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CASE REPORT

Primary malignant melanoma of the cervix: report of a case

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Abstract
Background To present a case of primary malignant melanoma of the cervix.
Case The patient was admitted with the complaint of vaginal bleeding. Gynecological examination revealed a dark, papillary mass on the posterior lip of the cervix. Histopathology showed a malignant neoplasm with increased vascularity, indicating the possibility of a primary uterine cervical melanoma. Diagnosis of malignant melanoma was confirmed with immunohistochemistry, which showed diffuse positive reactions for S-100 protein and HBM-45, with no reaction for epithelial markers, namely cytokeratin AE1/AE3 and epithelial membrane antigen. An extensive search for a melanotic lesion in skin and in uveal tract was performed to verify the distinct site of melanoma. The tumor was stage IB1 according to the International Federation of Gynecology and Obstetrics classification.The patient underwent radical Wertheim–Meigs hysterectomy, bilateral salpingo-oopherectomy, and retroperitoneal pelvic lympadenectomy. Radiotherapy or chemotherapy was not performed in the postoperative period. She is now free of the disease 10 months after the operation.
Conclusion Primary malignant melanoma of the cervix is a rare cervical malignancy.

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Introduction

Malignant melanoma, which is a common neoplasm of the skin and mucous membranes, makes up 1% of all cancers [1]. Approximately 3–7% of malignant melanomas in women develop within genital tract [2]. The vast majority of these cases occur in vulva and vagina; cervix is a rare site for melanoma with about 43 cases reported in the literature [3–6]. We present a rare case of primary malignant melanoma of the cervix in this report.

Case report

A 61-year-old, multiparous woman was admitted to the Department of Gynaecology at Kocaeli University with the complaint of postmenopausal bleeding for 4 months. Her past medical history was uneventful.

Her gynecological examination revealed a dark, papillary mass measuring 1.5 × 1.5 cm^2 on the posterior lip of the cervix. Vagina and parametrium were not involved. Cervical PAP smear showed round cells with enlarged hyperchromatic nuclei including intracytoplasmic pigment granules. A biopsy from the lesion was taken. Histopathology of the lesion showed a malignant neoplasm with increased vascularity, indicating the possibility of a primary uterine cervical melanoma (Figs. 1, 2).

Immunohistochemistry showed diffuse positive reactions for S-100 protein (Neomarkers, Freemont, CA, USA) and HBM-45 (Neomarkers, Freemont, CA, USA), which confirmed the diagnosis of malignant melanoma (Fig. 3) with

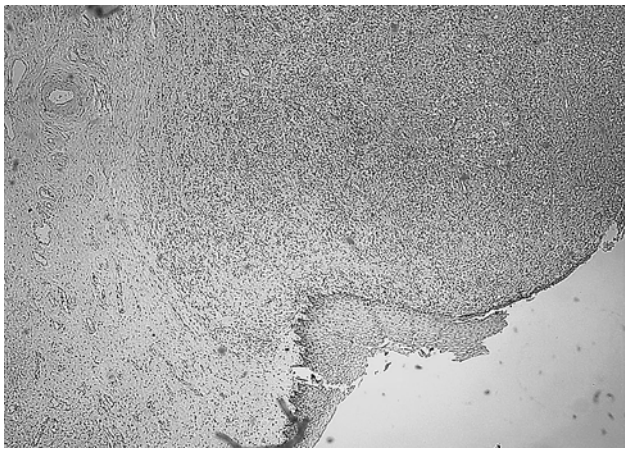

Fig. 1 The cervical biopsy demonstrated an ulcerated polypoid mass composed of a vascular cellular tumor in lower power (H&E, ×40)

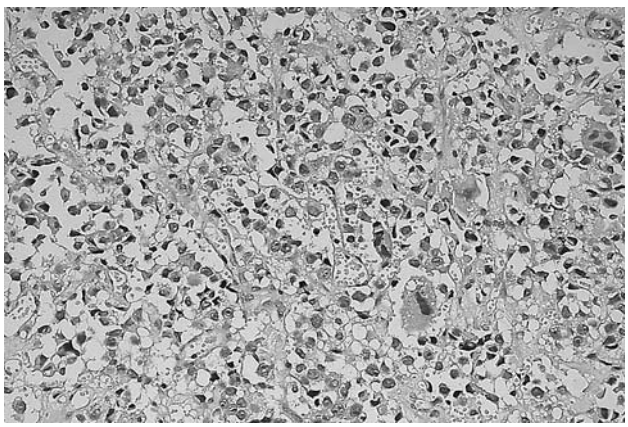

Fig. 2 The tumor cells showed large pleomorphic, hyperchromatic nuclei with prominent nucleoli and moderate amount of dense cytoplasm (H&E, ×400)

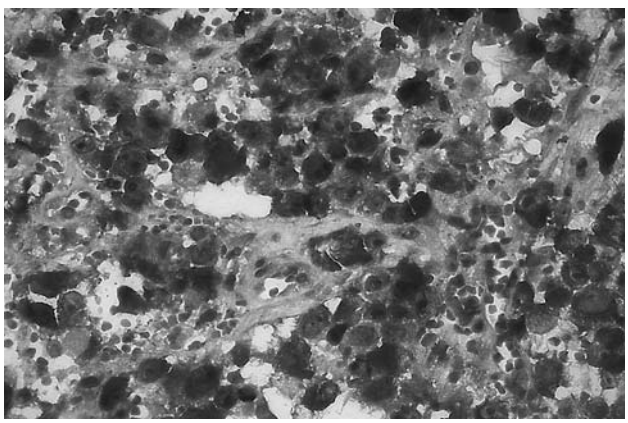

Fig. 3 Immunohistochemical stains revealed strong cytoplasmic reactivity for the melanoma-specific antibody HMB-45 (Immunohistochemistry HMB45, ×200)

no reaction for epithelial markers, namely cytokeratin AE1/AE3 (Neomarkers, Freemont, CA, USA) and EMA (Neomarkers, Freemont, CA, USA). Before incubation with primary antibody, antigen retrieval was induced through the utilization of either microwave oven or a pressure cooker.

An extensive search for a melanotic lesion in skin and uveal tract with ophthalmoscopy was performed to verify the distinct site of melanoma. Abdominal ultrasound, chest X-ray, intravenous pyelography were performed preoperatively, all negative for metastasis. The tumor was stage IB1 according to the International Federation of Gynecology and Obstetrics classification. The patient underwent radical Wertheim–Meigs hysterectomy, bilateral salpingo-oopherectomy, and retroperitoneal pelvic lympadenectomy.

Gross examination showed a 1.5 cm ulcero-noduler lesion involving ectocervical region. The lesion was dark on its cut-surface. Microscopic sections showed a cellular tumor composed of small cells proliferated in sheets with a 6 mm depth of invasion. The tumor cells had moderate amount of eosinophilic cytoplasm, predominantly monomorphic nuclei with rarely prominent eosinophilic nucleoli. A fair number of cells showed dark-brown intracellular pigment. The mitotic count was 2/mm^2. Immunohistochemical stains revealed strong reactivity for the S-100 protein and HMB-45. There was no sign of immunoreactivity for epithelial markers, like cytokeratin and EMA.

Neither radiotherapy nor chemotherapy was performed in the postoperative period. A follow-up examination was made 3 months after the operation. Her physical examination, laboratory parameters, and radiologic examinations were all normal. She is now free of the disease 10 months after the operation.

Discussion

Primary melanoma of the cervix is a rare entity. Genital tract melanomas involve the vulva/vagina and only 9–13% is diagnosed in the cervix [7]. Lately, a primary melanoma of the uterine cervix after supracervical hysterectomy has been reported [6]. Cervix is usually involved secondarily either as a result of local extension from vagina or vulva or as a result of hematogenous dissemination from a primary melanoma located elsewhere in the body [8].

Cervical melanoma originates from the melanocytic cells of the cervix [3, 7]. Melanoma in the uterine cervix may be melanotic or amelanotic. About half of the melanomas are amelanotic. Diagnosis of amelanotic melanomas may be difficult due to the absence of pigment. In our case, presence of pigment made the diagnosis easier. Patients may remain asymptomatic till they ulcerate, become infected which may cause vaginal bleeding and discharge [9].

Diagnosis is usually based on gynecologic examination, histopathology, and electron microscopy, and is confirmed by immunohistochemical staining with S-100 and HMB-45. Primary cervical melanoma must be differentiated from

secondary metastasis of melanoma existing elsewhere in the body. Morris and Taylor [10] have suggested the following diagnostic criteria: (1) the presence of melanin in the normal cervical epithelium; (2) the absence of melanoma elsewhere in the body; (3) the demonstration of junctional change in the cervix; (4) the metastases according to the pattern of cervical carcinoma. Particular attention should be given to the existence of melanoma in the skin and in the eye, which might have special importance for the diagnosis of primary lesion.

Very few cases have been diagnosed on cytology. Cervical smears may be negative if the overlying epithelium is intact. As the tumor is evident by speculum examination, the first diagnostic step is usually a biopsy for histological examination. Recently, morphological features of primary cervical melanoma in PAP smears have been published, raising the hope of early diagnosis [6]. Cervical smear usually shows scattered bizarre and pleomorphic cells containing melanin pigment. In the present case, histomorphologic features were specific for melanoma, and positive immunoreaction for melanocytic markers led us to diagnosis. Absence of any other primary site was suggestive of cervical melanoma. There was no junctional melanocytic activity or wide ulceration, which prevented the evaluation of junctional zone.

There is no consensus on optimal management strategy after diagnosis of a primary malignant melanoma due to the rarity of the lesion. The most common mode of treatment in literature is surgery, including radical hysterectomy, pelvic lymphadenectomy, and partial vaginectomy [3, 11]. There is lack of evidence on the efficacy of postoperative radiation or chemotherapy [12]. Radiotherapy can be useful in the palliation of an inoperable patient or as an adjuvant theraphy.

The prognosis of primary cervical melanoma is generally poor because diagnosis is usually made at an advanced stage [13]. The average survival time ranges from 6 months to 14 years, most patients dying within 3 years [14].

In conclusion, primary malignant melanoma of the cervix should be considered in differential diagnosis of cervical malignancies both by pathologists and gynecologists.

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