

Recent advances in the treatment of vaginal primary malignant melanomas

Editorial

Vaginal primary malignant melanoma (VPMM) is a very rare and equally aggressive clinical entity.¹⁻⁷ Apparently, VPMM represents only 0.3-0.8% of all malignant melanomas and less than 3% of all malignancies affecting the vagina.^{2,6,8} Furthermore, VPMM is the 2nd most common site among primary malignant melanomas of the female genital tract.^{6,8-10} Additionally, VPMM has an estimated annual incidence about 0.026/100,000 women per year with no essential differences among various racial or ethnic groups.^{6,8-10}

Nowadays, various treatment options have been proposed for patients with VPMM.^{1,3-5,7,11,12} However, most international scientific societies (ACOG, FIGO and ESMO) do not share any clear recommendation for the VPMM patients.^{11,12} To begin with, surgery remains the cornerstone treatment approach in patients with VPMM and it can either be conservative or radical.^{1,3-7,11-14} The most common type of conservative surgical operation is the wide local excision. Likewise, the most common forms of radical operation are vaginectomy and pelvic exenteration.^{6,11,14}

In patients with confined local disease in which wide local excision with clear margins is feasible, radical operations should be avoided because of the technical difficulties and related surgical morbidity with more side-effects and lower quality of life.^{1,3-7,11,12,15} In sharp contrast, in patients with extended disease where wide local excision with clear margins is impossible, more radical surgical approaches should be preferred in carefully selected patients.^{1,3-7,16}

It is also worth noting, that the lymph node dissection is absolutely essential in these patients, because there is a very low propensity for lymph node metastasis. This is the reason why, we do not recommend routine lymph node dissection in those patients.^{1,3,4,7,11} Apart from that, the procedure of lymph node dissection significantly increases morbidity, intraoperative and postoperative complications, prolongs hospital stay and diminishes quality of life, while it does not offer any survival benefit.^{1,3-5,7,11,12,17} Similarly, the elective lymph node sampling procedure has a controversial role in patients with VPMM.^{1,3-7,11-13} However, the sentinel lymph node biopsy approach has become very popular nowadays in VPMM patients.^{1,3-5,7,11,13,18} On the other hand, radiotherapy represents an equally effective treatment approach in patients with VPMM either in the form of vaginal brachytherapy or external pelvic radiotherapy.^{1,3-7,11,19,20}

Vaginal brachytherapy represents the primary treatment of choice especially in elderly patients with poor performance status and relevant co-morbidities.^{1,3-5,7,21,22} The administration of vaginal brachytherapy is well tolerated and associated with less side effects and improved quality of life.^{1,3-5,7,22} Moreover, vaginal brachytherapy minimizes the risk for local recurrences in patients with VPMM.^{1,3-5,7,16}

Likewise, external pelvic radiotherapy is the primary treatment of choice especially in patients with VPMM who are unable or unwilling to proceed to a surgical operation.^{1,3-7,11,19,20} Besides, external pelvic radiotherapy could be used as a preoperative treatment in order to reduce tumor size and enable a more conservative surgery. Apart from that, external pelvic radiotherapy is the adjuvant treatment

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of choice in high risk patients with VPMM (tumor size ≥ 3 cm, incomplete tumor resection and pelvic metastases)^{1,3-7,11,15,19,20} The application of external pelvic radiotherapy is not well tolerated and associated with significant long and short term morbidity and affected quality of life.^{1,3-5,7,22} Additionally, despite the reduced risk for local recurrences, external pelvic radiotherapy has no impact on overall survival.^{1,3-5,7,12,13,16}

Similarly, chemotherapy is another treatment option especially in patients with advanced stage VPMM. However, the clinical role of postoperative adjuvant chemotherapy in those patients remains controversial.^{1,3-5,7,23} In addition, postoperative adjuvant chemotherapy achieves only modest response rates and has no impact on overall survival.^{1,3-5,7,15}

In recent years, immunotherapy is an additional treatment approach especially in patients with VPMM and high risk for recurrence.^{1,3-5,7,13,24-26} The most common immunotherapeutic agents are interferon (IFN) and interleukin-2 (IL-2).^{1,5,13,24-26} The application of postoperative adjuvant immunotherapy is associated with significant toxicity and autoimmune disorders.^{1,3-5,7,24,25,27} Additionally, postoperative adjuvant immunotherapy offers survival benefits and reduces the risk for recurrences in patients with VPMM.^{1,3-5,7,13,24-26}

Biochemotherapy is the standard combination of chemotherapy and immunotherapy and represents a promising approach in patients with advanced stage VPMM.^{1,3-5,7,28} The application of postoperative adjuvant biochemotherapy is associated with significant toxicity.^{1,3-5,7,13,25} Moreover, the effectiveness of biochemotherapy in patients with advanced stage VPMM has not been established yet.^{1,3-5,7,28}

Overall, it is immediately evident that VPMM runs an aggressive clinical course with a propensity for early spread and metastasis, whilst most patients are usually being diagnosed at an advanced disease stage with distant metastase.^{1-7,11,13,16,26,29-32} This is the main

reason why, the 5-year overall survival in patients with VPMM is very low and ranges from 8.4 to 32.3%.^{2,11,13,16,26,29,30}

Conclusion

In conclusion, VPMM has an aggressive clinical behaviour with poor prognosis and low 5-year overall survival. Although, there are various treatment protocols, none of them is effective enough in minimizing the risk for recurrences and achieving high response rates.^{1-7,11,13,16,26,29,30}

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Conflicts of interest

None.

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