

### Clinical Characteristics, Management and Prognosis of Patients with Vaginal Primary Malignant Melanoma

Editorial

Androutsopoulos G\*, Decavalas G

Department of Obstetrics and Gynaecology, University of Patras, Medical School, Rion, Greece.

**\*Corresponding Author:**

Georgios Androutsopoulos MD,  
Assistant Professor, Department of Obstetrics & Gynecology, University of Patras, Medical School, Rion 26504, Greece.  
Tel: +306974088092  
E-mail: androutsopoulos@upatras.gr  
androutsopoulosgeorgios@hotmail.com

**Received:** January 25, 2015

**Published:** February 02, 2015

**Citation:** Androutsopoulos G, Decavalas G (2015) Clinical Characteristics, Management and Prognosis of Patients with Vaginal Primary Malignant Melanoma. *Int J Translation Community Dis.* 3(1e), 1-3. doi: <http://dx.doi.org/10.19070/2333-8385-150004e>

**Copyright:** Androutsopoulos G© 2015. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution and reproduction in any medium, provided the original author and source are credited.

Vaginal primary malignant melanoma (VPMM) is an extremely rare and highly aggressive tumor [1,2]. It accounts for less than 3% of all vaginal malignancies and 0.3-0.8% of all malignant melanomas [1-3]. It is the 2<sup>nd</sup> most common malignant melanoma of the female genital tract [4]. Until today, less than 300 cases of VPMM have been reported in the English literature [1,2,5,6].

The estimated annual incidence of VPMM is 0.026/100,000 women per year [2,3]. However between various racial or ethnic groups, there are no significant differences in VPMM annual incidence [3,7]. VPMM most commonly occurs in postmenopausal women [8-11]. The median age at diagnosis of VPMM, is 57 years [8-13].

Despite proposed theories, the precise pathogenesis of VPMM still remains unclear [14]. However, an attractive explanation is that VPMM arises from melanocytes located aberrantly in vaginal epithelium [14,15]. Those melanocytes are present in the basal layer of vaginal epithelium in 3% of healthy women [16]. According to this theory, active junctional changes is the initial stage in malignant melanoma development [17].

As VPMM located in areas not exposed to sunlight, it is obvious that ultraviolet radiation is not implicated in its pathogenesis [7].

Although VPMM may arise anywhere in the vagina, it most commonly occurs in the lower one third (34%) and the anterior (38%) vaginal wall [2,8,9,12,15,18,13]. VPMM lesions may be single or multiple, pigmented or nonpigmented [13,19]. Also, most of VP-

MMs are polypoid and ulcerated [14,19]. Moreover, the clinical appearance of nonpigmented VPMMs may be similar with vaginal epithelial tumors [14,19].

The most common symptoms and signs in patients with VPMM, are: vaginal bleeding (80%), vaginal discharge (25%), palpable vaginal mass (15%) and pain (10%) [5,6,8,9,11,12,14,20].

VPMM is a very aggressive tumor with a propensity of early spread and metastasis development [1,6,21,22]. The extensive vascular and lymphatic network of the vaginal mucosa, explains adequately the aggressive clinical behaviour of VPMM [8,10,20].

Most patients with VPMM, diagnosed with advanced stage disease [1,6,21,22]. More specifically, they have local recurrences in the pelvis and distant metastases in the lungs, liver, bones and brain [8,14]. However, many patients with distant metastasis have synchronous local recurrence in the pelvis [8].

The most common histologic cell type of VPMM, is: epithelioid (55%) [10,14,19]. Other less common histologic cell types of VPMM, are: spindle (17%) and mixed (28%) [10,14,19].

FIGO staging system for vaginal cancer does not incorporate tumor size and regional lymph node status and it is inappropriate for VPMM staging [2,12].

Although there are various treatment options, it has not defined yet an appropriate and effective treatment protocol for patients with VPMM [10,23].

Surgery is the baseline treatment in patients with VPMM [2,10,23,24]. The spectrum of surgical operation varies from conservative (wide local excision) to radical (vaginectomy, pelvic exenteration) [2,10,20]. In patients that wide local excision with clear margins is possible, the role of radical surgery remains unjustified [2,10,23,25]. However in highly selected patients that wide local excision is impossible, pelvic exenteration may be reasonable [2,13].

Lymph node dissection is not recommended in patients with VPMM, because the rate of lymph node metastasis is low [10]. Although lymph node dissection has no survival benefits for patients with VPMM, it leads to significant morbidity [10,23,26].

Moreover the role of elective lymph node sampling in patients with VPMM, remains controversial [2,10,23,24]. Recent years, sentinel lymph node biopsy has gained popularity [10,24,27].

Radiotherapy in patients with VPMM includes vaginal brachytherapy and external pelvic radiotherapy [2,10,28,29].

External pelvic radiotherapy is used as primary treatment for patients who are unable or unwilling to have surgery [2,10,28,29]. Also it is used as preoperative treatment, to reduce tumor size and enable a more conservative surgery [2,10,25,28,29]. Moreover it is used as postoperative adjuvant treatment for patients with tumor size ≥3 cm, incomplete tumor resection or pelvic metastases [2,10,11,23,28,29]. However, although external pelvic radiotherapy reduces the risk of local recurrences, it has no impact on overall survival [13,23,24].

Especially in elderly patients with bad performance status and relevant comorbidities, we prefer postoperative vaginal brachytherapy [5,11,30,31]. It is well tolerated and reduces the risk of local recurrences [13]. Moreover, it is associated with less side effects and better quality of life, compared with external pelvic radiotherapy [5,11,31].

The role of postoperative adjuvant chemotherapy in patients with advanced stage VPMM, remains controversial [32]. Postoperative adjuvant chemotherapy achieve only modest response rates and has no impact on overall survival [25].

Postoperative adjuvant immunotherapy with interferon (IFN) or interleukin-2 (IL-2), confers survival benefits in patients with VPMM at high risk for recurrence. [6,22,24,33-35]. Moreover, the combined use of IFN and IL-2 is superior to the single use of IL-2 [36]. However, the toxicity of immunotherapy is significant [6,22,33,34]. Moreover, IFN associated with the generation of autoantibodies and the induction of autoimmune disorders [37].

The role of combined use of chemotherapy and immunotherapy (biochemotherapy) in patients with advanced stage VPMM has not been established [38]. Moreover, the toxicity of biochemotherapy is significant [24,34].

Patients with VPMM have poor prognosis [35]. As most cases with VPMM diagnosed at advanced stage disease, the prognosis is very poor despite treatment modality [1,6,11,22].

Prognostic factors for patients with VPMM, are: tumor size, tumor growth, lymph node status and treatment method [8,12,23,35]. Among them, tumor size (<3 cm) is the most important prognostic factor [8,12,24]. Tumor thickness is only a weak predictor of survival, in patients with VPMM [8].

The 5-year overall survival of patients with VPMM is 8.4-32.3% [1,8,10,13,15,24,35]. Moreover the prognosis of VPMM is much more unfavourable, compared with other vaginal malignancies and cutaneous malignant melanoma [14].

## References

- [1]. Creasman W, Phillips J, Menck H (1998) The National Cancer Data Base report on cancer of the vagina. *Cancer* 83(5):1033-40.
- [2]. Piura B (2008) Management of primary melanoma of the female urogenital tract. *Lancet Oncol* 9(10):973-81.
- [3]. Weinstock M (1994) Malignant melanoma of the vulva and vagina in the United States: patterns of incidence and population-based estimates of survival. *Am J Obstet Gynecol* 171(5):1225-30.
- [4]. McLaughlin C, Wu X, Jemal A, Martin H, Roche L, et al (2005). Incidence

- of noncutaneous melanomas in the U.S. *Cancer* 103(5):1000-7.
- [5]. Androutsopoulos G, Decavalas G (2014) Vaginal primary malignant melanoma: a critical update. *J Community Med Health Edu* 4(2):e124.
- [6]. Terzakis E, Androutsopoulos G, Adonakis G, Zygouris D, Grigoriadis C, et al. (2011) Vaginal primary malignant melanoma: report of four cases and review of the literature. *Eur J Gynaecol Oncol* 32(1):122-4.
- [7]. Hu D, Yu G, McCormick S (2010) Population-based incidence of vulvar and vaginal melanoma in various races and ethnic groups with comparisons to other site-specific melanomas. *Melanoma Res* 20(2):153-8.
- [8]. Reid G, Schmidt R, Roberts J, Hopkins M, et al. (1989) Primary melanoma of the vagina: a clinicopathologic analysis. *Obstet Gynecol* 74(2):190-9.
- [9]. Levitan Z, Gordon A, Kaplan A, Kaufman R (1989) Primary malignant melanoma of the vagina: report of four cases and review of the literature. *Gynecol Oncol* 33(1):85-90.
- [10]. Miner T, Delgado R, Zeisler J, Busam K, Alektiar K, et al. (2004) Primary vaginal melanoma: a critical analysis of therapy. *Ann Surg Oncol* 11(1):34-9.
- [11]. Androutsopoulos G, Terzakis E, Ioannidou G, Tsamandas A, Decavalas G (2013) Vaginal primary malignant melanoma: a rare and aggressive tumor. *Case Rep Obstet Gynecol* 2013:137908.
- [12]. Xia L, Han D, Yang W, Li J, Chuang L, et al. (2014) Primary malignant melanoma of the vagina: a retrospective clinicopathologic study of 44 cases. *Int J Gynecol Cancer* 24(1):149-55.
- [13]. Jovinetz M, Erchepeborda M, Sun C, Soliman P, Eifel P, et al. (2010) Primary malignant melanoma of the vagina. *Obstet Gynecol* 116(6):1358-65.
- [14]. Gupta D, Malpica A, Deavers M, Silva E (2002) Vaginal melanoma: a clinicopathologic and immunohistochemical study of 26 cases. *Am J Surg Pathol* 26(11):1450-7.
- [15]. Irvin W Jr, Bliss S, Rice L, Taylor P Jr, Andersen W (1998) Malignant melanoma of the vagina and locoregional control: radical surgery revisited. *Gynecol Oncol* 71(3):476-80.
- [16]. Nigogosyan G, Delapava S, Pickren J (1964) Melanoblasts in Vaginal Mucosa. Origin for Primary Malignant Melanoma. *Cancer* 17:912-3.
- [17]. Allen A, Spitz S (1953) Malignant melanoma; a clinicopathological analysis of the criteria for diagnosis and prognosis. *Cancer* 6(1):1-45.
- [18]. Batsakis J, Suarez P (2000) Mucosal melanomas: a review. *Adv Anat Pathol* 7(3):167-80.
- [19]. Borazjani G, Prem K, Okagaki T, Twigg L, Adcock L (1990) Primary malignant melanoma of the vagina: a clinicopathological analysis of 10 cases. *Gynecol Oncol* 37(2):264-7.
- [20]. Piura B, Rabinovich A, Yanai-Inbar I (2002) Primary malignant melanoma of the vagina: case report and review of literature. *Eur J Gynaecol Oncol* 23(3):195-8.
- [21]. Nakagawa S, Koga K, Kugu K, Tsutsumi O, Taketani Y (2002) The evaluation of the sentinel node successfully conducted in a case of malignant melanoma of the vagina. *Gynecol Oncol* 86(3):387-9.
- [22]. Androutsopoulos G, Adonakis G, Ravazoula P, Kourounis G (2005) Primary malignant melanoma of the vagina: a case report. *Eur J Gynaecol Oncol* 26(6):661-2.
- [23]. Kirschner A, Kidd E, Dewees T, Perkins S (2013) Treatment approach and outcomes of vaginal melanoma. *Int J Gynecol Cancer* 23(8):1484-9.
- [24]. Vaysse C, Pautier P, Filleron T, Maisongrosse V, Rodier J, et al. (2013) A large retrospective multicenter study of vaginal melanomas: implications for new management. *Melanoma Res* 23(2):138-46.
- [25]. Leitaó MJ (2014) Management of vulvar and vaginal melanomas: current and future strategies. *Am Soc Clin Oncol Educ Book* e277-81.
- [26]. Reeves M, Coit D. Melanoma (2000) A multidisciplinary approach for the general surgeon. *Surg Clin North Am* 80(2):581-601.
- [27]. Abramova L, Parekh J, Irvin W Jr, Rice L, Taylor P, et al. (2002) Sentinel node biopsy in vulvar and vaginal melanoma: presentation of six cases and a literature review. *Ann Surg Oncol* 9(9):840-6.
- [28]. Petru E, Nagele F, Czerwenka K, Graf A, Lax S, et al. (1998) Primary malignant melanoma of the vagina: long-term remission following radiation therapy. *Gynecol Oncol* 70(1):23-6.
- [29]. Buchanan D, Schlaerth J, Kurosaki T (1998) Primary vaginal melanoma: thirteen-year disease-free survival after wide local excision and review of recent literature. *Am J Obstet Gynecol* 178(6):1177-84.
- [30]. Sause W, Cooper J, Rush S, Ago C, Cosmatos D, et al. (1991) Fraction size in external beam radiation therapy in the treatment of melanoma. *Int J Radiat Oncol Biol Phys* 20(3):429-32.
- [31]. McGuire S, Frank S, Eifel P. (2008) Treatment of recurrent vaginal melanoma with external beam radiation therapy and palladium-103 brachytherapy. *Brachytherapy* 7(4):359-63.
- [32]. Signorelli M, Lissoni A, Garbi A, Perego P, Mangioni C (2005) Primary malignant vaginal melanoma treated with adriamycin and ifosfamide: a case report and literature review. *Gynecol Oncol* 97(2):700-3.
- [33]. Jack A, Boyes C, Aydin N, Alam K, Wallack M (2006) The treatment of melanoma with an emphasis on immunotherapeutic strategies. *Surg Oncol*

- 15(1):13-24.
- [34]. Ives N, Stowe R, Lorigan P, Wheatley K (2007) Chemotherapy compared with biochemotherapy for the treatment of metastatic melanoma: a meta-analysis of 18 trials involving 2,621 patients. *J Clin Oncol* 25(34):5426-34.
- [35]. Huang Q, Huang H, Wan T, Deng T, Liu J (2013) Clinical outcome of 31 patients with primary malignant melanoma of the vagina. *J Gynecol Oncol* 24(4):330-5.
- [36]. Keilholz U, Conradt C, Legha S, Khayat D, Scheibenbogen C, et al. (1998) Results of interleukin-2-based treatment in advanced melanoma: a case record-based analysis of 631 patients. *J Clin Oncol* 16(9):2921-9.
- [37]. Abu-Shakra M, Buskila D, Ehrenfeld M, Conrad K, Shoenfeld Y (2001) Cancer and autoimmunity: autoimmune and rheumatic features in patients with malignancies. *Ann Rheum Dis* 60(5):433-41.
- [38]. Harting M, Kim K (2004) Biochemotherapy in patients with advanced vulvovaginal mucosal melanoma. *Melanoma Res* 14(6):517-20.