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Case report

Vulvar keratoacanthoma may be a malignant precursor: A case report and literature review

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ABSTRACT

Background: Keratoacanthoma is a relatively rare skin tumor, with vulvar keratoacanthoma being even more uncommon. Although the majority of keratoacanthomas exhibit a benign course, a subset of cases may show features of malignant potential, such as marginal invasion and recurrence.
Case: An 82-year-old female presented with a rapidly growing exophytic lesion on the left vulva, measuring 1.5 cm in diameter, accompanied by pruritus. The lesion had been present for two months. The patient underwent vulvar mass excision, and postoperative pathology revealed squamous cell hyperplasia with glassy cytoplasm and no significant cellular atypia. The surgical margins were clear. Three years later, the tumor recurred with disordered growth.
Conclusion: In terms of histological and clinical presentation, keratoacanthoma may overlap with classical well-differentiated squamous cell carcinoma. In rare cases, certain atypical keratoacanthomas may exhibit intravascular and perineural invasion, along with lymph node metastasis. By sharing our treatment experience of a patient with recurrent vulvar keratoacanthoma following surgery, we aim to provide a cautionary perspective for the clinical management of such cases.

1. Introduction

Keratoacanthoma (KA) is a rapidly growing skin tumor, typically originating from follicular cells exposed to sunlight. Lesions generally undergo spontaneous regression within 4 to 6 months, passing through three phases: proliferation, maturation, and degeneration. Clinically, these lesions present as firm, well-defined red or skin-colored elevations with a central thickened keratin plug, which may leave a depression upon removal (Tisack et al., 2021). KA may occur on various body parts; however, vulvar KA is extremely rare. In 1985, Rhatigan et al. first documented a case of vulvar KA in the literature. To date, only six cases of vulvar KA have been reported (Table1) .

There is considerable controversy in the field of dermatopathology regarding the distinction between KA and SCC. Many experts consider KA to be a rapidly growing benign squamous cell tumor, generally well-differentiated and self-limiting. However, KA may present clinically and histologically similar to SCC, As a result, some experts believe that KA should be classified as a well-differentiated subtype of SCC. The diagnosis of KA primarily relies on H&E staining, Studies have shown that the histological characteristics of KA on H&E staining include the presence of nuclear pleomorphism and mitotic figures, which are typically concentrated in the peripheral regions of the deep component of KA. In contrast, SCC generally exhibits mitotic figures scattered throughout the entire tumor area. Additionally, factors such as symmetry, the presence of a keratin plug, an abrupt transition zone between the tumor and the epidermis, a deep fibrotic band beneath the lesion, and intraepithelial neutrophilic microabscesses support the diagnosis of KA. Conversely, asymmetry, a gradual transition zone, and fibrosis surrounding the tumor nests are more frequently observed in SCC (Akay et al., 2017).

Although most KA patients have a favorable prognosis after complete excision of the lesion, a small number of cases occasionally exhibit invasive growth, with involvement of surrounding blood vessels and nerves (Hodak et al., 1993; Monroy et al., 2024). The malignant biological behavior of KA is inconsistent with benign tumors; furthermore, a very small number of KA cases may present with distant metastasis and

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tumor-related death (Hodak et al., 1993). Therefore, some scholars have suggested that this characteristic further supports the idea that KA could be considered a subtype of SCC. In the current case, the patient developed postoperative recurrence and disorderly tumor growth after recurrence, providing further evidence for KA being a subtype of SCC. Consequently, complete excision of the lesion and close postoperative follow-up are crucial for monitoring disease progression. This case highlights the importance of clinical vigilance, as the patient's neglect of the condition and refusal of follow-up led to an adverse outcome, serving as a significant warning for clinical practice.

2. Materials and methods

2.1. Clinical data

2.1.1. Clinical history

An 82-year-old female patient was admitted to our hospital in August 2020 due to the discovery of an external genital mass over the past two months. Two months prior to admission, during external genital hygiene, she noticed a mass approximately the size of a soybean. The mass was hard, with raised edges and a central crater-like depression. Over the past month, the patient reported progressive enlargement of the mass, accompanied by increasing pruritus around the external genital area, prompting her hospital visit.

2.1.2. Physical examination

Gynecological examination revealed atrophy of the external genitalia, consistent with aging. A mass approximately 1.5 cm in diameter was observed at the inferior aspect of the left labium majus, characterized by a keratinous plug, well-defined borders, no evidence of bleeding or ulceration, and hard consistency. The mass was mobile and tender upon palpation. Vaginal examination showed patent vaginal walls with minimal secretions; the cervix was smooth and atrophied, and both adnexa were unremarkable.

2.1.3. Past medical history

The patient has no chronic diseases, nor any history of immunosuppression. There is no history of human papillomavirus infection or exposure to toxic substances. The family history is non-contributory, with no hereditary or infectious diseases reported.

2.1.4. Auxiliary examinations

The results of the external genital exfoliative cytology examination indicate no abnormalities.

2.2. Treatment Methods

A contrast-enhanced abdominal CT was performed prior to the vulvar mass excision. The results showed no abnormalities. The patient underwent excision of the vulvar mass, with the excised tissue extending 5 mm beyond the clinically healthy surrounding tissue. This approach aimed to ensure complete removal of the tumor, reduce the likelihood of residual malignant cells, and minimize the risk of recurrence.

3. Pathological results

3.0.1. Histopathological Findings

Low-power microscopy showed hyperplasia of squamous epithelium with excessive keratinization (Fig. 1). High-power microscopy revealed pale pink cellular proliferation of squamous cells, with cytoplasm exhibiting a glassy appearance, and no significant cellular atypia was observed (Fig. 2).

3.0.2. Diagnosis

Postoperative pathology revealed keratoacanthoma of the vulva with clear surgical margins.

4. Follow-up

The patient did not attend follow-up appointments as scheduled. In December 2023, she presented to our emergency department due to extensive vaginal bleeding caused by the rupture of a vulvar mass. Physical examination revealed multiple "crater-like" lesions on the vulva, with keratinous protrusions in the center. The largest lesion was located on the right labia, approximately the size of a fist. The vulva exhibited structural erosion due to tumor invasion, and there was significant vaginal bleeding (Fig. 3). The patient's family refused further diagnostic workup and treatment, requesting only gauze compression for local hemostasis before leaving the hospital.

5. Discussion

Due to the extreme rarity of vulva KA, a review of the existing literature reveals that the six reported cases are all benign lesions, with an average age of approximately 50 years. The reported ages range from

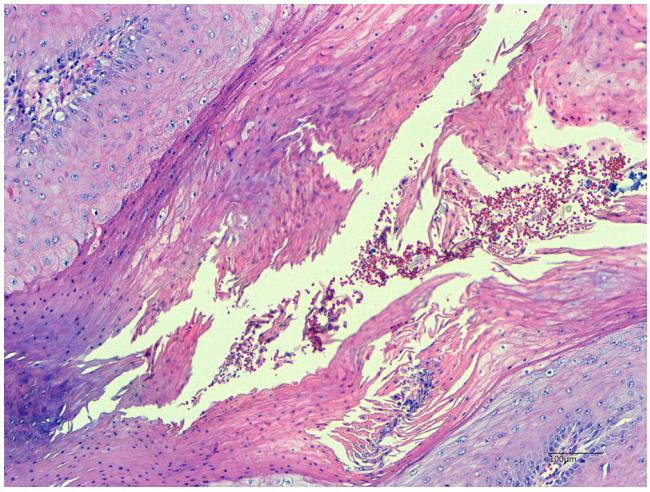

Fig. 1. Low-power microscopy shows hyperplasia of squamous epithelium with excessive keratinization exhibiting a crater-like appearance (HE × 100).

Table 1
Summary of Previously Reported Cases of Keratoacanthoma of the Vulva.

Reference	Age/year	Lesion Location	Size (cm)	Time of duration	Surgical approach	Follow up (months)
Rhatigan R M (Hadley et al., 2009)	65	Right labium majus	1.5	4 weeks	Excisional biopsy	24
Gilbey S[13]	54	Mid-right labium majus	1	4 weeks	Wide local excision	24
Chen W[12]	49	Left labium majus	0.8	4 weeks	Excisional biopsy	14
	44	Left labium majus	1	6 weeks	Excisional biopsy	138
Nascimento M C (Thiele et al., 2004)	79	Clitoris	0.9	Several months	Excisional biopsy	1
Ozkan F[11]	33	Clitoris	1	Several months	Excisional biopsy	14
Present case	82	Left labium majus	1.5	2 months	Excisional biopsy	40

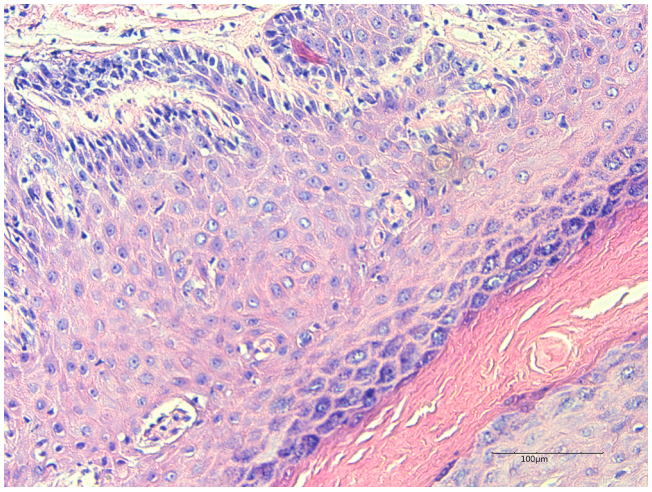

Fig. 2. High-power microscopy reveals pale pink cellular proliferation of squamous cells, with cytoplasm exhibiting a glassy appearance and no significant cellular atypia observed (HE × 200). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

a minimum of 33 years to a maximum of 79 years. All cases underwent complete excision of the vulvar lesions, and during the follow-up period, no recurrences or metastases were observed, with an average follow-up duration of about 40 months (1–138 months) (Table 1) .In this case, similar to previously reported cases, complete excision of the vulvar lesion was performed. Additionally, as in other reports, the vulvar intraepithelial neoplasia (VIN) and vaginal cytology examinations were negative. However, the patient did not attend timely follow-ups after surgery and only presented to the emergency department three years post-operation due to tumor recurrence, accompanied by significant vaginal bleeding. Due to the refusal of further treatment by the patient's family, no additional relevant examinations were conducted.

KA is clinically classified into four types, with the solitary type being the most common. The other types—multiple, marginally centrifugal, and disseminated eruptions—are relatively rare. An important characteristic of isolated KA is its self-limiting nature; it typically expands rapidly over a few weeks and resolves spontaneously within months. Patients often do not experience significant symptoms in the early stages, but as the tumor grows quickly, varying degrees of pruritus may occur (Zito and Scharf, 2024).

Despite being classified as a subtype of SCC, KA is characterized by its self-limiting nature and low likelihood of distant metastasis, leading to a preference for benign tumor diagnosis (Liang et al., 2020). Consequently, surgical excision is the preferred treatment for KA, and local wide excision can effectively prevent recurrence. To ensure complete removal of the affected tissue, it is essential to have clear surgical margins on intraoperative frozen sections. For vulvar KA, we typically extend the excision margin by 0.5 cm beyond the edge of the tumor, without the need for radical treatment or lymphadenectomy as would be required for malignant tumors. In the reported case, histological examination of the excised tissue revealed no significant atypical cells or typical infiltration, suggesting that the surgical margins were sufficient. Considering the patient's advanced age and the associated surgical risks, further intervention was not deemed necessary. However, the patient's postoperative recurrence raises important considerations. Reports indicate that the recurrence rate for KA following surgical intervention ranges from 4 % to 8 % (Ozkan et al., 2006). Although keratoacanthoma generally exhibits spontaneous regression, approximately 20 % of cases may exhibit neural, vascular, or intravascular infiltration, increasing the risk of recurrence. Some studies have shown that KA may deteriorate upon recurrence and has the potential to transform into well-differentiated SCC (Juhász and Marmur, 2018). In such instances, the

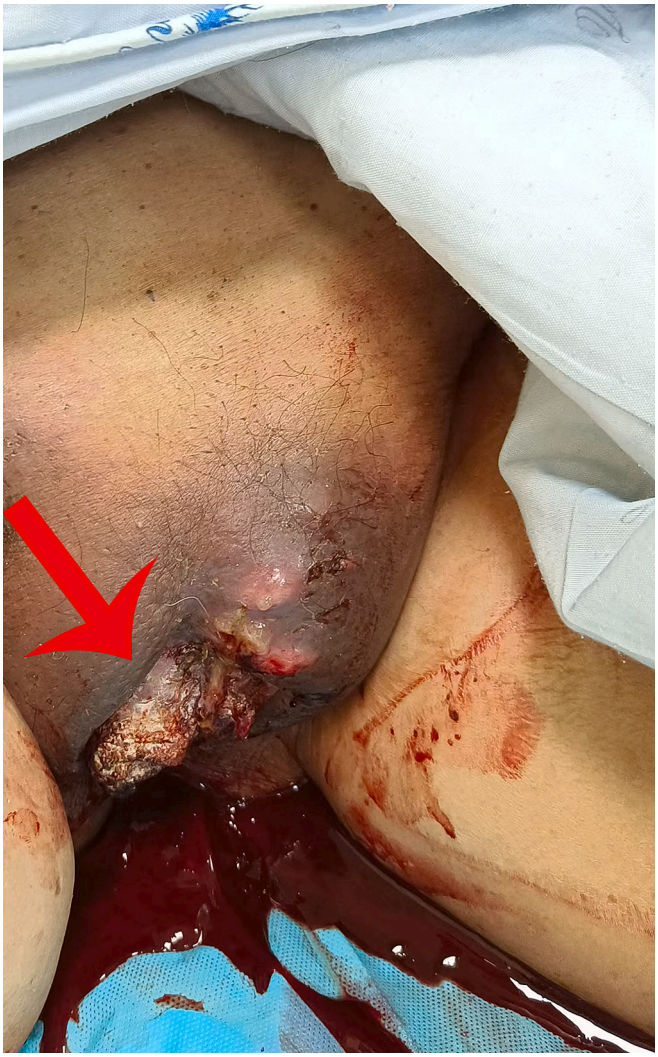

Fig. 3. Multiple "crater-like" lesions on the vulva, with keratinous protrusions in the center. The largest lesion is located on the right labium and is approximately the size of a fist. The vulva exhibits unclear structural boundaries due to tumor invasion, and there is significant vaginal bleeding.

initial presentation and recurrent lesions may share similar pathological features. Furthermore, besides the recurrence of KA following surgical excision, trauma incurred during the surgical process may also contribute to recurrence (Hadley et al., 2009). For patients with recurrent KA, a combined treatment strategy is recommended, including the combination of surgical excision and radiotherapy, intralesional triamcinolone injection, YAG laser treatment combined with local 5-fluorouracil injection, and the postoperative local application of imiquimod. These approaches have shown promising therapeutic effects (Thiele et al., 2004). This highlights the importance of postoperative follow-up and timely intervention upon recurrence. In this case, the patient did not undergo any follow-up or relevant examinations after surgery. When recurrence of vulvar lesions was later identified, the patient only sought medical attention after experiencing significant vaginal bleeding, leading to a passive clinical situation. This serves as a cautionary reminder for clinical practice. For special cases, particularly those with potential recurrence risk, we should maintain closer surveillance and timely interventions, which are vital for improving disease prognosis.

In our paper, we aim to share our experiences and emphasize the importance of diagnosing, differentiating, and conducting postoperative follow-up for vulvar KA. The incidence of vulvar KA is significantly lower than that of vulvar SCC, leading to a lack of relevant clinical

experience in patient management. This often results in a simplistic perception of KA as merely a benign tumor, with insufficient attention given to the rare cases that may progress malignantly. This case also has certain limitations. Due to the patient's recurrence and the lack of further pathological examination during follow-up, the pathological type after recurrence could not be determined. Considering the post-operative pathology and the disorganized growth pattern of the tumor after recurrence, along with relevant literature, we hypothesize that this patient is more likely to have experienced malignant transformation of the KA. However, since the patient did not follow up for a long period, it cannot be ruled out that inflammation progression may have led to the concurrent occurrence of KA and SCC. In light of the above discussion, this further underscores the importance of timely postoperative follow-up and comprehensive examinations, serving as a reminder for clinical management of patients.

6. Statement

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

CRediT authorship contribution statement

Fang Chen: Writing – review & editing, Writing – original draft. **Yang Wang:** Methodology, Investigation, Data curation. **Dina Haishaer:** Methodology, Investigation, Formal analysis, Data curation. **Feng Bai:** Writing – review & editing, Writing – original draft, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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