[6] The pigmentation of these lesions typically presents in shades of red, blue, brown, and black. In contrast, amelanotic lesions lack pigmentation, which is a defining characteristic of melanoma. Due to the exceptional rarity and diagnostic challenges associated with these cases, it is crucial to conduct a biopsy followed by immunohistochemical staining to ensure timely diagnosis, as cutaneous and mucosal melanomas possess unique presentations, genetic profiles, etiologies, risk factors, and prognosis.[7,8]

This report introduces an exceptionally rare instance of amelanotic mucosal melanoma located on the glans penis. To our knowledge, this represents the first documented case

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المقالة باللغة العربية

حالة نادرة من الورم الميلانيني المخاطي اللاصبغي للقضيب: أول تقرير حالة من الهند

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الورم الميلانيني المخاطي اللاصبغي للقضيب حالة نادرة للغاية. وعلى حد علمنا، هذه هي أول حالة يتم الإبلاغ عنها من الهند. في هذا التقرير، نناقش التحديات التشخيصية والعلاج والتكهنات المرتبطة بهذه الحالة النادرة. قدم رجل يبلغ من العمر 55 عاماً بتاريخ مرضي لقرحة غير ملتئمة في القضيب استمرت لمدة شهرين. تعكس هذه المدة تأخراً في التقديم للعلاج، حيث تم تأكيد التشخيص فقط بعد إجراء فحوصات تشخيصية شاملة، بما في ذلك التصوير والكيمياء النسيجية المناعية. تم إجراء استئصال جزئي للقضيب مع هامش 2 سم وخزعة العقدة الليمفاوية الحارسة. مرت فترة ما بعد الجراحة دون مضاعفات. حالياً، المريض تحت المتابعة الدقيقة. في حالات نادرة جداً مثل هذه، قد يؤدي عدم وجود تصبغ بالميلانين إلى تأخير عملية التشخيص والعلاج. في مثل هذه السيناريوهات، فإن المعرفة المتعلقة بهذه الحالة النادرة ستساعد الأطباء بشكل فوري في التشخيص المبكر، والذي سيكون مفتاحاً للعلاج الفعال وتحسين التكهنات للمريض .

الكلمات المفتاحية: لاصبغي، مخاطي، ورم ميلانيني خبيث، قضيب، تقرير حالة.

from India, with minimal existing literature on the subject globally. In this case report, we have elaborated on the diagnostic difficulties encountered, the treatment administered, and the associated prognosis.

Case Presentation

A 55-year-old male was referred to our facility with a 2-month history of a persistent, nonhealing ulcer on his penis. On examination, a nonpigmented ulceroproliferative lesion measuring 2.5 cm × 2.5 cm was noted on the glans penis (see ►**Fig. 1A**). Although the patient reported a 2-month history, this duration is indicative of delayed presentation rather than the confirmed onset of disease. The diagnosis was established only after a further comprehensive diagnostic workup, during which magnetic resonance imaging of the pelvis revealed a well-defined hypointense soft tissue lesion on T1-weighted images, affecting the glans penis and accompanied by small subcentimetric bilateral inguinal lymph nodes. A punch biopsy was performed, revealing a poorly differentiated carcinoma, which prompted a detailed differential diagnostic workup.

Histologically, the lesion appeared as a subepithelial tumor with an ulcerated overlying epithelium. Given the undifferentiated nature of the tumor on initial examination, immunohistochemistry (IHC) was conducted to further characterize the neoplasm. The IHC results demonstrated strong positivity for vimentin, HMB-45, and Melan A, with sporadic expression of S100 (►**Fig. 1–D**). Despite these findings, no melanin pigment was detected. This immunoprofile strongly supported a diagnosis of melanoma. To systematically rule out other differentials, additional histological and immunohistochemical evaluations were performed. The absence of Toker cells on hematoxylin and eosin staining, combined with negative IHC for CK7, SOX10, and carcinoembryonic antigen, effectively excluded extramammary Paget's disease. Likewise, the lack of p63 and p40 expression ruled out squamous cell carcinoma. These findings collectively reinforced melanoma as the most plausible diagnosis. A full-body positron emission tomography-computed tomography scan was performed to assess for distant spread and showed no evidence of metastatic disease. Subsequently, the patient underwent a partial penectomy with a 2-cm surgical margin. A sentinel lymph node biopsy (SLNB) was also performed and returned negative on frozen section analysis, thereby eliminating the need for radical lymph node dissection. The final pathological examination revealed clusters of poorly differentiated cells within the invasion into the corpora spongiosa (►**Fig. 1E**). The urethra remained unaffected, subepithelial layer exhibiting, and bilateral inguinal lymph nodes showed no evidence of metastasis. The pathological staging was classified as stage IIB according to the American Joint Committee on Cancer-tumor, node, and metastasis (AJCC-TNM), 8th edition. The patient's postoperative course has been smooth, and he remains clinically well nearly 2 years into regular follow-up, with no signs of recurrence or disease progression. Given the aggressive nature of amelanotic mucosal malignant melanoma of the penis and its high risk of local recurrence, nodal involvement, and distant metastasis, long-term surveillance is essential. In the absence of standardized protocols, follow-up has followed general mucosal melanoma guidelines, with clinical assessments every 3 to 6 months initially and annually thereafter. This case underscores the importance of early diagnosis, ongoing monitoring, and extended follow-up—not only for timely detection of recurrence and adjustment of therapy but also for improving prognostic insight and informing future management strategies for this rare malignancy.

Discussion

The incidence of amelanotic mucosal malignant melanoma on the glans penis is an extraordinarily rare occurrence. The diagnosis of this condition is particularly challenging due to

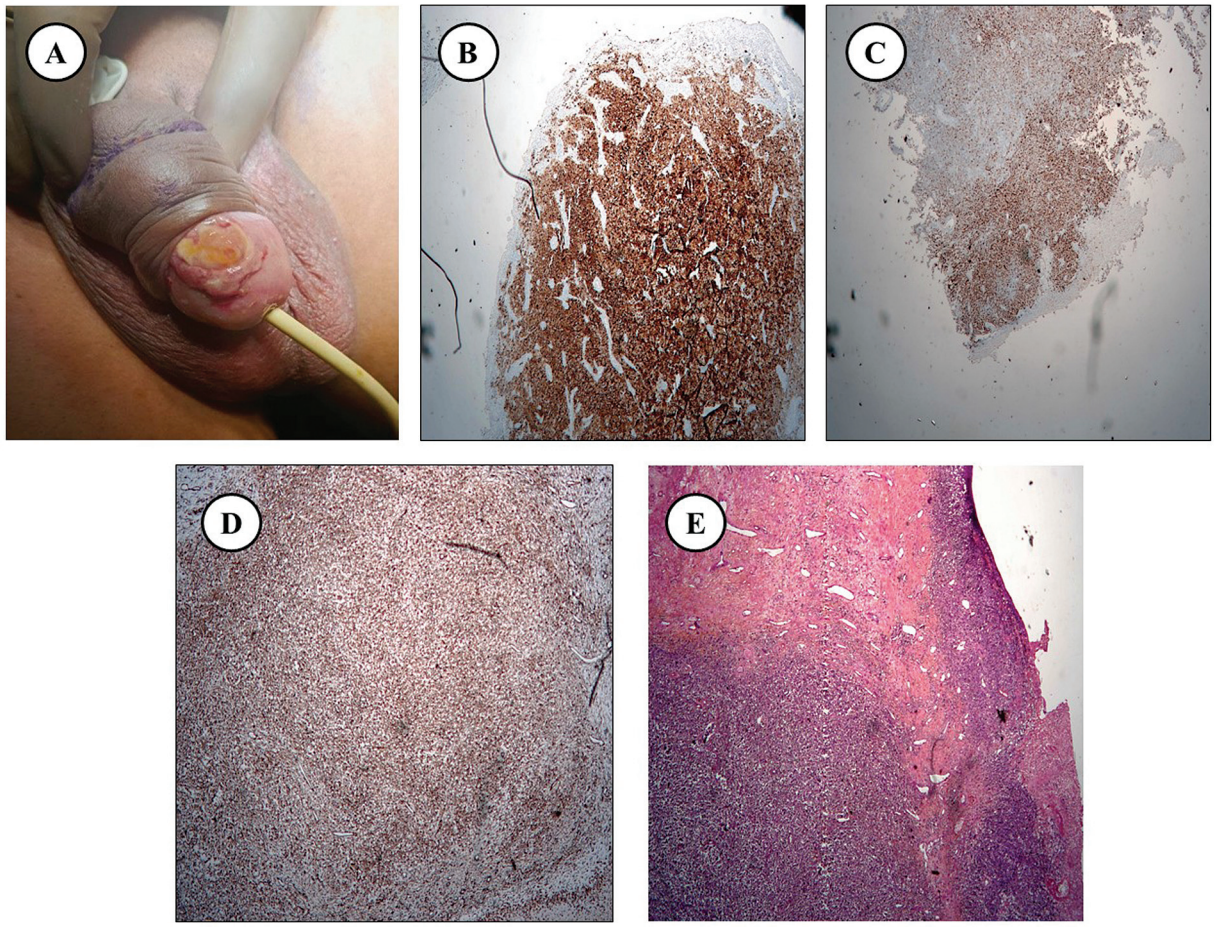

Fig. 1 (**A**) Nonpigmented ulceroproliferative lesion over the glans penis. (**B**) Positive for Melan A, (**C**) positive for HMB-45, (**D**) positive for vimentin, and (**E**) hematoxylin and eosin stain—poorly differentiated carcinoma negative for melanin pigment.

the limited availability of literature concerning its epidemiological data. A search of PubMed revealed only five previously published reports on this subject. The majority of cases have been documented in older men, particularly those in their sixth and seventh decades of life.[4] The prognosis for patients with this melanoma type is notably poor, with a 5-year overall survival rate estimated between 18 and 31%.[9] Clinically, these mucosal melanomas of the penis typically present as lesions that are bluish-black or brown in color, with or without ulceration. In rare cases, the absence of pigmentation can lead to diagnostic ambiguity and subsequent delays in management. In such penile lesions accompanied by palpable inguinal lymphadenopathy, pathological confirmation is essential, which can be achieved through fine-needle aspiration or core biopsy.[10]

The rarity of these lesions has contributed to the absence of definitive consensus guidelines for their staging and management. Previously, the three-stage classification system developed by Bracken and Diokno was utilized, where stage I indicated disease confined to the penis, stage II referred to metastasis to the regional lymph nodes, and stage III denoted disseminated disease.[11] More recently, the AJCC has introduced the TNM staging system, which classifies all lesions based on Breslow's depth of invasion, excluding urethral melanoma.[12]

Evidence from clinical experiences underscores the importance of clinical staging—categorized as localized, lymph nodal, or metastatic—as a vital prognostic determinant, often outweighing the significance of the disease's location at the time of diagnosis in predicting favorable outcomes. A comprehensive study by van Geel et al outlined specific characteristics that aid in evaluating the likelihood of recurrence and/or progression. These characteristics include tumor dimensions, patterns of regression, lymphovascular invasion, the existence of satellite nodules, growth orientation (vertical or horizontal), mitotic activity, ulceration presence, and the extent of invasion.[9]

Surgical treatment remains the cornerstone for managing primary mucosal melanoma of the penis; however, the appropriate extent of surgical intervention is still debated among clinicians. Current literature suggests that in individuals with stage I/IA melanomas affecting the glans and distal urethra, a radical surgical approach, which entails total penectomy and bilateral inguinal lymph node dissection, has proven advantageous.[4,13] On the other hand, organ-sparing surgeries that maintain a 2-cm negative margin—through methods such as local excision, urethrectomy, glans amputation, or partial penectomy—are deemed sufficient for achieving safe surgical outcomes.[13] The prevalent belief that radical surgeries lead to improved survival rates has been challenged by the findings of

Geelhoed and Myers.[14] Over time, the routine practice of bilateral inguinal lymphadenectomies in patients with stage A disease has been limited, primarily due to the low incidence of inguinal lymph node metastasis (~17%).[8] In these instances, SLNB has been utilized to ensure precise staging while minimizing the potential morbidities associated with standard therapeutic bilateral inguinal lymph node dissections. However, in patients identified with positive sentinel lymph nodes, the execution of bilateral ilioinguinal lymphadenectomy has been deemed necessary, given its demonstrated curative efficacy.[15] In stages B and C, patients diagnosed with non-localized mucosal melanomas accompanied by metastatic squamous cell carcinoma of the penis underwent routine bilateral ilioinguinal lymph node dissection primarily to address local complications such as pain, tumor mass effect, and tumor fungation, rather than to enhance survival outcomes.[16]

There is currently no case series in the literature that offers conclusive evidence for the use of adjuvant systemic therapy in patients with mucosal melanoma. A study by Lian et al involving 189 patients revealed that those treated with either chemotherapy (temozolomide and cisplatin) or immunotherapy (interferon a-2b) had improved survival rates compared with those who received no systemic adjuvant treatment following complete resection of stage II or III disease. Nonetheless, it is important to note that among the 189 patients, only one case involved penile melanoma, which limits the generalizability of these findings.[17] Additionally, the true efficacy of targeted therapies (e.g., imatinib, sunitinib, etc.) remains ambiguous.[18] In such cases, emerging evidence suggests that immunotherapy, particularly checkpoint inhibitors such as anti-programmed cell death protein 1 (PD-1) and anti-cytotoxic T-lymphocyte antigen 4 (CTLA-4) agents, shows promise in the treatment of mucosal melanoma.[19–22] Although responses are generally less robust compared with cutaneous melanoma, these therapies have demonstrated meaningful clinical benefit in select patients, offering a valuable option in cases where surgery alone may be insufficient or recurrence occurs.[20] However, robust clinical evidence is still required to fully validate their routine use in practice.

After evaluating all available options alongside the National Comprehensive Cancer Network guidelines (Version 2, 2023), the patient was deemed ineligible for chemotherapy and was placed under observation, given his stage 2 melanoma and the negative results from the SLNB.[23]

Conclusion

Amelanotic mucosal malignant melanoma of the penis is an extremely uncommon condition, and to our knowledge, this is the first case reported in India. The lack of melanin pigmentation in such cases often results in diagnostic delays and challenges in management. In the case presented, the amelanotic mucosal melanoma was localized to the glans penis. The patient underwent a partial amputation of the penis along with a SLNB, which returned negative for metastasis. As a result, no adjuvant therapy was recommended. The patient is currently under regular follow-up for nearly 2 years and remains clinically well, with no signs of recurrence or disease progression. In these rare occurrences, prompt diagnosis is crucial for effective treatment and improved prognosis.

Availability of Data and Materials

The data set used and/or analyzed during the current study is available from the corresponding author on reasonable request.

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Conflict of Interest

None declared.

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