Primary vaginal melanoma and long-term survivors*

W. A. Tjalma[1,2], *M.D., Ph.D.*; **J. M. Monaghan**[1], *M.B., F.R.C.S. (Ed.), F.R.C.O.G.*; **A. de Barros Lopes**[1], *M.B., Ch.B., M.R.C.O.G.*; **R. Naik**[1], *M.B., Ch.B. M.R.C.O.G., M.D.*; **A. Nordin**[1], *M.B., CR.B., M.R.C.O.G.*

[1]*Northern Gynecological Oncology Centre, Queen Elizabeth Hospital, Gateshead (U.K.)*
[2]*Division of Gynecologic Oncology, Antwerp University Hospital, Antwerp (Belgium)*

Summary

Vaginal melanoma is a rare and highly malignant disease. This report describes the characteristics and clinical course of all patients treated at one institute (Northern Gynaecological Oncology Centre, UK) over the last 25 years. Of a total of nine patients identified with a primary malignant vaginal melanoma, only one patient survived for more than five years. A literature review revealed only 21 reported cases with a survival greater than five years. The most important factor for survival appears to be the tumour size. Treatment modality varied equally within the group of long-term survivors (27% radical surgery, 27% wide local excision, 27% radiotherapy, 14% wide local excision and radiotherapy, and 5% unknown therapy). The prognosis of patients with primary malignant melanoma is poor, regardless of primary therapy (conservative or radical). Conservative treatment and accurate investigation of every discoloured lesion is recommended.

Key words: Vaginal melanoma; Treatment; Prognosis; Size.

Introduction

Melanomas are among the commonest of all human cancers and the incidence is steadily increasing. The increase is almost entirely attributed to sun exposure, but surprisingly, the incidence of vaginal melanomas also appears to be rising.

The first report of vaginal melanoma was in 1887 [1]. The tumour originates from melanocytes that are present in the vaginal mucosa of approximately 3% of women [2]. To date there have been 222 cases reported in the English literature. The overall 5-year survival is notoriously poor being between 0% and 21% and there appears to be no reliable prognostic indicator [3].

Treatment varies among conservative surgery, radical surgery, radiotherapy, chemotherapy and immunotherapy. Optimal treatment is debatable with none of the above-mentioned modalities having been shown to provide a survival advantage. This retrospective study reviews patients with a vaginal melanoma treated in one cancer centre (NGOC) over the last 25 years. Furthermore a survey of the literature is given for all patients with a survival of longer than five years. The aim of this study was to identify patients with a favourable outcome and to evaluate the most appropriate treatment.

Material and Methods

The medical records of all patients with a primary invasive vaginal cancer, treated between January 1974 and December 1999 at the Northern Gynaecological Oncology Centre (Gateshead, U.K.) were reviewed. Patients with metastatic lesions to the vagina were omitted from the review. The patients were staged according to FIGO guidelines. All follow-up examinations took place in the Northern Gynaecological Oncology Centre.

Results

Within this 25-year period 84 patients were treated for a primary vaginal cancer. Of these, nine had a malignant melanoma (11%). The mean age at diagnosis was 77 years (range 69-92). The symptoms were either pain (2) or discharge (7) with a clinical history varying between one and six months (median 3). The average parity was one with a range from zero to two. On physical examination, the tumours varied in size from 9-50 mm with a mean diameter of 18. The lesions were found in the upper one-third of the vagina in one case, in the lower one-third in six cases, in the middle one-third in one case and in one case the tumour involved the entire vaginal length. The tumour arose in the anterior wall in five patients and in the posterior wall in four.

The FIGO stage was I in five cases, II in one case, III in one case and IV in two cases. Two patients received local radiotherapy, one patient had a radical hysterectomy and upper vaginaectomy, and six patients had a wide local excision, of which two received whole pelvis radiotherapy. Six patients died of the disease, while one patient died of intercurrent disease and two patients are alive with disease. No patients were lost to follow-up and the median overall survival time was 24 months (range 4-63). None of the clinical-pathological factors appear to have any prognostic value. Figure 1 shows the overall survival curve.

*Presented at the XVI FIGO World Congress, Washington, D.C. (USA) 3-8 September, 2000

Revised manuscript accepted for publication September 10, 2000

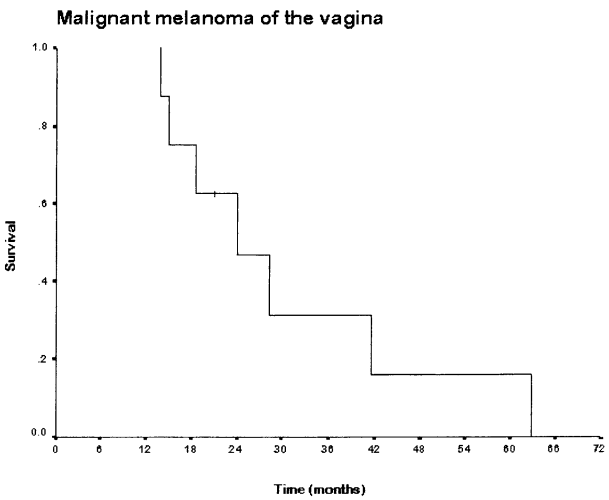

Figure 1. — Overall survival curve for nine patients with a primary malignant melanoma.

Discussion

Vaginal melanomas account for 2.6%-2.8% of all primary malignant vaginal tumours [4]. The number of melanomas are rising. In a recent report of the National Cancer Data Base 4% of the vaginal cancers registered were melanomas [5]. An overview in the NGOC between 1974-2000 showed that malignant melanomas accounted for 11% of the patients diagnosed with primary invasive vaginal tumours. In a previous report covering the period 1947-1979 only 2% of the primary vaginal tumours were melanomas [6]. The rise in incidence of malignant melanomas in an area of the body not exposed to ultraviolet radiation is difficult to explain.

Generally the prognosis of patients with vaginal melanomas is poor. A search of the English literature was performed to identify long-term survivors of vaginal melanomas. Patients with urethral melanomas were excluded and patients from population studies (tumour registry data) were not included due to a lack of clinical information [7, 8]. Only 22 patients were identified to have survived longer then five years [3, 4, 9-20] and only four of those survived longer then ten years (Table 1) [3, 4, 13, 20].

There did not appear to be any relationship between overall survival and location of the tumour, presence of symptoms, gravidity or parity [20], although debate does exist with respect to tumour thickness, tumour size and treatment. Recent reports by Reid *et al.* [16] and Buchanan *et al.* [20] found no correlation between tumour thickness and survival. However, it could well be that there is a correlation, as there is in vulvar melanoma, if tumours are detected with an invasion less than 1 to 2 mm [20]. On the other hand only two of the 22 patients who survived longer than five years had a thickness of less then 2.0 mm. As very early diagnosis of this disease is rare, the impact of thickness in prognosis of early stage disease can not be assessed.

Tumour size appears to be the greatest predictor of survival [3, 16, 21]. This is also reflected in our review of 5-year survivors: of the 18 patients with a known tumour size only two were greater than 30 mm.

The optimal treatment remains unknown. In the group of 5-year survivors, the treatment modalities were dispersed accordingly: six had radical surgery, six had wide

Table 1. — *Reported cases of primary vaginal melanoma with a survival of longer than 5 years.*

Author	Year	Age	Size (mm)	Depth (mm)	Treatment	Outcome	
						Status	Follow-up (y)
1. Mino *et al.*	1952	28	20	5.0	RS	NED	5.0
2. Casas *et al.*	1952	52	25	–	WLE+RT	NED	6.0
3. Ariel *et al.*	1961	47	60	–	RT	DOID	7.0
4. Ariel *et al.*	1961	52	20	–	RS	DOD	6.0
5. Davis *et al.*	1975	60	–	–	WLE	NED	16.0
6. Chung *et al.*	1980	72	25	1.0	RS	NED	12.75
7.		37	10	2.8	RS	NED	5.5
8.		71	10	3.0	WLE	DOD	5.0
9.		60	–	1.4	RT	DOD	7.6
10. Liu *et al.*	1987	55	–	–	WLE	DOD	5.8
11.		39	40	–	WLE	AWD	8.2
12. Harrison *et al.*	1987	58	15	–	RT	NED	7.7
13. Reid *et al.*	1989	81	10	9.0	WLE	DOID	5.7
14.		68	25	–	RS	DOD	6.0
15. Levitan *et al.*	1989	59	20	4.0	RT	DOD	9.0
16. Ronan *et al.*	1990	60	–	9.0	–	DOD	6.2
17. Geisler *et al.*	1995	58	–	7.0	RS	NED	8.0
18. Petru *et al.*	1998	65	20	5.0	RT	DOD	12.75
19.		54	30	5.0	WLE+RT	AWD	8.3
20.		69	30	6.0	RT	DOD	5.4
21. Buchanan *et al.*	1998	55	15	6.0	WLE	NED	13.0
22. Present	2001	71	10	11.0	WLE+RT	DOID	5.2

RS = radical surgery; RT = radiotherapy; WLE = wide local excision; NED = no evidence of disease; AWD = alive with disease; DOID = died of intercurrent disease; DOD = died of disease; – = not mentioned.

local excision, three had wide local excision and radiotherapy and six had radiotherapy alone. Findings of the present review confirm previous reports showing no significant differences in survival among radical surgery, wide local excision, radiotherapy or wide local excision with radiotherapy [16, 20]. Only one publication stated a survival benefit for radical surgery [21]. However there appeared to be a selection bias with younger patients and those with smaller lesions receiving radical surgery in preference to radiotherapy.

Based on the scarcity of literature on primary vaginal melanoma, no general recommendations for treatment can be made based on survival outcome. However, most reports favour conservative surgery (wide local excision) over extensive radical surgery or primary radiotherapy. Lesions close to the bladder, urethra or rectum may require a more radical approach in order to achieve adequate clearance of the melanoma.

Evaluation of regional lymph nodes provides important staging information and it may enhance regional control if involved with metastatic disease. However, comprehensive lymphadenectomy does not provide a survival benefit and may occasionally be associated with an increase in morbidity. Elective lymphadenectomy should therefore only be performed in patients with evidence of lymph node metastases [22]. Sentinel lymph node biopsy can be performed to assess the lymph node status and therefore the need for an elective lymphadenectomy.

Primary radiation therapy should be considered for patients who are unfit for surgery. The role of chemotherapy is unclear and there is as yet no reliable data on the use of interferon as adjuvant therapy.

Conclusion

Overall survival appears to be related to the size of the primary lesion. Currently there is no treatment shown to be superior with regard to survival, and conservative surgery appears equivalent to that of a radical approach. A wide local excision with a sentinel node biopsy seems to be the most appropriate treatment to date. Only in cases of metastatic lymph node involvement should a lymphadenectomy be considered. Survival can be improved by earlier detection. Therefore any discoloured lesion identified at the time of cervical screening or routine vaginal examination should be investigated to exclude vaginal melanoma.

References

[1] Parona F. A.: "Sarcoma primitivo melanotico fuso-cellulare al setto vesico-vaginale; esportazione del tumore e di porzione della vesico; guarigione temporia". *Ann. Univ. Med. Chir. Milan.*, 1887, *279*, 241.

[2] Nigogosyan G., DeLaPava S., Picken J. W.: "Melanoblasts in vaginal mucosa". *Cancer*, 1964, *17*, 1912.

[3] Petru E., Nagele F., Czerwenka K;, Graf A. H., Lax S., Bauer M. *et al.*: "Primary malignant melanoma of the vagina: long-term remission following radiation therapy". *Gynecol. Oncol.*, 1998, *70*, 23.

[4] Chung A. F., Casey M. J., Flannery J. T., Woodruff J. M., Lewis J. L.: "Malignant melanoma of the vagina - report of 19 cases". *Obstet. Gynecol.*, 1980, *55*, 720.

[5] Creasman W. T., Phillips J. L., Menck H. R.: "The National Cancer Data Base report on cancer of the vagina". *Cancer*, 1998, *83*, 1033.

[6] Al-Kurdi M., Monaghan J. M.: "Thirty-two years experience in management of primary tumours of the vagina". *Br. J. Obstet. Gynecol.*, 1981, *88*, 1145.

[7] Blaumeiser B., Tjalma W., Swaegers M;, van Dam P., Colpaert C., Buytaert P.: "Primary malignant melanoma of the female urethra". *Zentralbl. Gynakol.*, 2000, *122*, 179.

[8] Rikaniadis N., Konstadoulakis M. M., Kymionis G. D., Tsibloulis B., Peveretos P., Karakousis C. P.: "Long-term survival of a female patient with primary melanoma of the urethra". *Eur. J. Surg. Oncol.*, 1998, *24*, 607.

[9] Mino R. A., Livingstone R. G., Haynes J. F.: "Primary melanoma of the vagina". *Ann. West. Med. Surg.*, 1952, *6*, 648.

[10] Casas P. F., Pincena J., Garcia C. G.: "Malignant melanoma of the vagina". *Surg. Gynecol. Obstet.*, 1952, *94*, 159.

[11] Ariel I. M.: "Five-years cure of a primary malignant melanoma of the vagina by local radioactive isotope therapy". *Am. J. Obstet. Gynecol.*, 1961, *82*, 405.

[12] Ariel I. M.: "Malignant melanoma of the vagina". *Obstet. Gynecol.*, 1961, *17*, 222.

[13] Davis P. C., Franklin E. W.: "Cancer of the vagina". *South. Med. J.*, 1975, *68*, 1239.

[14] Liu L. Y., Hou Y. J., Li J. Z.: "Primary malignant melanoma of the vagina: a report of seven cases". *Obstet. Gynecol.*, 1987, *70*, 569.

[15] Harrison L. B., Fogel T. D., Deschel R. E.: "Primary vaginal cancer and vaginal melanoma: a review of therapy with external beam radiation and a simple intracavitary brachytherapy system". *Endocuriether. Hyperthermia. Oncol.*, 1987, *3*, 67.

[16] Reid G. C., Schmidt R. W., Roberts J. A., Hopkins M. P., Barrett R. J., Morley G. W.: "Primary melanoma of the vagina: a clinicopathologic analysis". *Obstet. Gynecol.*, 1989, *74*, 190.

[17] Levitan Z., Gordon A. N., Kaplan A. L., Kaufman R. H.: "Primary malignant melanoma of the vagina: report of four cases and review of the literature". *Gynecol. Oncol.*, 1989, *33*, 85.

[18] Ronan S. G., Eng A. M., Briele H. A., Walker J. D., Das Gupta T. K.: "Malignant melanoma of the female genitalia". *J. Am. Acad. Dermatol.*, 1990, *22*, 428.

[19] Geisler J. P., Look K. Y., Moore D. A., Sutton G. P.: "Pelvic exenteration for malignant melanomas of the vagina or urethra with over 3 mm of invasion". *Gynecol. Oncol.*, 1995, *59*, 338.

[20] Buchanan D. J., Schlaerth J., Kurosaki T.: "Primary vaginal melanoma: Thirteen-year disease-free survival after wide local excision and review of recent literature". *Am. J. Obstet. Gynecol.*, 1998, *178*, 1177.

[21] Van Norstrand K. M., Lucci J. A., Schell M., Berman M. L., Manetta A., DiSaia P. J.: "Primary vaginal melanoma: improved survival with radical pelvic surgery". *Gynecol. Oncol.*, 1994, *55*, 234.

[22] Yu L. L., Flotte T. J., Tanabe K. K., Gadd M. A., Cosimi A. B., Sober A. J. *et al.*: "Detection of microscopic melanoma metastases in sentinel lymph nodes". *Cancer*, 1999, *86*, 617.

Address reprint requests to:
W. A. TJALMA, M.D., Ph.D.
Division of Gynecologic Oncology
University Hospital Antwerp
Wilrijkstraat 10
2650 Antwerp (Belgium)
e-mail: wiebren.tjalma@uza.uia.ac.be