Primary Malignant Melanoma of the Vagina with a Survival of Longer than 5 Years after Recurrence: Case Report and Review of the Literature

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Abstract

Background: Primary malignant melanoma of the vagina is an aggressive and very rare malignancy. This tumor constitutes less than 3% of vaginal cancers and only 0.3-0.8% of all melanomas in women. The overall prognosis for patients with vaginal melanoma is poor. Furthermore, once a recurrence is noted, survival is extremely poor, with a mean survival time of 8.5 months. The result of bibliographic search for recurrent vaginal melanoma, only 3 cases have been reported to survive 5 years after re-treatment for recurrence. We report a case of vaginal melanoma with a survival of longer than 5 years after recurrence.

Case: A 38-year-old woman presented with amelanotic melanoma of the vagina and underwent an operation and adjuvant chemotherapy. Twenty months later, sacral lymph node metastasis was observed. We removed her metastatic foci by surgery, and 2 of 15 lymph nodes demonstrated metastasis of malignant melanoma. The patient underwent 5 courses of adjuvant chemotherapy. She is alive and without evidence of disease 141 months after recurrence.

Conclusion: While the prognosis of vaginal melanoma is poor, in certain cases, early detection and early treatment may improve the prognosis.

Keywords: Vaginal melanoma; Recurrence; Lymph node metastasis; Long time survival; Amelanotic melanoma

Introduction

Melanoma is the most serious form of skin cancer. Currently, the incidence of melanoma is rising worldwide. The risk factors for developing melanoma are both environmental and genetic, solar ultraviolet exposure is a major risk factor for melanoma in particular.

Some melanomas may also arise from the mucosal epithelium lining the respiratory, alimentary, and genitourinary tracts, all of which contain melanocytes besides from the skin. These melanomas are called mucosal melanomas and they are rare, account for approximately 1 percent of all melanomas [1]. An estimated 20% of mucosal melanomas are multifocal [2], compared with less than 5% of those arising in the skin, and approximately 40% of mucosal melanomas are amelanotic, compared with less than 10% of cutaneous melanomas [3]. Patients diagnosed with mucosal melanomas are older and they occur more commonly in females than males, primarily due to the development of disease in the genital tract.

Melanomas arising from the female urogenital tract occur primarily in the vulva and vagina (95% and 3%, respectively) [1]. Primary malignant melanoma of the vagina is an aggressive and extremely rare malignancy. This tumor constitutes less than 3% of vaginal cancers [4,5] and only 0.3-0.8% of all melanomas in women [6]. Vaginal melanomas generally carry a worse prognosis than those arising from cutaneous sites. Overall, a five year survival rate in patients with vaginal melanoma is notoriously poor, being between 13% and 19% [6,7], despite the various treatment modalities described. This is considerably lower than the five year overall rate for patients with melanoma of the vulva (47%), and strikingly lower than the five year overall survival rate for women with cutaneous melanoma (81%) [7].

Herein, we report a case of primary malignant melanoma of the vagina in 38-year-old female patient. She was treated in 1999 by operation and chemotherapy and developed recurrence 20 months later. She underwent surgery and adjuvant chemotherapy again. She has survived more than 5 years with no evidence of disease.

Case Report

A 38-year-old, married Japanese woman presented with abnormal vaginal bleeding of one months duration. She had been in good health and had no past medical or surgical history.

Physical examination disclosed an essentially healthy appearance and normal vital signs. On vaginal examination, there was a 1.7×1.4 cm raised, ulcerated and irregular lesion in the upper third of anterior vaginal wall, and a 1.3×0.6 cm raised, ulcerated and irregular lesion in the lower third of the posterior vaginal wall (Figure 1). Bilateral inguinal lymph node was not palpable, and the rest of pelvic examination was normal.

In the colposcopic examination, non-pigmented primary lesion was found with cutaneous melanoma (81%) [7].

Figure 1: Colposcopic findings. Non-pigmented primary lesion was found in vagina.

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Incisional biopsy was taken and sent for histopathological examination. Microscopic sections from the biopsy demonstrated amelanotic malignant melanoma. Immunohistochemical staining was negative for cytokeratin and positive for vimentin, S-100, HMB-45, thus confirming the diagnosis of amelanotic malignant melanoma (Figure 2). Preoperative Computed Tomography (CT) of the chest, abdomen and pelvis, Magnetic Resonance Imaging (MRI) of the pelvis and isotopic bone scanning and Gallium scanning did not disclose abnormal findings. A total hysterectomy, total vaginectomy with pelvic lymphadenectomy and vaginal reconstruction using sigmoid colon were performed. Pathologic analysis revealed a residual malignant melanoma and tumor thickness was 2 mm. All lymph nodes were negative.

Postoperatively, 5 courses of adjuvant chemotherapy were given (2 courses with dacarbazine, nidan and vincristine; and 3 courses of dacarbazine alone). Twenty months later, routine CT revealed a metastasis of sacral lymph nodes (Figure 3). A lymphadenectomy was performed, and 2 of 15 lymph nodes demonstrated metastasis of malignant melanoma (Figure 4). After operation, 5 courses of chemotherapy with dacarbazine alone were given. She is alive and without evidence of disease 141 months after recurrence.

Discussion

Primary malignant melanoma of the vagina is defined as melanoma originating in vaginal wall without involvement of the vulva and/or the uterine cervix. Vaginal melanoma appears to originate from melanocytes that are present in the vaginal mucosa. It has been shown that melanomas occur more commonly in the lower third of the vagina and more often on the anterior vaginal wall [8,9].

Forty percent of vaginal melanoma lack pigmentation (amelanotic) [3]. In the amelanotic variety, the diagnosis may be difficult. Immunohistochemistry is helpful for diagnosis. Melanoma is usually negative for cytokeratine and S-100 may be only focally positive. HMB-45 positivity and suggestive histomorphology is specific for melanocytic lesion. We had a case of two non-pigmented tumor foci, the upper third of anterior vaginal wall and the lower third of posterior wall. No one doubted that the tumors were malignant melanoma, where immunohistochemical examination revealed them as amelanotic melanoma.

The most appropriate treatment for vaginal melanoma has been the subject of some debate. Some authors have found no difference in the overall five-year survival among conservative surgery, radical surgery, radiation, and chemotherapy [8,10]. Surgery seemed to play the most important role in treatment providing local control of the tumor in a better way than that resulting from radiotherapy [11]. Achieving negative margins in these cases can be difficult without pelvic exenteration, given the high frequency of multifocality and anatomic constraints. No evidence has been available so far regarding which is the best surgery technique. Thus, surgery may be combined with radiotherapy or chemotherapy in select cases. Although a number of adjuvant chemotherapy regimens have been tested in the effort to reduce recurrence rate in high-risk melanoma, none of the agents, such as dacarbazine, used either alone or in combination proved beneficial in randomized clinical trials. Recently the most promising results have been reported with Interferon alpha (IFNα), which has become the standard of care for patients with resected node-positive cutaneous melanoma. Some clinical trials have shown that high dose IFNα as adjuvant therapy for cutaneous melanoma makes statistically significant improvements in relapse-free survival [12]. ECOG 1684 [12], a randomized clinical trial as IFNα adjuvant therapy of high-risk resected cutaneous melanoma, demonstrated statistical survival benefit, while all other trials with IFNα [13-16] could not prove
Patients who have a limited site of metastatic disease may be amenable largely based upon experience in patients with cutaneous melanoma. In case of recurrence or metastatic mucosal melanoma, tumor size is the best prognostic factor. There was no difference in patient outcomes among five treatment groups: (1) wide excision, (2) radical surgery, (3) radiation therapy, (4) wide excision plus radiation therapy, and (5) others. They concluded that tumor size (<3 cm versus ≥ 3 cm) is very poor because of the high incidence of local recurrence and metastases at disease presentation. This may be explained by the extensive lymphatic and vascular supply to the lamina propria of the vaginal mucous membranes. Patients with vaginal melanoma have the five year survival rate of 13 to 19% [6].

Buchanan et al. analyzed 67 cases of primary vaginal melanoma, only 18 cases had survived 5 years or more, and only 3 had survived ten years or more [18]. They analyzed outcomes on these cases on the basis of treatment tumor size and so on. There was no difference in patient outcomes among five treatment tumor groups: (1) wide excision, (2) radical surgery, (3) radiation therapy, (4) wide excision plus radiation therapy, and (5) others. They concluded that tumor size (<3 cm versus ≥ 3 cm) is the best prognostic factor.

The common sites of recurrence of vaginal melanoma are vagina, vulva and groin [19]. Once recurrence occurs, prognosis of melanoma is usually poor. In case of recurrence or metastatic mucosal melanoma, data on the systemic treatment of patients with metastasis are very limited, and treatment of metastatic vaginal mucosal melanoma is largely based upon experience in patients with cutaneous melanoma. Patients who have a limited site of metastatic disease may be amenable to surgical resection and complete surgical resection of limited metastatic disease can result in prolonged relapse free survival. In case of recurrent or metastatic cutaneous melanoma, useful anticancer drugs include Dacarbazine, nitrosoureas, vinca alkaloids, bleomycin, platinum analogues, or taxanes. Among these drugs, Dacarbazine is the only cytotoxic drug approved in the United States for the treatment of patients with metastatic melanoma. Dacarbazine has not been shown to prolong survival. Currently, approaches have been shown to provide clinical benefit for patients with recurrent and metastatic melanoma include Interferon alpha (IFNα), high-dose Interleukin-2 (IL-2), ipilimumab and vemurafenib.

As far as we examined documents regarding vaginal melanoma, only 23 cases have been reported to survive 5 years and only 10 of these were still alive, with no evidence of disease, at the time of reporting (Table 1). As for the primary treatment of long-term survivor, Buchanan et al. reported that the only patients who had a treatment simply with wide local excision of the lesion survived >10 years without recurrence [18]. They concluded radiation therapy appears to offer results comparable to those of surgery. In our review of literature about long-term survivor of vaginal melanoma, radiation therapy was chosen as the primary treatment to 6 cases. Only 3 cases have been reported to survive 5 years after re-treatment for recurrences [19-21]. Mino et al. reported that a case with local recurrence after 5 years and 3 months, has survived 8 years after resection (pelvic exenteration) [20]. The case reported by Davis and Franklin had a local recurrence after 9 years of the primary treatment; she had been alive by resection twice after 12 years and 10 years [21]. Another case, there had been recurrent inguinal lymph node after 28 months, had survived with surgery [19]. For the 3 cases, surgery was performed for recurrence disease, resulting in good survival. In these cases, although tumor size was less than 3 cm, the patient developed metastasis to a lymph node 20 months later. It was discovered on routine CT examination, and was extracted by an operation immediately, which led to the long-term prognosis. Although there are only anecdotal reports on the efficacy of treatment for metastatic disease of vaginal melanoma, further considerations and accumulation of cases are needed.

Conclusion

While the prognosis of vaginal melanoma is poor, in certain cases, early detection and early treatment may improve the prognosis.

References


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RS: Radical Surgery; RT: Radiotherapy; WLE: Wide Local Excision; NED: No Evidence of Disease; AWD: Alive With Disease; DOD: Died of Intercurrent Disease; DOD: Died of Disease; NM: Not Mentioned

Table 1: Vaginal melanoma: Five-year survivors.


