International Journal of Research in Dermatology
Mercado-Figueroa H et al. Int J Res Dermatol. 2026 Jan;12(1):63-66
http://www.ijord.com

DOI: https://dx.doi.org/10.18203/issn.2455-4529.IntJResDermatol20254123

Case Report

A rare malignancy in an uncommon location: case of a 25-year-old female patient with infiltrative vulvar basal cell carcinoma

Hillary Mercado-Figueroa[1], Jose Silva-Martinez[1], Itzamar Pastrana-Echevarria[2]*, Alexandra Ortiz-Orama[2]

[1]Department of Obstetrics and Gynecology, Hospital Episcopal San Lucas, Ponce, Puerto Rico
[2]Department of Graduate Medical Education, Hospital Episcopal San Lucas, Ponce, Puerto Rico

Received: 24 September 2025
Accepted: 14 November 2025

***Correspondence:**
Dr. Itzamar Pastrana-Echevarria,
E-mail: 121ipastrana@uccaribe.edu

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ABSTRACT

Basal cell carcinoma (BCC) of the vulva accounts for less than 1% of all BCCs. Herein this report describes a case of a 25-year-old female with vulvar BCC that was presented as an ulcerated mass lesion with erythema, fissuring and bleeding in the upper region of the right labium majus. After biopsy, the histopathology results showed basal cell carcinoma, mixed nodular and infiltrative type with focal areas of squamous metaplasia confirmed by IHC staining for common BCC markers. The reasoning for this clinical case is to report the atypical presentation and unique histopathology, for future consideration as a differential diagnosis when encountering genital lesions and to contribute to an ideal treatment. Vulvar BCCs remain a rare tumor of the vulva, which has excellent prognosis if managed appropriately. Therefore, any persistent lesion in the vulvar region should be biopsied and examined histologically regardless of the age of the patient.

Keywords: Basal cell carcinoma, Vulvar cancer, Genital skin tumors, Squamous metaplasia

INTRODUCTION

Basal cell carcinoma (BCC) is the most common cutaneous malignancy and the most frequently diagnosed cancer in humans.[1] About 5.4 million of BCC are diagnosed each year in the United States, affecting nearly one in five Americans.[1,2] BCC is typically a highly curable cancer that rarely results in metastasis or death.[3] It usually affects UV-exposed areas, with nearly 85% of cases involving the head or neck; less frequently, it may involve the trunk and extremities.[1,3]

However, BCC occurring in non-UV-exposed areas is uncommon, and vulvar involvement is particularly rare. Moreover, 20% of BCC can arise on non-sun exposed skin and Vulval BCC accounts for less than 1% of all BCCs.[4] Among the vulvar BCC the most common location is the labium majus, followed by the clitoris.[5] Its pathogenesis of BCC is largely attributed to defective signaling through the Hedgehog (HH) pathway, which forms the molecular basis of tumor development.[6]

Vulvar BCC typically presents in elderly patients, with an average patient age of 70 years; very few cases describing this malignancy in young adults have been reported. The etiology is unknown but several risk factors have been associated with vulvar BCC as older age, chemicals exposures (e.g., arsenic), prior radiation exposure, trauma, syphilis, chronic skin inflammation, weakened immune system, and genetic syndromes such as Gorlin syndrome.[7,8]

In terms of its clinical presentation, BCC typically presents as a shiny, pink or flesh colored papule or nodule with surface telangiectasia.[1] Patients often give a history of crusting and recurrent bleeding causing them to seek medical evaluation as the tumor may enlarge and ulcerate over time.[1] Vulvar BCC is mostly asymptomatic but

among patients who report symptoms the most common one is pruritus.[7]

Diagnosis confirmation relies on skin biopsy of the lesion, including shave, punch or excisional biopsy.[1] The characteristic features of the BCC include nests of basaloid cells palisading at the periphery and disorganized central arrangements.[1] Several histologic subtypes have been identified including nodular (the most common), superficial, infiltrative, mixed, basosquamous, infundibulocystic and morpheaform variants.[3] Importantly, histologic aggressive ones such as infiltrative, morpheaform and infundibulocystic vulvar BCCs are associated with higher recurrence rates and have been reported scarcely in the literature.[3]

Management for vulvar BCC is surgical, primarily wide local excision, Mohs micrographic surgery (MMS) or in some cases vulvectomy.[3,9] Prognosis for vulvar BCC is excellent and local recurrence has been reported at a range from 0% to 21%. The case of a 25-year-old female patient with previous history of ALL treated with chemotherapy and ionizing radiation who has developed nodular and infiltrative type vulvar BCC. The goals of this case report are to highlight an atypical presentation of this rare malignancy as a differential diagnosis when encountering genital lesions, and to review risk factors, pathophysiology and optimal management strategies.

CASE REPORT

25-year-old nulligravid female patient with past medical history of acute lymphocytic leukemia (ALL), type 2 diabetes mellitus, mixed hyperlipidemia, vitamin D3 deficiency, and intellectual disability came to the clinic for evaluation of a progressive enlarging vulvar mass. The lesion was located in the upper quadrant of the right labium majus. The patient reported that the lesion first appeared approximately six months ago. Over time, the mass kept growing, accompanied by pruritus, localized pain and occasional bleeding. Her symptoms persisted despite the use of topical antifungals and over the counter barrier ointments, which had been applied without medical guidance.

The patient denied fever, systemic symptoms, prior trauma to the area, or prior similar lesions. She had no personal or family history of cutaneous malignancies. She reported previous exposure to radiation for the management of her ALL. She had never been sexually active, and there was no history of sexually transmitted infections.

On physical examination, an erythematous plaque with areas of superficial fissuring and bleeding was observed on the upper quadrant of the right labium majus. No inguinal lymphadenopathy was appreciated, and the remainder of the pelvic examination, including inspection of the vaginal mucosa of the cervix, was within normal limits. No additional skin lesions were noted elsewhere on the body.

A biopsy of the vulvar lesion was performed. Histopathological evaluation revealed features consistent with basal cell carcinoma, nodular and infiltrative type (Figures 1A and B) with focal areas of metaplasia. Immunohistochemical staining (IHC) was performed to further characterized the lesion and confirmed diagnosis: P16 patchy positive, BerEP4 positive (Figure 1C), P-63 positive, KI-67 high proliferative index, SOX10 negative, and EMA negative. These findings supported the diagnosis of basal cell carcinoma with aggressive histological features. The patient was then referred for further evaluation and management by a gynecologic oncologist.

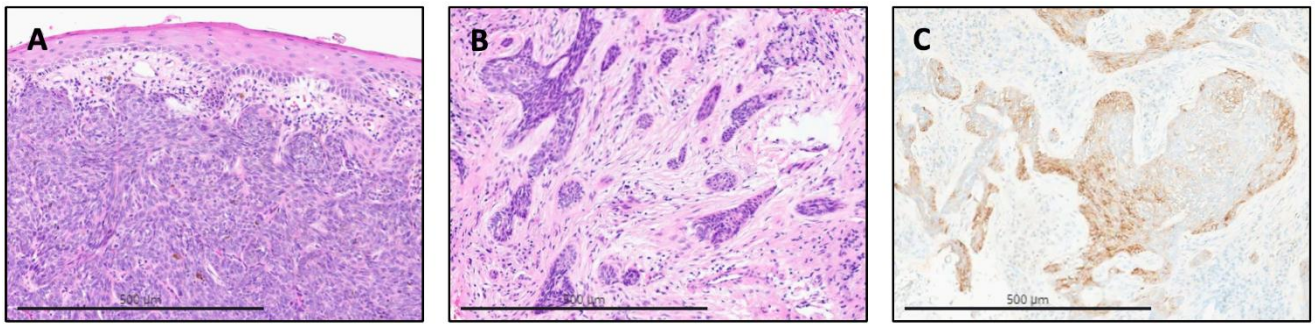

Figure 1: Histopathological features of a 25-year-old patient with vulvar basal cell carcinoma, (A) benign epidermis with underlying basaloid tumor (H&E x10), (B) infiltrative component of basaloid tumor (H&E x10), and (C) berep4 positive staining in basaloid cells (ICH x10).

DISCUSSION

This case highlights a rare presentation of a basal cell carcinoma located in a non-sun exposure area, the upper right quadrant of the labium majus in a young Hispanic patient evaluated at a southern clinic in Puerto Rico. BCC typically arises in sun-exposed areas, most commonly the head and neck.[1] However, VBBC is a rare type of skin cancer that originates from the basal cells of the vulvar epithelium, accounting for less than 5% of all vulvar malignancies.[3,10] Of the VBBC reported in the literature the majority occur in postmenopausal women of advanced age, usually the seventh or eighth decade, making this case particularly unusual.[3,11]

The pathogenesis of BCC is strongly linked to chronic sun exposure as it can damage DNA by increasing the likelihood of transcription errors or by direct damage of DNA replication, leading to cellular mutations that can activate pro-oncogenes or deactivate tumor suppression genes. Among the tumor suppression genes mutations in Tp53 and PTCH1 have been associated with BCC.[12] However, the occurrence of VBCC in a non-sun-exposure region as the vulva suggests additional contributing risk factors. Reported risk factors for VBBC include chronic exposure to ultraviolet (UV) radiation, trauma, tanning bed use, syphilis, prior cutaneous malignancies, immuno-suppression, and genetic syndromes.[3] The patient had a history of ALL, previously treated with ionizing radiation, making this a highly associated risk factor for VBCC. Furthermore, the patient had multiple comorbidities such as diabetes mellitus, mixed hyperlipidemia and intellectual disability which may have contributed to delayed diagnosis and added complexity to her overall care.

The patient presented a gradually enlarging lesion in the upper right quadrant of the labium majus, which is the most common location for VBCC followed by the clitoris.[5] The patient reported associated pruritus, pain and bleeding. Macroscopically, BCC often appears as a pink pearly nodule with telangiectasias, ulceration or a brown pigment.[5] On physical examination, the patient presented with characteristic findings as erythema, fissuring and ulceration with bleeding.

Although nonspecific, these symptoms are consistent with the clinical behaviour of VBCC, which is often a slow growing but locally invasive tumor. While most BCC was indolent, metastasis thought rare has been reported. One case series identified twelve of 446 cases (2.7%) being metastatic.[3] Of the 12 cases, seven were reported to invade subcutaneous tissue and only two extending to the pubic bone.[3] Even though distant node metastasis and hematogenous spread is rare, it can occur. These findings underscore the importance of recognizing metastatic potential, even in classically low risk malignancies like BCC.

VBCC is diagnosed through histopathological analysis of a biopsy specimen. Its histology is essentially the same as BCC which is characterized by a basaloid epithelium composed of basaloid tumor cells with basophilic nuclei and scant cytoplasm.[5,13] Several histopathological subtypes have been described in the literature and among them the most common ones are nodular and superficial.[5] In the patient the lesion was diagnosed as nodular and infiltrative basal cell carcinoma with focal areas of metaplasia. These subtypes are considered more aggressive than the superficial or nodular forms alone.

Immunohistochemistry (IHC) supported the diagnosis: staining positive for common BCC markers, including P16, BerEP4, p-63 and KI-67. Specifically, the BerEP4 marker which is a monoclonal antibody has been widely used and is considered a reliable marker for the diagnosis of BCC.[14] In contrast, SOX10 and EMA were negative which helps rule out other cancers such as melanoma, actinic keratosis, squamous cell carcinoma or melanocytic hyperplasia.[15,16] Moreover, p-63, a transcription factor of the p53 family, was positive. This marker plays a critical role in the differentiation of several tissues including the squamous epithelium.[17] Additionally, KI-67 which is a protein that is found only in cells that are dividing was also positive and serves as a marker for cellular proliferation.[18]

The mainstay treatment for VBCC is complete surgical excision with histological clear margins. Moreover, treatment modality selection depends on lesion size, location, depth and patient specific factors. Options include surgical excision, Mohs micrographic surgery, laser ablation, radiation therapy and in rare cases topical treatment.[10,19] In the patient, given her young age and multiple comorbidities, a multidisciplinary approach was pursued. She was referred to a gynecologic oncologist for specialized management.

The literature review identified very few cases of VBCC in women under 30 years of age. Most reported cases involve postmenopausal older patients, and few have documented prior radiation exposure as a precipitating factor. For example, Celik et al. described VBCC with clitoral involvement in a 72-year-old woman without prior radiation exposure, highlighting the typical advanced age of presentation.[20]

The patient's young age and prior exposure to ionizing ration for ALL distinguish her case from most published reports. The contrast between her presentation and the current literature underscores the importance of considering additional pathogenic influences and tailoring clinical suspicion accordingly, especially in patients with atypical risk profiles.

It is important to note that the indolent behavior and local invasiveness of VBCC may necessitate long-term follow-up and surveillance for local recurrence. BCC in the genital area is at high risk for recurrence however the prognosis of VBCC is favorable.[11] Regular clinical examinations and imaging studies may be recommended to monitor for disease recurrence and assess treatment response. Additionally, patient education on self-examination of the vulvar area may be emphasized to promote early detection of any potential lesions.

CONCLUSION

This case report highlights a unique presentation of VBBC in a young nulligravid female patient with history of acute lymphocytic leukemia and other comorbidities. The diagnosis was confirmed by histopathological examination and IHC staining for common BCC markers. The management approach should be individualized based on the patient's overall health status and preferences, and long-term follow-up for surveillance of local recurrence is important. Further research is needed to better understand

the risk factors, pathogenesis, and optimal management strategies for VBBC in patients with complex medical histories.

ACKNOWLEDGEMENTS

Authors would like to thank the medical team, hospital staff and the patient for their contributions to this case report.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Mercado-Figueroa H, Silva-Martinez J, Pastrana-Echevarria I, Ortiz-Orama A. A rare malignancy in an uncommon location: case of a 25-year-old female patient with infiltrative vulvar basal cell carcinoma. Int J Res Dermatol 2026;12:63-6.