Primary Malignant Melanoma of the Uterine Cervix: Rare Case Report

https://doi.org/10.32635/2176-9745.RBC.2023v69n4.4410

Melanoma Maligno Primário do Colo do Útero: Relato de um Caso Raro

Melanoma Maligno Primario del Cuello del Útero: Informe de un Caso Raro

Carlos Anselmo Lima[1]; Adriana Cardoso Batista Albuquerque[2]; Érika de Abreu Costa Brito[3]; Marcela Sampaio Lima[4]

ABSTRACT

Introduction: Primary cervical melanoma is a rare and often challenging diagnosis, particularly in the presence of amelanotic lesions, where confirmation should be made through immunohistochemical methods. Despite aggressive treatment, the prognosis for this disease is typically poor. **Case Report:** A 79-year-old woman with a history of vaginal bleeding from a malignant cervical lesion. Initially, colposcopy examination revealed an ulcerated lesion of the exocervix, and biopsy confirmed a malignant neoplasm. However, following a radical abdominal hysterectomy, histopathological examination displayed a malignant epithelioid neoplasm, confirmed a malignant melanoma of the cervix through immunohistochemical assays. The patient received adjuvant chemotherapy and radiation therapy, but eventually experienced recurrence and died. **Conclusion:** The present report assesses a patient with an uncommon diagnosis of cervical melanoma, which, despite aggressive treatment, had an unfavorable outcome. However, thorough skin surveillance should be performed to correctly diagnose it as primary.

Key words: cervix uteri; uterine cervical neoplasms; melanoma.

RESUMO

Introdução: O melanoma cervical primário é um diagnóstico raro e frequentemente desafiador, especialmente na presença de lesões amelanóticas, cuja confirmação deve ser feita por métodos imuno-histoquímicos. Apesar do tratamento agressivo, o prognóstico para essa doença costuma ser ruim. **Relato do caso:** Mulher, 79 anos, com histórico de sangramento vaginal decorrente de uma lesão cervical maligna. Inicialmente, a colposcopia revelou uma lesão ulcerada no exocérvix e a biópsia confirmou ser um tumor maligno. No entanto, após uma histerectomia abdominal radical, o exame histopatológico mostrou tratar-se de uma neoplasia maligna epitelioide, confirmada como um melanoma maligno do colo do útero por meio de exame imuno-histoquímico. A paciente recebeu quimioterapia adjuvante e radioterapia, mas eventualmente apresentou recorrência e veio a óbito. **Conclusão:** O presente relato avalia uma paciente com um diagnóstico incomum de melanoma cervical que, apesar do tratamento agressivo, teve um desfecho desfavorável. No entanto, uma vigilância cutânea minuciosa deve ser realizada para diagnosticá-lo corretamente como primário.

Palavras-chave: colo do útero; neoplasias do colo do útero; melanoma.

RESUMEN

Introducción: El melanoma cervical primario es un diagnóstico raro y a menudo desafiante, especialmente en presencia de lesiones amelanóticas, donde la confirmación debe hacerse mediante métodos inmunohistoquímicos. A pesar del tratamiento agresivo, el pronóstico de esta enfermedad suele ser malo. **Informe del caso:** Mujer, 79 años, con antecedentes de sangrado vaginal debido a una lesión cervical maligna. Inicialmente, el examen colposcópico reveló una lesión ulcerada del exocérvix y la biopsia confirmó que se trataba de una neoplasia maligna. Sin embargo, después de una histerectomía abdominal radical, el examen histopatológico mostró una neoplasia epitelioide maligna, confirmada como un melanoma maligno del cuello uterino mediante pruebas inmunohistoquímicas. La paciente recibió quimioterapia adyuvante y radioterapia, pero finalmente sufrió una recurrencia y falleció. **Conclusión:** El presente informe evalúa a una paciente con un diagnóstico poco común de melanoma cervical, que, a pesar del tratamiento agresivo, tuvo un resultado desfavorable. Sin embargo, para diagnosticarlo correctamente como primario, se debe realizar una vigilancia exhaustiva de la piel.

Palabras clave: cuello del útero; neoplasias del cuello uterino; melanoma.

[1]Universidade Federal de Sergipe (UFS), Hospital Universitário, Rede Ebserh. UFS, Programa de Pós-Graduação em Ciências da Saúde e Programa de Pós-Graduação Profissional em Gestão e Inovação Tecnológica em Saúde. Aracaju (SE), Brazil. E-mail: ca.lima01@gmail.com. Orcid iD: https://orcid.org/0000-0003-4269-7320
[2,3,4]UFS, Hospital Universitário, Rede Ebserh. UFS, Programa de Pós-Graduação em Ciências da Saúde. Aracaju (SE), Brazil. E-mails: drikascb@msn.com; kostabrito@hotmail.com; marcelasampaio@yahoo.com.br. Orcid iD: https://orcid.org/0000-0001-8046-7812; Orcid iD: https://orcid.org/0000-0003-0050-1799; Orcid iD: https://orcid.org/0000-0003-1738-4023
Corresponding author: Carlos Anselmo Lima. Rua Cláudio Batista 505 – Palestina. Aracaju (SE), Brazil. CEP 49060-676. E-mail: ca.lima01@gmail.com

INTRODUCTION

The diagnosis of primary melanoma in mucosal sites is uncommon, accounting for less than 4% of all melanoma cases. These lesions are primarily found in the oral cavity, esophagus, anus, conjunctiva, and vulvovaginal epithelium, and are difficult to diagnose due to the absence of melanin, a characteristic feature of cutaneous melanomas[1].

Primary melanoma of the uterine cervix is an extremely rare condition, with only a few cases reported in the world literature[2-4]. Unlike non-cutaneous melanomas, primary cervical melanomas often present in advanced stages and have a more aggressive course, leading to a poorer prognosis[5]. Confirmatory diagnosis typically requires immunohistochemical assays, and staging tests are performed to assess the presence of metastasis[6].

The purpose of this study is to report an unusual case of primary melanoma of the cervix, including its diagnosis, management, and follow-up until the patient's death. In compliance with the current legislation, the study was submitted, reviewed and approved by the Institutional Review Board of "*Universidade Federal de Sergipe*" CAAE (submission for ethical review) number 71636723.2.0000.5546 and approval report number 6,319,121, in compliance with Resolution 466/2012[7] of the National Health Council.

CASE REPORT

A 74-year-old Brazilian female of African descent presented with vaginal bleeding. Three days later, she was evaluated by a gynecologist who identified and performed a biopsy on a cervical lesion. The initial biopsy confirmed the diagnosis of squamous cell carcinoma of the cervix. Following this, one-month post-biopsy, the patient was admitted to the Oncologic Facility for a comprehensive gynecologic examination. The examination revealed a 4-cm cervical lesion that exhibited no invasion into the vagina or parametrium. Subsequent assessments including blood, urine, and cardiac tests, chest x-ray, and abdominal ultrasound were performed, ruling out any extra-uterine involvement. Based on clinical and imaging evaluations, the lesion was staged as FIGO (International Federation of Gynecology and Obstetrics, 2009[8]) IB1.

Forty-four days after the initial symptoms, the patient underwent a radical abdominal hysterectomy with pelvic lymphadenectomy. Histopathological examination revealed a malignant 3.5 cm width, 1.4 cm deep epithelioid neoplasm, consisting of papillary and fusocellular areas, limited to the exocervix and negative pelvic lymph nodes, consistent with previously determined clinical staging. She had an uneventful post operative course.

Due to the diagnosis of an epithelioid neoplasm, immunohistochemistry (Table 1) was performed and revealed expression of the proteins S-100 (Figure 1) and Melan-A (Figure 2), indicating malignant melanoma. The lack of cutaneous lesions led to a final diagnosis of primary melanoma of the uterine cervix.

Following the processing of the surgical specimen and subsequent immunohistochemical analysis, there was a remarkable delay in reaching the final diagnosis. Eighty-two days post-surgery, the patient underwent adjuvant treatment comprising dacarbazine (D1-D3), carmustine (D1), and cisplatin (D1-D3) concurrently with external beam radiation (whole pelvic 45 Gy; 28 Fr/1.8 Gy), followed by brachytherapy (24 Gy at point C; 4 Fr/6 Gy). The patient did not experience any major complications during the adjuvant treatment, and extended granulocytopenia was prevented with filgrastim. Eleven months after completing brachytherapy, the patient was diagnosed with lung metastasis, peritoneal

Table 1. Immunohistochemical markers, melanoma of the uterine cervix

Antibodies	Clone	Result
Cytokeratins – 40, 48, 50, 50.6 kDa	AE1/AE3	Negative
Protein p63	Dak-p63	Negative
P16 (INK4)	G175-405	Negative
Cytokeratin 5/6	D5/16B4	Negative
Protein S-100	Polyclonal	Positive
Melan A (MART-1)	D5/16B4	Positive
Desmin	D33	Negative
Myogenin	F5D	Negative
Chromogranin A	DAK-A3	Negative

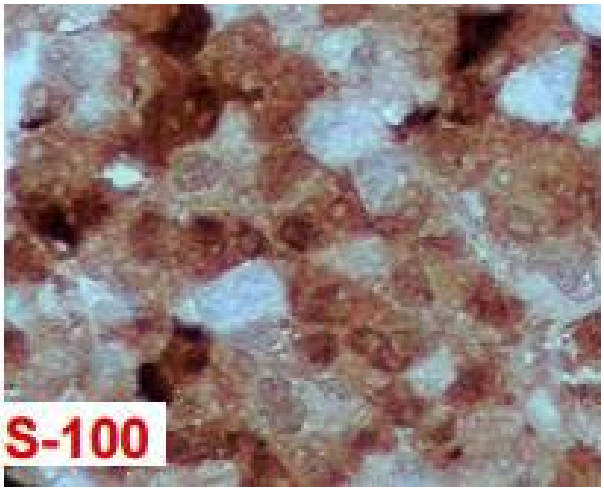

Figure 1. Immunohistochemical expression of protein S-100

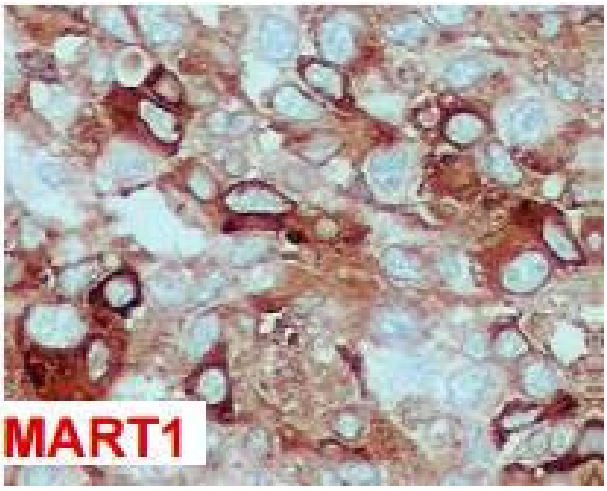

Figure 2. Immunohistochemical expression of MART-1

recurrence, and ascites, and succumbed to these conditions within two months.

DISCUSSION

The diagnosis of primary melanoma of the uterine cervix is achievable due to the description of melanocytic cells in cervical epithelium[9,10]. The scarcity of this condition is well documented, as most of the literature consists in case reports[2,11,12]. The present case was diagnosed in an older patient with a deep lesion, which was challenging to diagnose, and despite undergoing surgery, chemotherapy, and radiation therapy, proved incurable.

Patients with primary melanoma are often diagnosed after 60 years of age[9]. Discharge or bleeding is typically the main presenting symptom; however, early lesions are frequently detected in asymptomatic patients during gynecological examination[6]. In the present case, the onset of bleeding prompted the patient to seek specialized care immediately, initiating her first treatment 44 days after the onset of symptoms. This duration is described in the literature with varying degrees but is often reported as relatively short[6].

The initial biopsy in this case was not accurately diagnosed. Most lesions are amelanotic and thus, immunohistochemistry is necessary for confirmation of diagnosis. Expressions of protein S-100, Melan-A, and HMB-45 are often seen[13-15]. The former two proteins were present in this case. No cervical alterations caused by HPV (Human Papilloma Virus) were detected, and p16 (INK4), which is a surrogate marker for persistent HPV infection[16], was not expressed.

The tumor was initially clinically staged as FIGO IB1 cervical cancer and later confirmed through pathological examination (pIB1). However, following immunohistochemical confirmation of melanoma, the authors inferred a grim prognosis for such an aggressive neoplasm and highlighted limited treatment options[17]. Radical surgery is advocated as the preferred approach, though the necessity of lymphadenectomy remains a subject of debate in the absence of metastasis evidence[18].

Adjuvant chemotherapy and radiation therapy are usually administered, and neoadjuvant chemotherapy-radiation treatment may also be used[3]. The adjuvant treatment, however, took longer to commence due to a lengthier diagnostic process. Whether this extended period between surgical treatment and the initiation of adjuvant therapy contributed to a poor outcome cannot be conclusively stated, as cervical melanoma is known to be an aggressive neoplasm. This likely remained the primary factor influencing the unfavorable progression of the case. Dacarbazine has been extensively utilized, showing response rates of 15 to 20%; treatment regimens involving cisplatin, vinblastine, and dacarbazine/bleomycin did not yield superior results[19].

More recently, the use of immune check point inhibitors appears to be a favorable option. In one study with nivolumab[20], two patients with post-operative recurrence were in remission at 33 and 17 months respectively. In another study, pembrolizumab[21] for high-risk stage III skin melanoma resulted in statistically significant longer recurrence-free survival compared to placebo, whereas, for aggressive cervical melanoma, poor response to the medication led to an overall survival of only six months[22].

In this case, a conventional treatment regimen, supplemented with carmustine, was selected considering the aggressiveness of the disease, but unfortunately, it proved unsuccessful.

CONCLUSION

Melanoma of the uterine cervix is a rare condition that is frequently difficult to diagnose definitively. Upon confirmation of diagnosis through immunohistochemistry, a thorough search for skin and other mucosal lesions should be conducted to determine the presence of metastases. Given the rarity and poor prognosis of cervical melanoma, multi-center studies may be necessary to establish the optimal treatment approach.

ACKNOWLEDGEMENT

The authors thank the following physicians for their support in managing treatment approaches: Lícia Violeta de Souza, Iraldo Jasé dos Santos, José Geraldo Dantas bezerra, and Maria Luciene Santos.

CONTRIBUTIONS

Carlos Anselmo Lima and Marcela Sampaio Lima contributed to the study design, data collection and critical analysis of the results. Carlos Anselmo Lima, Adriana Cardoso Batista Albuquerque and Érika de Abreu Costa Brito contributed to the wording of the manuscript. All the authors revised and approved the final version for publication.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

FUNDING

None.

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Recebido em 29/9/2023
Aprovado em 11/12/2023

Scientific-Editor: Anke Bergmann. Orcid iD: https://orcid.org/0000-0002-1972-8777