

Amelanotic malignant melanoma of the vagina

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Primary vaginal malignant melanoma is an uncommon disease. Especially amelanotic variants are extremely rare. We have discussed an unpigmented vaginal malignant melanoma that was not suspected histologically but was confirmed by immunohistochemical techniques. Immunohistochemical techniques may usefully complement diagnostic histopathology in such unusual cases. [Turk J Cancer 2000;30(3):126-130]

Key words: vagina, amelanotic malignant melanoma

Malignant melanoma (MM) of the vagina is a rare tumor. It accounts for less than 1% of all MM, and less than 3% of all primary malignant tumors of the vagina (1). In a review of reported cases, Stellato et al. (2) found less than 150 cases of primary melanoma of the vagina in the literature. The histologic appearance of melanoma may be heterogeneous. In fact, especially amelanotic melanomas may be diagnosed as poorly differentiated carcinomas or sarcomas (3,4). In such cases immunohistochemical techniques (IHC) have been valuable as a diagnostic aid (1,3,5-7).

In contrast with the majority of cases reported, we described here a case of amelanotic MM of the vagina diagnosed by immunohistochemistry.

Case Report

A 65 year old woman, gravida 11, para 11 was referred to Obstetric and Gynecology Department of Cumhuriyet University School of Medicine. She had blood tinged vaginal discharge and a nodule present in the vagina. A gynecological examination revealed a nodule measuring approximately 70x30 mm involving one third of the right wall of the vagina. Also in the right inguinal region 20 mm palpable lymph node was found. No other abnormalities were found during general and pelvic examination. Her past history was of no relevance. As a diagnostic aid, biopsies were taken from the vaginal nodule. Macroscopically the lesion appeared as a greyish yellow, soft, nonencapsulated nodular mass measuring approximately 30x20x10 mm. Light microscopic examination showed anaplastic spindle cells with marked variation in size and

shape, with prominent nuclei and nucleoli and frequent atypical mitotic figures. Tumor cells formed fascicular and storiform patterns. The mucosa overlying the tumor showed ulceration. Junctional activity and melanin pigment were absent. Based on these histologic features malignant mesenchymal tumor or poorly differentiated carcinoma was considered and differential diagnosis was undertaken by means of IHC. Avidin biotin peroxidase complex (Dako, USA) was used as detection system (8). Low and high molecular weight of (LMW, HMW) cytokeratin (Dako, USA), epithelial membrane antigen (EMA) (Dako, USA), vimentin (Dako, USA), actin (Dako, USA), S-100 (Biogenex, USA), desmin (Biogenex, USA), neuron specific enolase (NSE) (Biogenex, USA), HMB-45 (Dako, USA) and leucocyte common antigen (LCA) (Biogenex, USA), were performed. The tumoral cells showed strongly diffuse positive reaction with vimentin, S-100, HMB-45 (Figure 1) and focally positive reaction with NSE, and LMW cytokeratin (Figure 2). Based on these IHC results the case was interpreted as amelanotic MM. Histochemically Masson Fontana's ammoniated silver nitrate method was also performed, however, melanin pigment was not observed.

The case was reexamined for the presence of pigmented lesion. However, no significant nevi or melanotic lesion was observed. Besides she had a negative upper abdominal and pelvic CT scan, chest X-ray, lung tomograms and routine blood tests. Thus the case was considered as primary amelanotic MM of the vagina. The patient had been discharged and sent to an oncology center for further treatment.

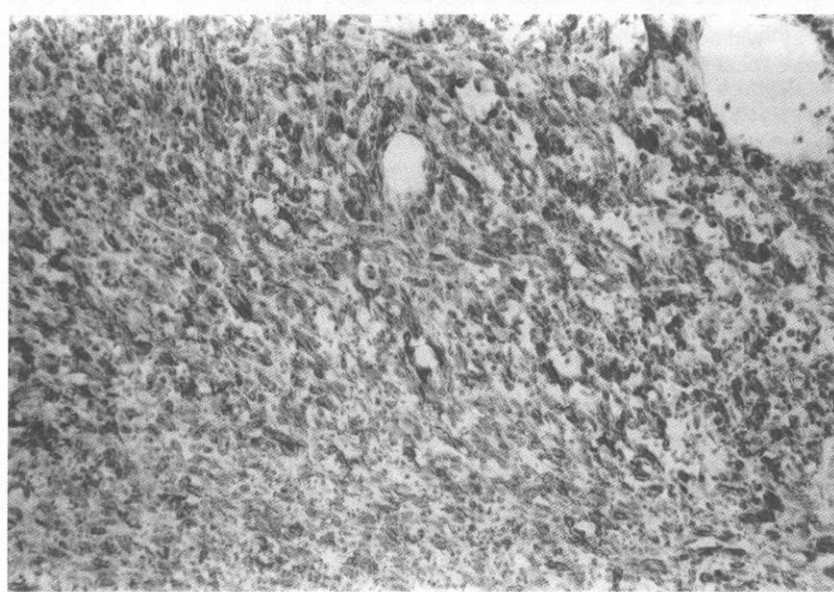


Fig 1. Avidin biotin method using antibody anti HMB-45 reveals a strong intracytoplasmic positivity of malignant cells (Avidin Biotin X100)

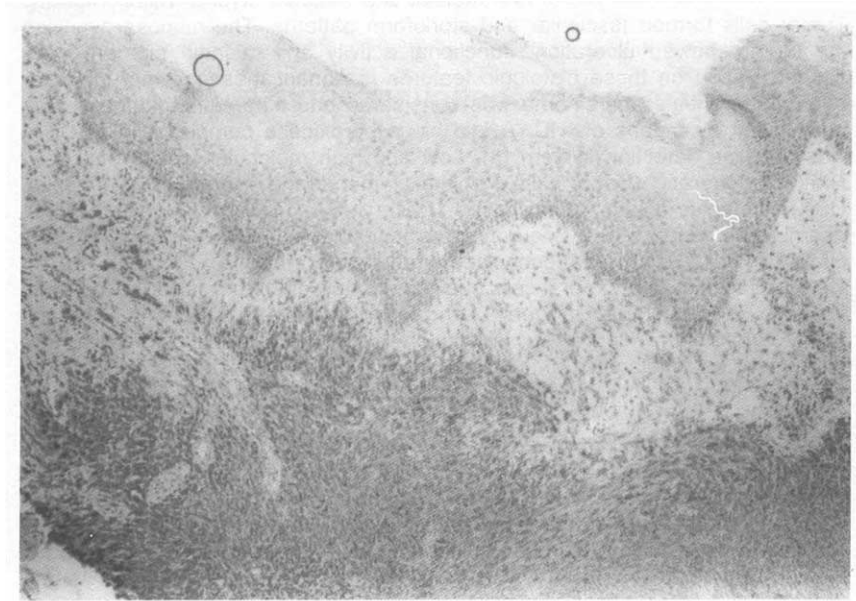


Fig 2. Avidin biotin method using antibody low molecular weight cytokeratin reveals focal positivity of malignant cells (Avidin Biotin X50)

Discussion

Vaginal MM, arisen from melanocytes, which may be present in the epithelium of the vagina, is a rare gynecological malignancy (1,4,7). This rare entity is primarily a disease of postmenopausal women. The most common symptoms are vaginal bleeding, vaginal discharge and feeling a mass in the vagina. It is mostly localized in the anterior wall in lower one third of the vagina (1). Our present case has been in postmenopausal period and abnormal vaginal bleeding and discharge had been present for seven months. A gynecologic examination revealed a nodule in the lower one third of the right wall of the vagina.

Although more than 50% of the gynecological MM have pigmentation, amelanotic melanomas have been also rarely reported (1,3,9). It only accounts for 6% of vaginal melanoma (3). Hasumi et al. (4) had presented four vaginal MM cases one of which was amelanotic and had no junctional activity. Also Brozjani et al. (1) reported 10 vaginal MM cases, three of which were amelanotic. Amelanotic MM could not be determined clinically as well as histopathologically if appreciable amounts of melanin pigment is absent. Besides, if mucosa overlying the tumoral cells show ulceration, junctional activity could not be demonstrated histologically. Both absence of junctional activity and melanin pigmentation arise a problem in the diagnosis (1,3,4,9).

Varied histologic appearance of amelanotic lesions may be mistaken as sarcoma or highly undifferentiated carcinoma. In such lesions malignant fibrous histiocytoma (MFH), malignant peripheral nerve sheath tumor and

hemangioendotelioma must be considered in the differential diagnosis (1,3,4,7,10). MFH cells may originate from multipotential mesenchymal cells with a capacity to differentiate to fibroblast like cells, epithelial cells, smooth muscle cells and Schwannian cells. Thus in these tumor cells positive immunoreactivity with S-100, desmin, cytokeratin and vimentin may be obtained (7,10). In our present case melanin pigment and junctional activity were absent. Tumor had a storiform pattern composed of large anaplastic and pleomorphic spindle shaped cells as though mesenchymal tumor. Also histochemically Masson Fontana's ammoniated silver nitrate method did not reveal pigment. The primary diagnosis of the case was therefore MFH before performing IHC.

Problems arise in the diagnosis when tumor cells have an appearance of the undifferentiated carcinoma or sarcoma especially if pigmentation is absent. In such cases, conventional histologic methods has been unsatisfactory. Thus histochemical and IHC techniques have been used in the differential diagnosis (3,4,6,7). For this purpose, immunohistochemically, a panel of antibodies including S-100, HMB-45, vimentin, cytokeratin, LCA and NSE have been performed to bring up the nature of the tumor cells. S-100 protein is nearly always positive in melanomas. Unlike carcinomas, melanomas express vimentin that is usually associated with mesenchymal tissues. HMB-45 antigen is useful to differentiate melanomas from nonmelanoma tumors. Also tumor cells of neuroectodermal origin such as melanocytes expresses NSE. EMA and CEA are useful in distinguishing epithelial from mesenchymal tumors and LCA is useful to differentiate lymphoid malignancies (6,7). Besides, a few cytokeratin positivity have been reported in melanomas (6,11). The anomalous cytokeratin expression by tumor limits the diagnosis of melanoma and raises a question of undifferentiated carcinomas. In such unusual cases the concomitant detection of additional tumor associated antigens must have been performed to reach a final and correct diagnosis (11).

In the present case we used a panel of antibodies immunohistochemically. In the first step we performed vimentin, S-100, cytokeratin, EMA, LCA to differentiate epithelial, mesenchymal and lymphoid tumors. Strongly positive reaction with S-100 and vimentin revealed a mesenchymal origin of the tumor. However positive cytokeratin reactivity raised the question of a highly undifferentiated carcinoma. We enhanced our IHC panel using NSE and HMB-45. NSE was positive focally however HMB-45 was diffusely positive in tumor cells, and the case was diagnosed as amelanotic MM. We did not have an opportunity to examine whole tumoral nodule as only a small biopsy specimen had been sent as a diagnostic aid. After the diagnosis; patient had been referred to an oncology center for further treatment.

The presence of melanocytes has been reported in the vagina and their presence provides an origin for MM of the vagina. Primary tumor may be associated with adjacent intraepithelial lesion in some of MM cases. Superficial spreading MM, lentigo maligna are said to be precursor lesions of MM (4,6). In our present case as tumoral nodule was not surgically removed, we examined only biopsy specimens. Thus we could not be able to evaluate the adjacent lesions of the tumor.

Prognosis of the vaginal MM is very poor. Even small lesions often produces widespread metastases. Initial therapy is wide local excision of the primary

tumor with pelvic lymphadenectomy followed by radiotherapy (1,3,4,7).

As a result, postmenopausal woman having bloody discharge and feeling mass in the vagina should be considered carefully. In tumor cells showing marked variation in histopathologic aspects and revealing any specific type of neither mesenchymal nor epithelial tumor, MM should be remembered even though the lesions are not pigmented and junctional activity is absent. Application of IHC provides useful information about the nature of the tumor and helps to differentiate the unusual lesions.

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