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CASE REPORT

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Vaginal Mucosa Melanoma with Giant Cell Phenotype: A Case Report

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ABSTRACT

Melanomas are malignant tumors that arise from pigmented cells, melanocytes. In the female genital tract, they represent 18% of all mucosal melanomas. The first vaginal melanoma was described in 1887, and approximately 500 cases have recently been documented in the literature. Currently, vaginal melanoma represents <5.5% of all vaginal neoplasms and 0.4 to 0.8% of all melanomas in women. We present the case of a 60 year-old woman with transvaginal bleeding and dysuria. Colposcopy reported an exophytic lesion located on the anterior vaginal wall, pigmented and bleeding upon contact. The clinical diagnosis was cervical carcinoma, a biopsy was taken and sent to the Surgical Pathology service where the histopathological diagnosis of melanoma with multinucleated giant cell phenotype of the vaginal mucosa was concluded, it also presented pigmentation and osteoid stromal metaplasia.

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KEYWORDS
Melanoma of the vaginal mucosa; Multinucleated giant cells; Histological variants; Immunohistochemistry; BRAF

INTRODUCTION

Melanomas are malignant tumors that arise from pigmented cells, melanocytes. Most melanomas are of cutaneous origin, according to the literature, only 0.8%-3.7% of melanomas occurs in the mucosa [1].

In the female genital tract, it represents 18% of all mucosal melanomas, with the vulva being the most frequent site (70%-76.7%), followed by the vagina (19.8%-21%) and the cervix (9%) [2-4].

Vaginal melanoma accounts for <5.5% of all vaginal neoplasms and 0.4% to 0.8% of all melanomas in women. The age of presentation varies from 57 to 68 years of age, predominantly in postmenopausal women (80%) of Caucasian descent [2-6]. These are limited to the lower third and the anterior wall of the vagina, suggesting that they are associated with conditions of chronic inflammation, viral infections, and irritating substances [6,7]. Clinically, it presents with vaginal bleeding, unifocal or multifocal ulceration (20%), pigmentation in most cases, and an average size of 3.0 cm. Local recurrence is common in approximately 40% of patients [2,8-14].

The survival rate according to the Surveillance, Epidemiology and Final Results (SEER) Program survival at 5 and 10 years is 27% and 18% respectively [15]. There are reports of distant metastases in the lung, liver, and bone [2]. Melanoma is known for a wide range of histologic patterns that can mimic other malignancies. In addition to the classical and historical forms, lentigo maligna melanoma with superficial and nodular extension, more variants have been described. These can be classified into four groups according to their architectural pattern, cytological characteristics, and stromal change [9].

Multinucleated cell melanoma occurs in rare cases, multinucleated cells tend to show large nuclei and a higher degree of pleomorphism and/or hyperchromasia compared to benign nevi. Cases of melanoma with giant cells of the Touton type and osteoclast are considered within this group and can be positive for histiocytic markers such as CD68 [10].

Stromal changes with osteocartilaginous metaplasia are very unusual, it usually occurs in acral lentiginous and primary mucosal melanomas. Various theories, such as trauma, stromal induction by melanoma, and mesenchymal metaplasia of neoplastic cells, are used to explain bone and cartilage formation [9].

CASE REPORT

A 60 year-old woman with a reported gynecological-obstetric history: 2 gestations of those 2 normal deliveries, 0 abortions, and menarche at 13 years and menopause at 50 years, mammography and cervical cytology never performed. Her condition began

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five months earlier with transvaginal bleeding and dysuria. Colposcopy showed an exophytic lesion located on the anterior vaginal wall, pigmented and bleeding on contact; with a partial vision of the exocervix and endocervix, erythematous, and with mucopurulent discharge.

A biopsy was taken and sent to Department of Surgical Pathology, Hospital General de México "Dr. Eduardo Liceaga", for its diagnostic evaluation. In the service, a bottle with formaldehyde was received, referred with the clinical diagnosis of "cervical cancer"; with multiple fragments of irregular shape and surface, with a combined measurement of 3.0 cm x 1.5 cm x 1.0 cm, of friable consistency, reddish brown coloring, mostly covered with hemorrhagic remains. Microscopic evaluation revealed non-keratinized, ulcerated flat stratified residual epithelium and an epithelial-type lesion, 40% formed by multinucleated giant cells of the osteoclast type (Figure 1), with moderate and eosinophilic cytoplasm, pleomorphic nuclei, and dense chromatin; in a background of atypical cells, some binucleated, with abundant extravasated erythrocytes and few inflammatory cells. Two foci of osteoid metaplasia were identified, surrounding the neoplastic cells (Figure 2), as well as a few neoplastic cells with cytoplasmic melanin pigment.

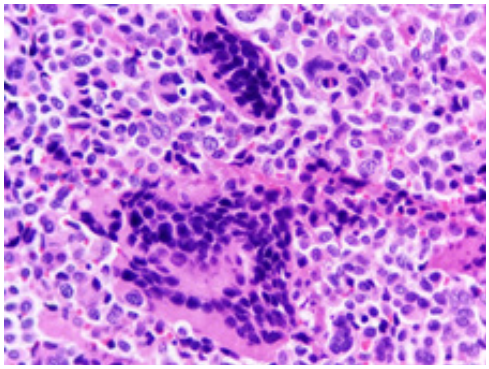

Figure 1. Mucosal melanoma with multinucleated giant cell phenotype "monster cells", H-E 40x.

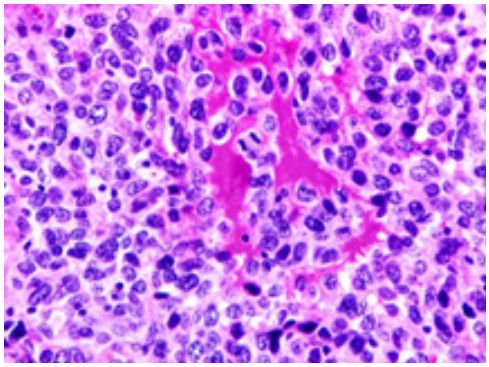

Figure 2. Osteoid metaplasia with individual neoplastic cells, H-E 40x.

The histopathological diagnosis was malignant melanoma of the vaginal mucosa. Immunohistochemistry (IHC) markers were performed for Microphthalmia Transcription Factor (MITF), HMB-45, PS100, and Melan-A, which were positive with expression in giant cells and individual neoplastic cells; confirming the diagnosis issued (Figure 3). BRAF was included in the panel as a possible therapeutic route targeting the specific mutation, which showed positivity with mild intensity in multinucleated giant cells. The case was consulted with one of the authors at the UMAE Hospital de Especialidades, Centro Médico Nacional Bajío, IMSS, agreeing with the final diagnosis.

The patient did not continue the treatment and follow-up issued by the Oncology Department of the same hospital; the course and outcome of the patient are unknown.

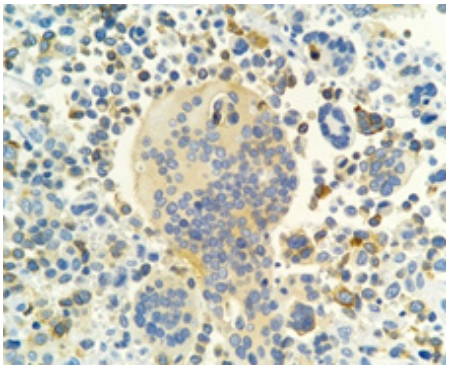

Figure 3. Immunohistochemistry marker BRAF positive giant cells and individual neoplastic cells, 40x.

DISCUSSION

The first vaginal melanoma was described in 1887 and approximately 500 cases have recently been reported in the literature [3]. We describe an entity that, due to its location and morphology, is infrequent. The cases reported in the literature of melanomas with a giant cell phenotype were all cutaneous and mostly in the head and neck region. Macroscopic pigment is a feature of melanoma and must be differentiated from other pigmented melanoses, such as melanosis, lentigo, and nevi, particularly dysplastic nevi [3]. Diagnosis of primary mucosal melanoma, especially in sites where it rarely arises, is of crucial importance to exclude the possibility of a metastatic lesion [2]. In general, melanoma can present a wide range of architectural patterns, cytological characteristics, and stromal changes; sometimes in combination with these, which makes diagnosis more complex and challenging when pigmented areas are absent.

Unlike other solid malignancies, histologic subtypes of primary melanoma are not frequently reported in pathology reports.

The SEER cut-off analysis shows that the histological subtype is an independent predictor of survival in melanoma [13], contrary to the location and adjacent invasion.

The morphological examination continues to be the gold standard for diagnosis, due to the wide morphology that it presents, studies with IHC biomarkers are often required for diagnostic confirmation [11]. Among all IHC markers, S100 and SOX10 are the most sensitive to melanocytic lesions, although they lack specificity. Melanoma-recognized T-cell augmentation (MART-1), MITF, and HMB-45 are frequently used because they have higher specificity and reasonable sensitivity in differentiating most conventional melanomas from histological non-melanocytic mimics [2].

The 8° edition of the American Joint Committee on Cancer (AJCC) included the TNM system for the staging of mucosal melanoma of the head and neck, but the establishment of appropriate systems for the other locations is necessary [3]; historical adaptations such as the Ballantyne system, where it is classified as stage I: localized disease, stage II: regional lymph node involvement, and stage III: distant metastatic disease; serve for the non-exclusive staging of an organ [14]. The future existence of a universal staging system for mucosal melanomas could provide adequate classification, treatment planning, and prognosis; also allow meaningful comparison of results from various institutions to define the best treatment options [3].

CONCLUSION

To date there is no effective systemic therapy; most studies focus on genetics and underlying molecular events. Therefore, mutation analysis of proto-oncogene tyrosine kinase (c-KIT), Neuroblastoma Rat Sarcoma (NRAS), and proto-oncogene B-Raf serine/threonine kinase (BRAF) are recommended at diagnosis initial and recurrence in all patients with female genital melanoma. In our case, BRAF expression made the patient a candidate for one of the specific drugs such as Vemurafenib (Zelboraf), Dabrafenib (Tafinlar), and Encorafenib (Braftovi); Unfortunately, with loss of clinical follow-up due to abandonment of treatment, the outcome of this case is unknown.

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