INTRODUCTION

Melanoma is a malignant tumor developed from melanocytes. Melanoma represents 1%–3% of all cancers and is the most severe skin tumor. It is the leading cause of death from skin cancer. Generally, malignant melanoma is observed in areas of the skin exposed intermittently and intensely to sunlight and UV radiation.1

Primary melanomas of the male genital tract are very rare and represent <1% of all malignant melanomas; they are associated with high mortality and often late diagnosis.2

We report the observation of a patient followed for metastatic melanoma of the penis. And through this observation, we will illustrate the epidemiological, clinical, and therapeutic characteristics of malignant melanoma of the penis.

CASE PRESENTATION

A 70-years-old man without any specific medical history presented to our institution with skin lesions of the penis gland that have appeared for 3 months. His physical examination revealed hyperchromic, grayish, nodular, and ulcerated lesions. The largest of which was 1 cm in diameter on the penile gland and around the urethral meatus, associated with a fixed right inguinal lymphadenopathy of 3 cm in diameter.

A surgical biopsy of the skin lesion with histopathological and immunohistochemical studies established the diagnosis of malignant melanoma of the penis in the metastatic stage. This case was managed by palliative immunotherapy and is currently under treatment by Pembrolizumab. Malignant melanoma of the penis represents an exceptional situation, in which only rapid diagnosis at an early stage allows treatment with optimal therapeutic results.

KEYWORDS
immunotherapy, melanoma, rare localization

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CASE REPORT

Unusual penile localization of melanoma

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Abstract
Penile’s melanoma is a rare situation, often associated with late diagnosis and high morbidity and mortality. We report the case of a 70-year-old man. He represented progressive skin lesions of the penile gland. A surgical biopsy with histopathological and immunohistochemical studies established the diagnosis of malignant melanoma of the penis in the metastatic stage. This case was managed by palliative immunotherapy and is currently under treatment by Pembrolizumab. Malignant melanoma of the penis represents an exceptional situation, in which only rapid diagnosis at an early stage allows treatment with optimal therapeutic results.

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VI and VII measuring 20 and 16 mm, respectively, with a right inguinal and iliac lymphadenopathy (Figure 4).

The patient received treatment with immunotherapy (pembrolizumab 200 mg/21 days). After 2 years of immunotherapy follow-up, a partial response of targeted lesions was observed. Regarding the immunotherapy tolerance profile, biological hypothyroidism was noted and was treated with hormonal substitution treatment (Figure 5).

3 | MATERIAL AND METHODS

We used the PubMed database for a literature review. We used the terms “melanoma” and “penis” to search for manuscripts published in English on this topic. Then, we selected all literature reviews, case series, and case reports (Table 1). All articles that did not contain useful information or did not correspond to the subject of the study were excluded.

4 | RESULTS

Only 13 reports (with 28 patients) were reported from 1948 to 2022 in a literature review on penile’s melanoma. The majority of publications are case reports. Stillwell et al.⁷ and Bechara et al.¹² have published a series of cases, which respectively report 11 and six patients with melanoma of the penis. The average age of reported patients is 62 years. At the time of diagnosis, the majority of cases were at the localized or locally advanced stage, only two patients were
metastatic from the outset, and in three cases the tumor was in situ. Conservative surgical treatment (local excision or partial amputation) is the most described treatment in these publications. Radical amputation was reported in only four cases. However, lymph node dissection was mainly indicated in case of clinical suspicion of lymph node involvement (12 patients). Adjuvant chemotherapy was indicated in three patients at high risk of recurrence (T4b or lymph node involvement) and only once in a metastatic patient. Median event-free survival was 50 months.

**DISCUSSION**

Penis melanoma was first described by Murchison in 1859. And since then, several cases and series of cases have been reported. Malignant melanoma of the penis remains extremely rare. It represents <1.4% of all malignant tumors of the penis and <1% of extraocular melanoma. Malignant melanoma of the penis develops mainly in the penile gland (55%), followed by the foreskin (28%), while it is rarely in the penis shaft (9%) and the urethral meatus (8%). The diagnosis of malignant melanoma of the penis is often late and usually at an advanced stage. This delay in diagnosis can be explained mainly by the frequency of differential diagnoses. But, also by the private site of the lesion, which bothers the patient to consult early. Clinically, penis melanoma should be suspected in the presence of any skin lesions (ulcerated or nodular) accompanied by a change in the color of the skin (blackish or brownish appearance). Dermoscopy is a non-invasive technique that highlights the morphological characteristics of small lesions.

There are four clinical forms of malignant melanoma: Lentigo malignant melanoma, superficial melanoma, lumpy melanoma, and acral lentiginous melanoma. Faced with these different presentations, penile’s melanoma poses a real diagnostic problem. Among the differential diagnosis of this entity, we cite squamous carcinoma, penile nevi, Kaposi sarcoma, or reactions like penile psoriasis. The diagnosis is essentially histological on biopsy samples of the lesions. In light of the American Joint Committee on Cancer (AJCC) recommendations, the histology report should include information on at least: the type of melanoma, anatomical site, maximum vertical thickness, mitotic rate, presence of ulceration, and clearance of the surgical margins.

For a patient with unresectable or metastatic disease, screening for BRAF, NRAS, and c-Kit mutations seems mandatory. Once the diagnosis of melanoma has been established, an exhaustive extension assessment must be carried out to look for a secondary localization, ideally a PET scan and a cerebral MRI except for low-risk lesions classified as pT1a which do not require any balance sheet.

For the localized stages, the treatment of melanoma of the glans penis is essentially surgical, with a wide excision of the primary tumors with safety margins of 0.5 cm for the melanoma in situ, 1 cm for the tumors of a thickness up to 2 mm. Currently, the aggressive surgical approach based on total amputation of the penis associated with bilateral dissection of the ilio-inguinal ganglion has become increasingly rare. Lymph node dissection should not be indicated systematically. Sentinel lymph node biopsy is preferred in melanoma.

**FIGURE 4** Appearance of lesions before (A) and after (B) four injections of immunotherapy.
**FIGURE 5** Thoraco-abdomino-pelvic CT scan showing hepatic lesions.

**TABLE 1** Summary of cases reported in the literature of penile's melanoma

| Autour and year | Number of reported cases | Age (years) | Pathologic stage | Breslow (mm) | Treatment | Adjuvant therapy | Follow-up (months) |
|-----------------|--------------------------|-------------|------------------|-------------|-----------|------------------|-------------------|
| Roberts et al.3 | 1                        | 62          | -                | -           | RA        | -                | 30 (without event) |
| Schneiderman et al.4 | 1                        | 50          | RxN0M0           | -           | PA + LND  | -                | 4 (local relapse)  |
| Gojaseni et al.5  | 1                        | 54          | RxN+M0           | -           | RA + LND  | Melphalan        | 24 (without event) |
| Myskow et al.6   | 1                        | 67          | T4bN0M0          | 4.5 mm      | LE        | Vinodesine weekly (6 cycles) | 5 (metastasis relapse) 8 months later (death) |
| Stillwell et al.7 | 11                       | 65          | TxN0M0           | -           | PA        | -                | 8 (died of M)      |
|                 |                          | 58          | T3bN0M0          | -           | PA        | -                | 282 (died of PE)   |
|                 |                          | 57          | T4aN+M0          | -           | LE + LND  | -                | 13 (died of M)     |
|                 |                          | 55          | T5N+M1           | -           | PA + LND  | Radiotherapy     | 6 (died of M)      |
|                 |                          | 67          | T2bN+M0          | -           | PA + LND  | -                | 24 (died of M)     |
|                 |                          | 53          | T6N+M0           | -           | PA + LND  | -                | 48 (died of M)     |
|                 |                          | 65          | T2N0M0           | -           | LE        | -                | 96 (died of M)     |
|                 |                          | 66          | T2aN0M0          | -           | PA        | -                | 126 (died)         |
|                 |                          | 70          | T in situ        | -           | LE        | -                | 192 (without event) |
|                 |                          | 70          | T3N0M0           | -           | PA        | -                | 78 (died)          |
|                 |                          | 80          | T2bN0M0          | -           | PA + LND  | -                | 12 (without event) |
| Manivel et al.8  | 1                        | 81          | T4bN2Mx          | -           | PA + LND  | -                | 2 (death)          |
| Brundrick et al.27 | 1                        | 51          | TxN0M0           | -           | RA + LND  | -                | 5 (nodal recurrence) |
| Rashid et al.9   | 1                        | 62          | T5N+M0           | 1.9 mm      | RA + LND  | No               | -                 |
| Demitsu et al.10 | 1                        | 50          | T in situ        | -           | LE        | No               | 3 (without event)  |
| Hanksins et al.11 | 1                        | 75          | T4bN0M0          | 5 mm        | LE        | -                | -                 |
with a tumor thickness of >1 mm. And for a patient with positive sentinel nodes, complete lymphadenectomy should be discussed in a multidisciplinary meeting as it may have benefits in terms of relapse-free survival without benefit in terms of overall survival.\(^{23}\)

For metastatic patients with BRAF mutation, the recommended first-line treatments are anti-PD1 or combined BRAF/MEK inhibitors, whereas, in the case of wild-type BRAF, anti-PD1 is preferable in the first line.

Two and five-years overall survival in a patient with penis melanoma is 63% and 31%, respectively. And this is related to the diagnosis, often in the advanced stage of the disease.\(^{25,26}\)

Hence, the interest of raising awareness both: the patients to seek the doctor’s advice in the face of any skin lesion of the penis and the doctors not to hesitate to do a complete clinical examination of patients whenever possible.

### 6 | CONCLUSION

Penile’s melanoma represents a very rare localization that is frequently confused with other lesions, in particular infectious. Only an early consultation, a biopsy of the lesion with histological study, and confirmation of the diagnosis at an early stage will improve the prognosis of this tragic disease.

### AUTHOR CONTRIBUTION

All authors read and approved the final manuscript.

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### Conflict of Interest

The authors declare that they have no competing interest.

### Data Availability Statement

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

### Consent

Written informed consent was obtained from the patient to publish this report in accordance with the journal’s patient consent policy.

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