

## Necrotizing fasciitis arising from squamous cell carcinoma of the vulva

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### Abstract

Necrotizing fasciitis (NF) is a devastating soft tissue infection affecting fascias and subcutaneous soft tissues. While it is associated with several risk factors, including malignancy, alcoholism, liver disease, drug use, malnutrition, diabetes, male gender and old age, few case reports in the literature describe its rare connection with genital malignancy. Vulvar squamous cell carcinoma (SCC) is the fourth most common malignancy, representing 5% of all gynaecological tumours among women. NF due to vulvar SCC is a rare complication. In this article, we present the 1991 case of a 58-year-old diabetic female patient with NF due to vulvar SCC. While surgical intervention was successful, the prognosis for vulvar SCC was poor because of late detection.

### Introduction

Vulvar squamous cell carcinoma (SCC), which is a rare type of cancer that occurs mainly in the external female genital tract, is mostly seen in women over the age of 60. Generally, 95% of vulvar carcinomas are SCCs, and the remaining 5% are melanomas, sarcomas and basal cell carcinomas.<sup>1</sup> Two different pathways in the development of vulvar SCC have been reported. The first occurs predominantly in postmenopausal women with a history of lichen sclerosis or lichen planus developing in differentiated vulvar intraepithelial neoplasia and is associated with a poor prognosis. The other is more common in younger patients and is related to high-risk papillomavirus (HPV) infection that develops in a high-grade squamous intraepithelial lesion.<sup>2</sup>

Although the prognosis is generally

good for patients in the early stages of cancer, those in the advanced stages can experience metastasis of the cancer from its original site to locoregional nodes and/or distant organs by lymphatic embolization or hematogenous diffusion.<sup>3</sup>

The most commonly described symptom of vulvar cancer is a long history of itchiness. With the progression of symptoms, vulvar bleeding, dysuria, discharge and pain occur. The lesion, which chronically transforms into ulceration and leucoplakia, may show microbial spreading; however, it rarely leads to the development of necrotizing fasciitis (NF).<sup>4</sup>

NF is a rapidly progressing and fatal infection of the superficial fascia and subcutaneous tissues that can occur as a result of surgical incision, episiotomy, unrecognized trauma and regional infection in sites such as Bartholin's glands.<sup>5</sup> NF development due to vulvar SCC is very rare and has been reported in only one instance in the literature.<sup>6</sup> Here, we present a case of vulvar SCC that developed as a result of lichen sclerosis that had rapidly progressed to NF by the time of diagnosis.

### Case report

A 58-year-old female multipara with no relevant medical or surgical history presented to the emergency department with a swelling on her left labia that had been developing over the course of six days. It had opened and begun to drain two days prior. The complaints started about three months earlier in the form of itchiness in the genital area and a small pimple on the left labium majus. Additionally, pain and a high temperature in the right puborectal region were noted. She had a high fever with a body temperature of 38.9°C, pulse rate of 120 beats/minute and blood pressure of 140/90 mmHg. Her medical history included a diagnosis of diabetes mellitus and hypertension. The patient was admitted to general surgery with the diagnosis of a complicated skin and soft tissue infection and referred to dermatology.

Dermatological examination showed diffuse erythema and oedema starting from the right mons pubis, including the labium majus and minus, and reaching to the right gluteal region. On the left labium majus and minus, a long, fragile, vegetant, exophytic ulcerated tumour mass of 2×7 cm was observed (Figure 1). Her laboratory work-up revealed low haemoglobin of 9.5 g/dL, high glucose of 495 mg/dL, an elevated white blood cell count of 43,140, increased erythrocyte sedimentation rate (ESR) of 70

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and c-reactive protein (CRP) of 33.03 mg/dL. Empirical antibiotic therapy was started in the form of piperacillin/tazobactam, and a surgery consult was requested. A

pelvic CT scan showed cutaneous ulceration over the left labia and air in the subcutaneous fat of the left groin and left lower abdominal wall (Figure 2).

An incisional biopsy was conducted on the lateral part of the right labium majus. Histopathological examination revealed keratin pearls with atypical mitosis and apoptotic and dyskeratotic cells, including in the dermis and epidermis. Acanthosis, nuclear enlargement of the epithelium and pleomorphism were observed in all layers (Figure 3a, b). In the biopsy taken from the atrophic area of the contralateral region were present epidermal atrophy, loss of elastic fibres in the papillary dermis, inflammatory infiltration of T cells and sclerosis findings consistent with LS (Figure 3c).

The patient was clinically and pathologically diagnosed as having a “well-differentiated vulvar carcinoma on the basis of Lichen Sclerosus.” In addition, PCR and special staining to exclude HPV were negative. Due to the patient’s rapidly deteriorating condition, the decision was made to perform immediate exploratory surgery. The Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score was 8, which is highly significant for NF. Bacteriology confirmed a diagnosis of NF with a  $\beta$ -haemolytic group *Streptococcus* culture. Exploratory surgery of the pelvic and abdominal regions performed by general surgery confirmed the diagnosis of necrotizing soft tissue infection originating at the left vulva and spreading to the abdominal wall. Several additional areas of necrosis in the abdominal wall were discovered and debrided. After additional debridement of the genital and abdominal areas, both areas were closed with incisions. A triple parenteral antibiotic combination (ampicillin-sulbactam + ornidazole + ciprofloxacin) was used. The patient’s clinical condition and inflammatory markers improved significantly in the first 24 hours postoperatively. After postoperative recovery, she was discharged on the 12<sup>th</sup> day following the completion of her systemic treatment. However, due to the rapid doubling of the tumour, approximately two weeks after the biopsy, the diameter of the mass at the biopsy site reached 5×11 cm (Figure 4). For further examination and treatment of vulvar SCC, she was referred to the oncology department. Lymphovascular and perineural invasions were found. Of all the inguinal lymph nodes dissected, four presented metastasis of vulvar SCC, four nodes from the left side and one from the right. According to TNM stabilization, our patient had SCC stage IIIC.

## Discussion

Vulvar NF is a surgical emergency with high morbidity and mortality rates. This anatomic placement can be fatal, with vulvar and perineal forms associated with mortality as high as 50%.<sup>7</sup> NF is divided into two types. Type I is a synergistic polymicrobial infection of both aerobes and anaerobes, most commonly seen in diabetes, peripheral vascular disease and postoperative patients. Causative bacteria are *Staphylococcus aureus*, *Streptococci*, *Enterococci*, *E. coli*, *B. fragilis* and *Clostridia*. Type II, which is a monomicrobial infection of group A *Streptococci* (*Streptococcus pyogenes*) and methicillin-resistant *S. aureus*, has been seen in patients without underlying comorbidity. Most vulvar NF infections fall into the type I group.<sup>8</sup>

There are many factors that can lead to NF, such as diabetes, immunodeficiency, peripheral vascular disease, increased age, hypertension, obesity and exposure to radiation (7). In addition to existing risk factors and based on a gynaecological point of view, NF also commonly involves endomyometritis, parametritis, adnexitis and cellulitis.<sup>9</sup> Also, among the few reported cases of NF originating in the vulva, the affected patients are typically diabetic like our patient. However, the probability of vulvar SCC leading to vulvar NF is very rare compared to the other causes of NF. The association of vulvar SCC with NF and its impact on the prognosis of NF has not been discussed adequately in the obstetric literature. Apart from the predisposing factors listed above, the development of NF as a complication of vulvar SCC has been reported in only one case.<sup>6</sup> In our case, both the patient’s risk factors and low socioeconomic status, which led her to ignore years of vulvar complaints (chronic itchiness, burning, bleeding), led to and delayed the diagnosis of the malignancy that caused NF.

The vulva is a unique skin area that acts as a transition between the skin’s cutaneous epithelium and the mucosa of the female urogenital system. The vulvar region contains one of the densest area of microbial flora.<sup>10</sup> Typically, the disruption of the integrity of the skin and mucous membranes due to malignancy and the alteration of the hemodynamic of the factors modulating vulvar microflora activate pathogenic microorganisms, and the infection progresses through the subcutaneous tissue and fascia.<sup>2</sup> Tissue ischemia secondary to peripheral vascular compromise, decreased phagocytosis and decreased chemotaxis of polymorphonuclear leukocytes, and hyperglycaemia also promote bacterial growth.

Clinical symptoms appear 1–2 days after the infection has spread. The affected area is initially very painful, but it displays no visible change. With the progression of symptoms, reddish-purple skin discoloration, bullous rash, systemic toxicity and wound anaesthesia occur. These symptoms are the result of tissue ischemia leading to denervation and vascular thrombosis.<sup>7</sup>

In our patient, the spreading of the infection in the vulvar area was facilitated by the loose areolar tissue in the subcutaneous layers and the contiguity of the vulvar fascial planes with the groin and anterior abdominal wall. The patient was initially admitted to the medical ward and a surgical consultation was requested several hours later.

Considering that delayed treatment of NF can lead to high mortality rates, early diagnosis is crucial. However, as there is no definitive diagnostic test, diagnosis often depends on the physician’s approach. Valuable and validated diagnostic tools currently available are the LRINEC score, with a positive predictive value of 92.0%, and CRP.<sup>11</sup> Also, due to its wide availability and high resolution compared to radiography or ultrasound, CT is the primary imaging method used in the diagnosis of NF. Gas accumulation in the soft tissue is a CT finding, but its absence does not exclude the diagnosis if NF is clinically suspected.<sup>12</sup> In our case, the high LRINEC score and the overlap of the radiological findings with NF were a guide for emergency surgical intervention.

Early and aggressive surgical debridement with broad spectrum antibiotic coverage is still the main treatment for NF. Systemic antibiotic treatment often consists of a penicillin, clindamycin and an aminoglycoside (e.g. GAC regimen: gentamicin, ampicillin, and clindamycin) until the patient stabilizes.<sup>5</sup> Hyperbaric oxygen therapy in addition to surgery and antibiotics has been found to decrease morbidity and mortality.<sup>13</sup> In our patient, adequate necrotic material was removed at the first opportunity to reduce the risk of further progression, regardless of the remaining defect. After 12 days of combined antibiotics therapy, she completely recovered from NF.

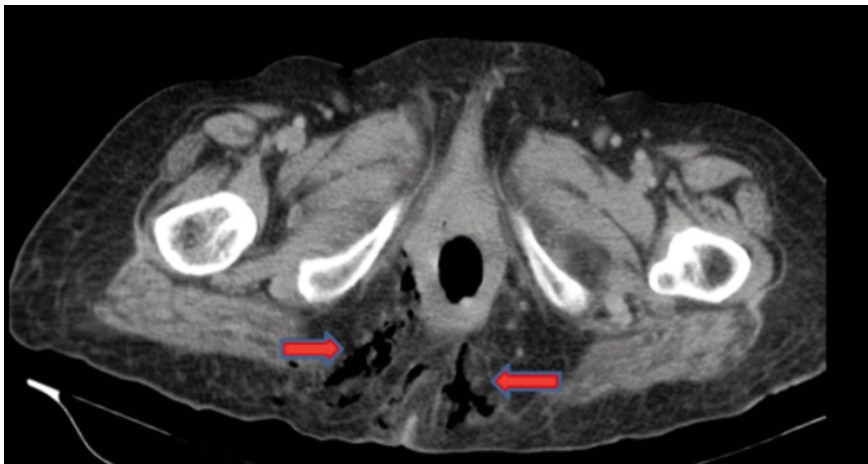
Therefore, the management principles in this case should be twofold: 1) to control the infection quickly and precisely through the extensive and radical debridement of necrotic tissue and 2) then to identify and treat the underlying condition (in this case, removing the vulvar SCC). Therefore, we referred the patient to the gynaecologic oncology department for further treatment. Careful clinical and imaging-based follow-up will enable us to determine whether a long-term cure has been achieved.



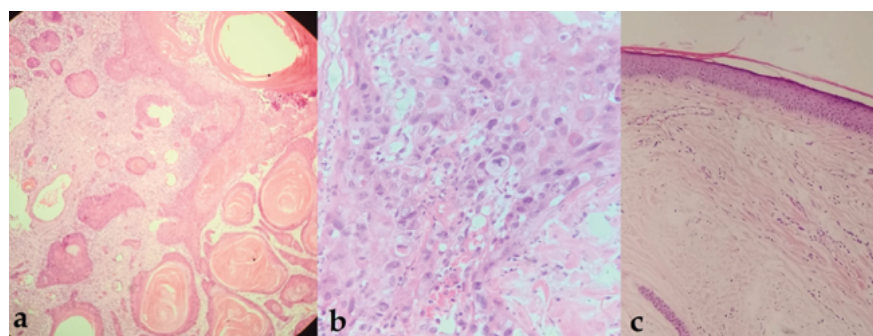
**Figure 1.** Diffuse erythema and oedema starting from the right mons pubis, including the labium majus and minus, and reaching to the right gluteal region. On the left labium majus and minus, a long, fragile, vegetant, exophytic ulcerated tumour mass of 2×7 cm.



**Figure 4.** Due to the rapid doubling of the tumour, approximately two weeks after the biopsy, the diameter of the mass at the biopsy site reached 5×11 cm.



**Figure 2.** A pelvic CT scan showed cutaneous ulceration over the left labia and air in the subcutaneous fat of the left groin and left lower abdominal wall.



**Figure 3.** a) Keratin pearls with atypical mitosis and apoptotic and dyskeratotic cells, including in the dermis and epidermis (H&E 40x). b) Acanthosis, nuclear enlargement of the epithelium and pleomorphism were observed in all layers (H&E 200x). c) Epidermal atrophy, loss of elastic fibres in the papillary dermis, inflammatory infiltration of T cells and sclerosis findings consistent with LS (H&E 100x).

## Conclusions

This case highlights the importance of considering the rare underlying causes of NF. Vulvar SCC should be sought as a rare potential aetiology in patients with NF of the genitalia as early diagnosis and subsequent emergency surgical intervention are essential to avoid negative patient outcomes, including death.

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