

Clinical characteristics and current treatment approach of vaginal primary malignant melanoma

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Abstract

Vaginal primary malignant melanoma (VPMM) is a very rare clinical entity. Most patients with VPMM usually have no specific symptoms or signs (abnormal vaginal bleeding, abnormal vaginal discharge, palpable vaginal mass and pain).

VPMM has a very aggressive clinical behaviour. Moreover, patients with VPMM are usually diagnosed at advanced stage disease. The extensive vascular and lymphatic network of the vaginal mucosa is a plausible explanation for the aggressive clinical course of VPMM.

Surgery is the baseline treatment for the majority of patients with VPMM. Surgical operation may be either conservative (wide local excision) or radical (vaginectomy, pelvic exenteration). Lymph node dissection is not recommended in patients with VPMM, because the possibility for a lymph node metastasis is very low.

Radiotherapy is another effective treatment option for patients with VPMM. In particular, the use of radiother-

apy includes vaginal brachytherapy and external pelvic radiotherapy.

Chemotherapy is most commonly used in patients with advanced stage VPMM, but its clinical role remains controversial. Immunotherapy is usually reserved as postoperative adjuvant treatment and offers survival benefits in patients with VPMM who are in high risk for recurrence. Biochemotherapy is characterized by the combined use of chemotherapy and immunotherapy and is considered for patients with advanced stage VPMM.

It becomes apparent that although there are various treatment options for patients with VPMM, because of the rarity of the condition, universally-accepted effective treatment protocols have not been established so far.

Key words: vaginal primary malignant melanoma; clinical characteristics; treatment, surgery

Introduction

Vaginal primary malignant melanoma (VPMM) is a very rare and at the same time a very aggressive clinical entity in the field of gynecological oncol-

ogy.¹⁻⁷ It is interesting to note that among all malignant melanomas only 0.3-0.8% are VPMMs.^{1,2,8} Moreover among the various vaginal malignancies, less than 3% are VPMMs.^{1,2,8} Besides, VPMM rep-

resents the 2nd most common localization of malignant melanoma within the female genital tract.⁹

The estimated annual incidence of VPMM, is only 0.026/100,000 women per year.^{2,8} Regarding its annual incidence, there are no significant differences between various racial or ethnic groups.^{8,10} Nevertheless, its exact pathogenesis still remains unclear; but ultraviolet radiation probably does not seem to trigger the formation of VPMM.^{10,11}

Clinical characteristics

Symptoms and signs

Establishing a clinical diagnosis of VPMM can be very laborious.^{3-7,11-15} Most patients with VPMM usually have no specific symptoms and signs.^{3-7,11-15} Abnormal vaginal bleeding is the commonest clinical finding among patients with VPMM (80%).^{3-7,11-15} Some patients with VPMM will complain of abnormal vaginal discharge (25%).^{3-7,11-15} A smaller proportion of patients with VPMM will illustrate a palpable vaginal mass (15%).^{3-7,11-15} Finally, few patients with VPMM will complain of pain (10%).^{3-7,11-15}

It should be also mentioned that VPMM most commonly occurs in postmenopausal women; the median age at diagnosis of VPMM is 57 years.^{5,13-17}

Clinical appearance

VPMM may arise anywhere in the vagina.^{2,13-15,18,19,17} The anterior vaginal wall is the most common location of VPMM (38%).^{2,13-15,18,19,17} Additionally, VPMM commonly occurs in the lower third of the vagina (34%).^{2,13-15,18,19,17}

VPMM lesions may be single or multifocal.^{17,20} Apart from that, VPMM lesions may be pigmented or nonpigmented.^{17,20} No standard colposcopic features exist, while the clinical appearance of nonpigmented VPMM lesions shares many features with the appearance of vaginal intraepithelial (VaIN) lesions.^{11,20}

Cell types of VPMM

There are 3 main histologic types of VPMM.^{11,16,20} The majority of VPMM cases belong to the epithe-

lioid cell type (55%); and fewer VPMM cases belong to the mixed cell type (28%).^{11,16,20} Finally, the minority of VPMM cases are assigned to the spindle cell type (17%).^{11,16,20}

Clinical behavior

It should be noted that VPMM illustrates an extremely aggressive clinical behaviour predominantly attributed to its tendency for early spread and its indigenous propensity for early metastasis.^{1,3-7,21}

Patients with VPMM are usually diagnosed at an advanced disease stage.^{1,3,4,21} Upon initial presentation, many VPMM patients already harbor distant metastases most commonly located in the lung, liver, bones and brain.^{11,13} Following initial treatment, many patients with VPMM have local recurrences in the pelvis.^{11,13}

The extensive vascular and lymphatic network of the vaginal mucosa represents a plausible explanation for the aggressive clinical behaviour of VPMM.^{12,13,16}

The outcome for women with VPMM is determined by prognostic factors like tumor size, tumor growth, lymph node status and treatment method.^{13,15,22,23} Among them, tumor size >3 cm is the most important prognostic factor.^{13,15,24}

With an estimated 5-year overall survival of VPMM patients ranging from 8.4-32.3%^{1,13,16-18,22,24}, it becomes apparent that the prognosis of patients with VPMM is very poor.²² Even compared with other vaginal malignancies or cutaneous malignant melanoma, the prognosis of patients with VPMM is most unfavourable.¹¹

The FIGO staging system for vaginal cancer does not incorporate tumor size and regional lymph node status.^{2,15} Therefore, the implementation of the FIGO staging system in patients with VPMM should be avoided, because it is inappropriate and merits significant alterations.^{2,15} Perhaps the implementation of the AJCC cutaneous melanoma staging system for patients with VPMM, represents a better approach.²⁵

Current treatment approach

Nowadays, various treatment options are available

for VPMM patients.^{16,23} However, no universally accepted, appropriate and effective treatment protocol exists for these patients.^{16,23}

Surgery

Surgery is the baseline treatment, for the majority of VPMM patients.^{2, 16, 23, 24} Surgical operation may be conservative or radical.^{2, 12, 16} Wide local excision is the most common form of conservative surgical operation.^{2, 12, 16} Radical surgery can either consist of vaginectomy or the ultra-radical pelvic exenteration.^{2, 12, 16}

If wide local excision with clear margins is possible, then opting for a radical surgical operation is not necessary.^{2, 16, 23, 26} However, if wide local excision with clear margins is unfeasible, then the performance of a radical surgical operation is justified in carefully selected patients.^{2, 17}

It must be noted that lymph node dissection is not recommended in patients with VPMM, because of the very low possibility for lymph node metastasis.¹⁶ Besides, lymph node dissection in patients with VPMM has no survival benefits, while it can also lead to significant iatrogenic morbidity.^{16, 23, 27}

Elective lymph node sampling in patients with VPMM has a controversial surgical role.^{2, 16, 23, 24} Nevertheless, practicing sentinel lymph node biopsy in patients with VPMM, is getting more popular.^{16, 24, 28}

Radiotherapy

Radiotherapy is another effective treatment option, for patients with VPMM.^{2, 16, 29, 30} In particular, radiotherapy options in those patients include *external pelvic radiotherapy* and *vaginal brachytherapy*.^{2, 16, 29, 30}

External pelvic radiotherapy can be used as primary treatment for patients who are unable or unwilling to proceed to a surgical operation.^{2, 16, 29, 30} External pelvic radiotherapy can be also used as preoperative treatment for VPMM patients in whom it reduces tumor size and enables a more conservative surgery.^{2, 16, 26, 29, 30} Furthermore, external pelvic radiotherapy can be used as postoperative adjuvant treatment for patients with tumor size ≥ 3 cm, incomplete tumor resection or pelvic metastases.^{2, 5, 16, 23, 29, 30}

Studies have illustrated that external pelvic radiotherapy reduces the risk of local recurrences, despite having no impact on overall survival.^{17, 23, 24} Furthermore, external pelvic radiotherapy is associated with side effects and impaired quality of life.^{5, 6, 31}

Conversely, vaginal brachytherapy can be used as primary treatment especially in elderly patients with bad performance status and relevant co-morbidities.^{5, 6, 31, 32} Vaginal brachytherapy also reduces the risk of local recurrences.¹⁷ However, vaginal brachytherapy is better tolerated and is associated with diminished side effects and improved quality of life.^{5, 6, 31}

Chemotherapy

Chemotherapy is another treatment option for patients with advanced stage VPMM.³³ However, the clinical role of postoperative adjuvant chemotherapy in those patients remains controversial.³³ Studies have illustrated that postoperative adjuvant chemotherapy can only achieve modest response rates and has no impact on overall survival.²⁶

Immunotherapy

Immunotherapy represents a novel approach for patients with VPM; the most common immunotherapeutic agents being interferon (IFN) and interleukin-2 (IL-2).^{3, 4, 22, 24, 34, 35}

Postoperative adjuvant immunotherapy offers survival benefits in patients with VPMM and high risk for recurrence.^{3, 4, 22, 24, 34, 35} Furthermore, the combined use of IFN and IL-2 is more effective than the individual use of IL-2.³⁶

Nonetheless, the use of immunotherapeutic agents has significant toxicity.^{3, 4, 34, 35} Moreover, the use of IFN is associated with the formation of autoantibodies and the induction of autoimmune disorders.³⁷

Biochemotherapy

Biochemotherapy is a promising approach for melanoma patients; in this case women with advanced stage VPMM.³⁸ Essentially it is characterized by the combined use of chemotherapy and immunotherapy.³⁸

The effectiveness of biochemotherapy in patients with advanced stage VPMM has not been established yet.³⁸ Furthermore, the combined use of chemotherapy and immunotherapy has significant toxicity.^{24,35}

Conclusion

It becomes apparent that VPMM is a very aggressive clinical entity in the field of gynecological oncology.¹⁻⁷ Although there are various treatment options for patients with VPMM, no effective treatment protocol has been established so far.^{16,23} ■

Conflict of interest

We declare that we have no conflict of interest.

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