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Primary Melanoma of the Female Genital System: A Report of 10 Cases and Review of the Literature

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Abstract. *Background: Primary melanoma of the female genital system are extremely rare (2-3%). Patients and Methods: A retrospective review was undertaken of patients with primary melanoma of the female genital system treated from 1990-2003 at Rostock University Hospital, Germany. Different treatments (sentinel node biopsy, inguinofemoral lymphadenectomy, en bloc resection, adjuvant Interferon-alpha-therapy, adjuvant chemotherapy) are discussed. The complicated classification is reduced to a clinical path for daily use (UICC stage and invasion depth of Breslow, Clark's level and Chung's level). Results: We report on 10 patients, aged 26 to 76 years, with primary melanoma of the female genital tract. Seven women developed a vulvar melanoma and one woman a malignant melanoma of the cutaneous inguinal region, while another 2 women had an unusual primary location of the malignant melanoma, the cervico-vaginal region (n=1) and the left ovary (n=1). Conclusion: Initial surgical modality did not influence long-term survival, but affected disease-free survival significantly.*

Primary melanomas of the female genital system are extremely rare (2-3%). They have been reported to occur in the vulva, vagina, uterus, cervix and ovaries, but the latter are not common and rarely curable (1). Despite its rarity, vulvar melanoma is the second most common vulvar malignancy after squamous cell carcinoma and represents between 3-4% (2, 3) and 8-10% (4) of all vulvar malignancies. Although the biological behavior of vulvar and vaginal melanoma is similar to cutaneus melanoma (5), the prognosis is very poor, as there is a high risk of local progression as well as distant metastases. Malignant melanoma can form metastases primarily in the skin, tissue, the lymph nodes and the lung ("limited disease") as well as in other organ systems (visceral, ossary and cerebral system: "extensive disease") (6). If there is a minimal suspicion of melanotic change, the affected area has to be removed completely and to be examined (immuno-) histopathologically (Vimentin, S-100-Protein, HMB45). Different types of melanoma can be categorized according to clinical and histological parameters: superficially spreading melanoma (SSM), nodular melanoma (NM), acral lentiginous melanoma (ALM) and lentigo-maligna-melanoma (LMM).

A retrospective review was undertaken of patients with primary melanoma of the female genital system, treated from 1990-2003 at Rostock University Hospital, Germany. The purpose of this analysis was to determine whether less radical surgery, such as that performed for cutaneous nonvulvar melanoma, makes a difference for the outcome of the patients. Different treatments (sentinel-lymphadenectomy, inguinofemoral lymphadenectomy, *en bloc* resection, adjuvant Interferon-alpha-therapy, adjuvant chemotherapy) are discussed.

Patients and Methods

From January 1990 to December 2003, ten patients were diagnosed with primary malignant melanoma of the female genital system at the University Hospital Rostock, Department of Obstetrics and Gynecology, Rostock, Germany. A retrospective review of clinical, pathological and surgical data was done to identify the outcome of patients at different stages of disease following different surgical procedures. Clinical features, type of surgery, adjuvant therapy, recurrences and distant metastases were recorded. Using the data of the pathological review, all patients were staged using the 2002 AJCC and UICC histological classification for malignant melanoma (Table I) (7). The complicated classification was reduced to a clinical path for daily use (UICC stage and invasion depth of Breslow, Clark's level and Chung's level, Tables I and II).

Abbreviations: AJCC, American Joint Committee on Cancer; FIGO, International Federation of Gynecology and Obstetrics; 5-YSR, Five-year survival rates; MRI, Magnetic resonance imaging; UICC, International Union against Cancer.

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Key Words: Vulvar melanoma, melanoma of the vagina, uterine cervix melanoma, ovarian melanoma.

Table I. *TNM classification and UICC-Stages 2002 for malignant melanoma (6).*

PTx	Primary tumor can not be evaluated.		
pT0	No primary tumor.		
Ptis	Melanoma *in situ* (Clark Level I).		
pT1	Tumor 1 mm or less thick.		
pT1a	Clark's level II or III, without ulceration.		
pT1b	Clark's level IV or V *or* with ulceration.		
pT2	Tumor 1-2 mm thick.		
pT2a	Without ulceration.		
pT2b	With ulceration.		
pT3	Tumor 2-4 mm thick.		
pT3a	Without ulceration.		
pT3b	With ulceration.		
pT4	Tumor more than 4mm thick.		
pT4a	Without ulceration.		
pT4b	With ulceration.		
N1	1 regional lymph node		
N1a	Microscopical.		
N1b	Macroscopical.		
N2	2-3 regional lymph nodes or satellite/in-transit metastase(s) without lymph node metastases.		
N2a	2-3 regional lymph nodes, microscopical.		
N2b	2-3 regional lymph nodes, macroscopical.		
N2c	Satellite/in-transit metastase(s) without lymph node metastases.		
N3	>4 regional lymph nodes; compound lymph nodes; satellite/in-transit metastases with regional lymph nodes.		
Stadium 0	PTis	N0	M0
Stadium I	pT1a, pT1b, pT2a	N0	M0
Stadium II	pT2b, pT3a, pT3b, pT4a	N0	M0
Stadium III	Every T	N1, N2, N3	M0
Stadium IV	Every T	Every N	M1

Table II. *Microstaging systems used to predict prognosis from vulvar melanoma (27).*

Clark's levels (invasion of cutaneous melanoma of non genital origin) (8)	Level I	*In situ* lesions; neoplastic cells confined to the epithelium.
	Level II	Lesions penetrate the basement membrane and extend into the loose papillary dermis.
	Level III	Melanoma invading and usually filling the papillary dermis, accumulating at the interface.
	Level IV	Invasion of the deep reticular dermis.
	Level V	Melanoma invading the subcutaneous adipose tissue.
Breslow (depth of invasion of cutaneous melanoma) (9)	(1)	0.75 mm or less
	(2)	0.76 to 1.50 mm
	(3)	1.51 to 2.25 mm
	(4)	2.26 to 3.0 mm
	(5)	Greater than 3.0 mm
Chung's level (involvement in melanoma of the vulva) (13)	Level I	Tumor confined to the epithelium.
	Level II	Lesion penetrates the basement membrane and extends into the dermis or lamina propria to 1 mm or less from the granular layer or its estimated position in the epidermis, or from the outermost epithelial layer.
	Level III	Melanoma penetrating between 1 and 2 mm into subepithelial tissue.
	Level IV	Invasion beyond 2 mm, but not into underlying fat.
	Level V	Melanoma invading the subcutaneous adipose tissue.

Results

Between January 1990 and December 2003, 10 patients with primary melanoma of the female genital system were diagnosed in our hospital. The clinical features, pathological characteristics, stages, type of surgery, adjuvant therapy, recurrences and distant metastases are given in Table III.

Seven women developed a vulvar melanoma (Figures 1 and 2) and one woman a malignant melanoma of the cutaneous inguinal region, while another two women had an unusual primary location of the malignant melanoma: the cervico-vaginal region (n=1, Figure 3) and the left ovary (n=1, Figures 4 and 5).

The median age was 53.3 years (range 26-76) for patients suffering malignant melanoma of the female genital tract. The median age of patients with vulvar melanoma was 48.4 years (range 26-67), the woman with malignant melanoma of the cervico-vaginal region was 67 years old, of the cutaneous inguinal region 56 years and with ovary melanoma 76 years old at the time of diagnosis.

After a long symptom-free time, the first clinical symptoms were mostly unspecific. A dark-pigmented lesion in the external genitalia was the most common sign present (6 out of 10: 60%), followed by pruritus (40%) and increasing fluor vaginalis, vaginal bleeding (20%) or pain. The patient with the melanoma of the ovary complained

Table III. *Patients' data.*

Patients	Age (a) FD	Central location (Histology)	Exulceration	TNM-classif. (DDG-Stage)	Infiltration depth	Primary treatment	Follow-up
1. FI	63 FD: 1/98	Labium minus dextrum near clitoris: SSM formed in NZN	-	pT1a cN0 cM0 R0 Stage I	Breslow 0.85mm Clark's II Chung's II	WLE SD 1-2cm	→5a+11m pd: CR
2. WM	50 FD: 2/03	Labium majus dextrum: MM Labium maj sin: Lentigo maligna	+	pT3b pN0 (0/25) M0 L0 R0 Stage IIB	Breslow 2-4mm Clark's IV Chung's IV	HVLNE r SD 2cm ing-fem LNE re+ing LNE li →IFN-alpha	→10m pd: CR
3. GA	67 FD: 2/91	Clitoris: LMM	+	pT3b cN0 cM0 Stage IIB	Breslow 3mm Clark's IV Chung's IV	WLE SD 2cm →Radiation inguinal region (GHD 54 Gy)	→5a+6m pd: Exitus letalis (sudden heart death) in CR
4. AE	36 FD: 3/91	Suburethral: Multiform MM	-	pT4a pN0 (0/7) cM0 Stage IIB	Breslow 18+2mm Clark's V Chung's V	WLE + ing LNE bil SD 0.7cm →Immuno-CHT: Dacarbacin (6xDTIC)+ IFN-alpha (4-8/1991)	→7m pd (10/91): several LR (left parietal vaginal wall) →Exenteration →3a pd (94): Exitus letalis
5. BM	48 FD: 3/98	Labium majus sinistrum: spinosus cells to polymorphic cells MM Labium majus dextrum: Melanoma *in situ* developed of junctional nevus	+	pT4b pN0(0/18) cM0 R0 Stage IIC	Breslow 12mm (8mm invasion of subcutis) Clark's V; Chung's V	RVLNE SD 3-5cm ing-fem LNE li+ing LNE re) →IFN-alpha	*13m pd (4/99): Progression (Mis→ WLE) *1a+4m pd (07/99):1. LR (r vaginal wall) =>DE +® (GD:51Gy) *2a+9m pd (12/00):2. LR(r post commisur) =>DE + ® (GD 36 Gy) Temodal therapy (since 12/00) *3a+7m pd (10/01): Basaliom (right nose) *3a+8m pd (11/01): 3. LR=>PE+® (GD 40Gy) *4a+1m pd (4/02): 4. LR=>PE+® (GD 40Gy) → 5a+9m pd: CR
6. BU	49 FD: 6/92	Labium minus sinistrum: Malignant nodular Melanoblastoma-LMM	+	pT4b N1a (1/25): Inguinal (1/12) =>N1 ing. re. Pelvin (0/13)	Breslow 4+2mm, (10x10mm); Clark's IV Chung'sIII	RVLNE SD 3-4cm Ing. LNE bil: r N1 →pelv LNE bds +BSO	* 8a pd (07/00): Breast cancer right (invasive ductal,pT1c (1.3cm) LCIS pN0 (0/12) cM0 L0 R0 G2: Operation, Radiation,

continued

Table III (*continued*)

Patients	Age (a) FD	Central location (Histology)	Exulceration	TNM-classif. (DDG-Stage)	Infiltration depth	Primary treatment	Follow-up
				cM0 Stage IIIB		→Immuno-CHT: Dacarbacin (6xDTIC: 07-11/92)+ IFN-alpha (07/92-11/94)	Tamoxifen 20mg until 2005 → 11a+6m pd: CR
7. BP	26 FD: 4/91	Labium minus sinistrum near clitoris: uniform, round and spinal cells MM	+	pT4b N1b (1/32) N1 ing. re cM0 Stage IIIC	Breslow 12mm Clark's V Chung's V	RVLNE (+clitoridectomy SD 3-4cm ing LNE bil: r N1) →pelv LNE bds →Immuno-CHT: Dacarbazin (6xDTIC) + IFN-alpha (06-10/1991)	*8m pd (12/91): hepatogen mets *11m pd (3/92): pulmonal mets *1a+4m pd (8/92): Progression of pulmonal mets *1a+6m pd (10/92): breast mets *1a+7m pd (11/92):cerebral mets →1a+8m pd (12/92): Exitus letalis
8. PS	51 FD: 8/90	Cutaneous left inguinal region near vulva: SSM	+	pT3b pN0 (0/2) cM0 Stage Iib	Breslow 2.5mm (16x10x2.5 mm) Clark's IV Chung's IV	WLE + ing LNE l SD 3-4cm →CHT	*4a+9m later (05/95): last contact: CR
9. ME	67 FD: 5/99	Cervico-vaginal region Suburethral: spinal, pleomorphic and clear cell MM	+	pT2b pN0(0/37) cM0 R0 Stage IIA	Breslow 1.9-2mm (1.3cm) Clark's IV Chung'sIII	Radical WLE + ing+pelv LNE bil (Colpohysterectomy, BSO) SD 3-4cm →IFN-alpha	*2m later CCT (07/99):cerebral metastases → 10m later (03/00): Exitus letalis
10. PA	76 FD: 11/95	Left ovary: epithelioid cell MM + benign Thecofibroma	+	pT1c cN0 M1 Stage IV	40x40x10 mm	abdominal HE+ BSO,AE, omentectomy partial => CHT refuged	At FD: pulmonal and peritoneal metastases →7m pd (6/96): LC

a...years, AE...appendectomy; BSO...bilateral salpingo-oophorectomy; CHT...chemotherapy; FD...first diagnosis; HE...hysterectomy; HV...hemivulvectomy; IFN...Interferon, ing...inguinal, l...left, LC...last contact with the doctors, LNE...lymphadenctomy, LR...local recurrence, m...month, ®...radiation, r...right; RV...radical vulvectomy; RVLNE...radical vulvectomy with lymphadenectomy; SD...safety distance,; WLE... wide local excision.

abdominal pain and ascites (patient 10). The time between the first symptom and diagnosis ranged from less than one month in four patients, less than four months in five patients and one year in one patient (patient 9).

The primary therapeutic approach was surgery in all patients. There were different surgical treatments depending on the location and surgical characteristics of the primary lesion. More than half of the patients (n=6) had to undergo radical surgery. Surgical treatments ranged from wide local excision, hemivulvectomy or radical vulvectomy with bilateral inguinal lymphadenectomy, or more radical surgery (30%). Five out of seven patients with vulvar melanoma had to undergo bilateral inguinal lymphadenectomy (71.4%). In histopathological examinations, two of these patients with vulvar melanoma (28.6%) presented tumor in the groin lymph nodes. The reason for not performing inguinal lymphadenectomy in one of the two patients was multimorbidity and the high risk of extended surgery. This woman received adjuvant radiation of the groin region (patient 3). The reason that the second woman with

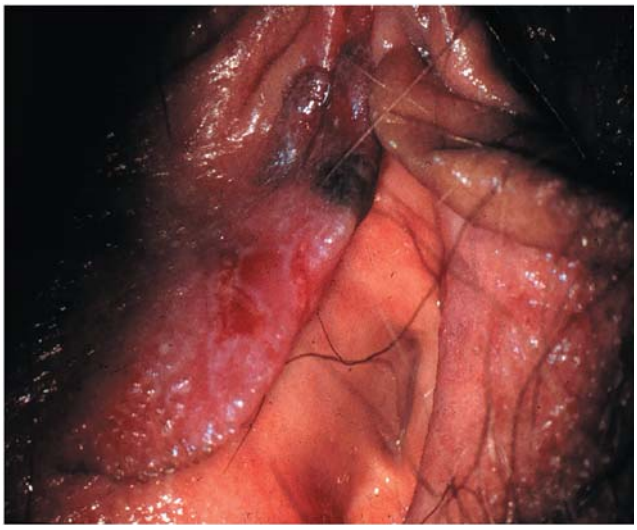

Figure 1. *Malignant melanoma of the right minor labia (patient 2).*

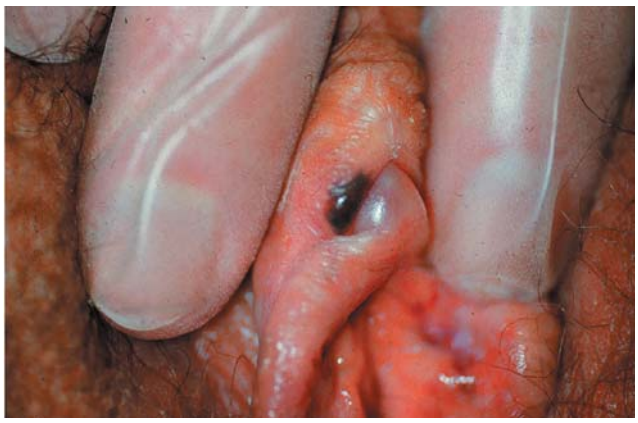

Figure 2. *Malignant melanoma of the clitoris (patient 1).*

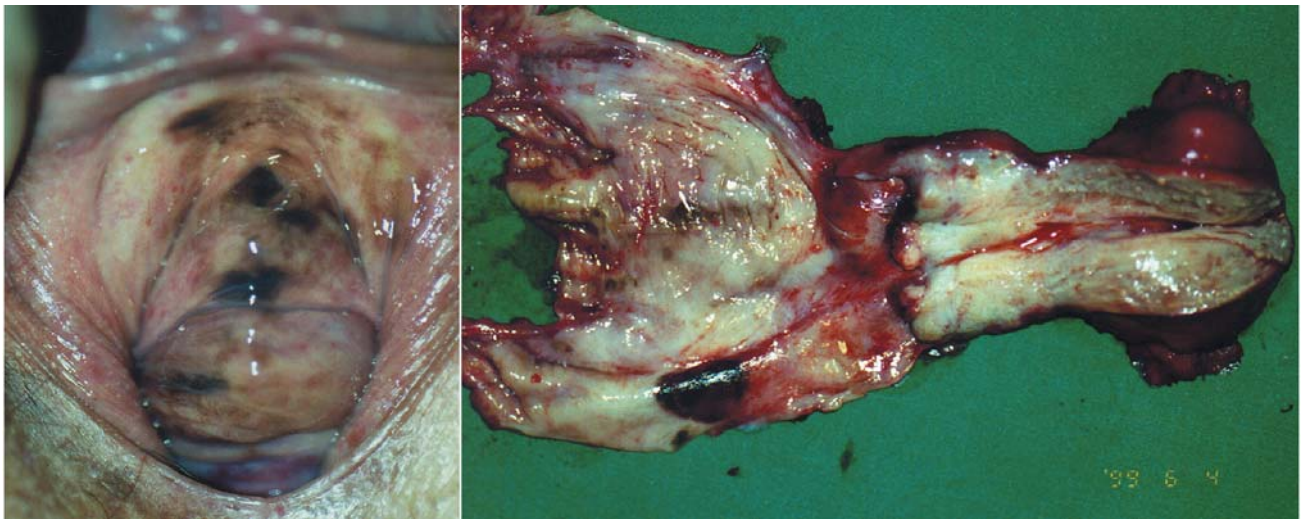

Figure 3. *Malignant melanoma of the cervico-vaginal region with operative tissue (patient 9).*

malignant melanoma of the vulva did not receive lymphadenectomy was the early diagnosis in DDG Stage Ia, at which stage radical surgery is not required (patient 1).

Patients with primary locations close to the introitus, suburethral or cervico-vaginal regions had to undergo radical vulvectomy for security distance (patients 5-7), occasionally with resection of the urethra (patient 4) or with colpohysterectomy (patient 9).

Different histological types are reported (SSM, NM, ALM, LMM and pleomorphic melanoma). On microstaging, the Breslow depth was between 0.85 to 18 mm, Clark's level II to V and Chung's level II to V. In six patients immunohistological investigations were done. The melanoma cells were positive for S-100 protein, HMB-45 and Vimentin (Figures 6 and 7). Three patients had postoperative complications (secondary healing in three cases, inguinal lymphocyst in one case).

Six out of ten women had adjuvant immunotherapy with IFN-alpha, since the invasion depth was more than 1.5 mm or lymph node metastases had already occured. Three patients had a combined immunochemotherapy with Dacarbacin (6 cycles DTIC + IFN-α) owing to the tumor thickness (18 mm; patient 4) or contralateral lymph node metastases (patients 6 and 7).

The average follow-up was 48.4 months (range, 10-138 months), but one of the patients was diagnosed in 2003 with

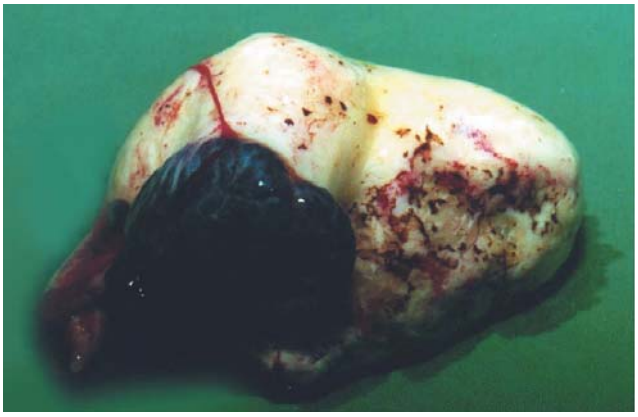

Figure 4. *Malignant melanoma of the left ovary (patient 10).*

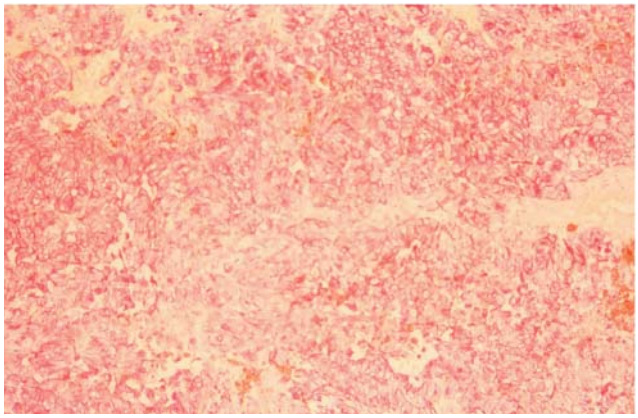

Figure 6. *Immunohistology. The tumor cells react positively for HMB-45 (original magnification x80, patient 10).*

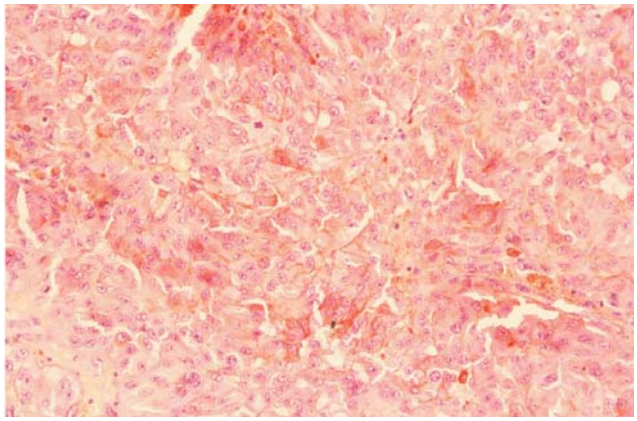

Figure 5. *Large tumor cells with melanin pigment (HE, x80, patient 10).*

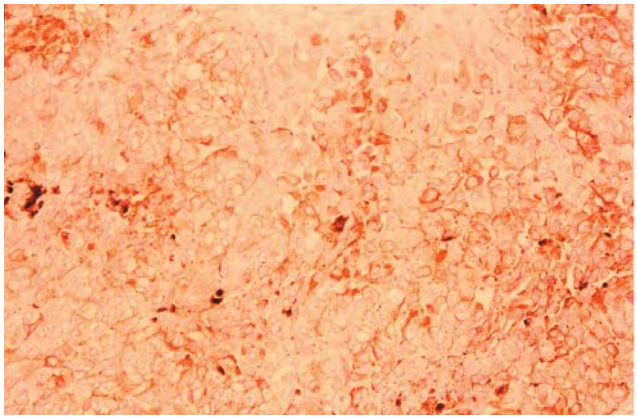

Figure 7. *Immunohistology. The tumor cells react positively for S-100 (original magnification x80, patient 10).*

a very early stage of melanoma and has been followed for 10 months (patient 2). Three out of ten patients (30%), with follow-up longer than five years, were still alive and disease-free at the last visit. One woman with follow-up of four years and nine months was still alive and the malignant melanoma in complete remission. Four patients (40%) died at 10 to 66 months after the initial diagnosis. One of these four patients died five years and six months after the first diagnosis because of a sudden heart incident, but the malignant melanoma was still in complete remission (patient 3). The other three patients died of widespread malignant melanoma and had either an unusual primary location of the malignant melanoma [suburethral (patient 4; died 36 months after first diagnosis) and cervico-vaginal region (patient 9; died 10 months after first diagnosis] or a wide-spreading malignant melanoma at time of first diagnosis (minor labia, stage IIIC; patient 7; died 20 months after first diagnosis). The outcome of the patient with malignant melanoma of the left ovary (patient 10) is not reported, her last contact with the doctors being 7 months after initial diagnosis.

Two of the seven women with vulvar melanoma developed local recurrences (28%, patients 4 and 5) and the patients with malignant melanoma, melanoma of the cervico-vaginal region and the wide-spread melanoma (patient 7) developed distant metastases (three in ten: 30%).

Discussion

The patients' median age was 53.3 years when the melanoma was first diagnosed (Table II), which confirms that vulvar melanoma occurs especially in postmenopausal women. For precise assessment of the prognosis of patients with cutaneous melanoma, the Clark's tumor invasion level (8) and Breslow's tumor thickness (9) classification were used (Table I). The prognosis of malignant melanoma is not only determined by

tumor size, but by tumor invasion. This is the reason for using the 2002 AJCC- or UICC-classification of malignant melanoma of the skin, which reveals tumor thickness and tumor invasion, and not the FIGO-classification of gynecological tumors. The correlation between progression-free survival and AJCC- or UICC-classification is higher than with FIGO-classification (5). The worse prognosis of vulvar melanomas (5-YSR 8-55, mean 36%) (10, 11) in comparison to malignant melanomas of the skin (10-YSR 75-80%) (12) is probably due to the morphological peculiarity of vulvar skin. The subepithelial tissues of the clitoris and labia (the lack of a defined papillar dermis) differ in morphology from the rest of the skin of the body (13). This is considered in the classification with a modified Clark system, the Chung's level (13, 14) (see Table II). The 5-YSR of primary malignant melanoma of the cervix uteri is only 14% (15) despite radical tumor surgery. The vaginal melanoma was a rare localization (16, 17) with a poor prognosis (patient 9, Figure 3). The worst prognosis belongs to malignant melanoma with primary localisation of the ovaries. These survival rates correlate with the outcome of our patients.

The recommended treatment for vulvar melanoma has been radical vulvectomy with bilateral inguino-femoral lymphadenectomy, regardless of lesion size, thickness, or depth of invasion (13, 18). However, most authors conclude that radical surgery does not improve the survival of patients with early disease when compared to local excision (19). However, such radical surgery, which is disfiguring and associated with severe morbidity (lymphedema, secondary disabilities), has not been shown to improve the survival of patients with vulvar malignant melanoma and, thus, has been questioned (3, 20, 21). But a small safety distance could be accompanied with a high risk of local progression. With regard to malignant cutaneous melanoma, the recommendations for treatment of vulvar melanomas with thin lesions (<1 mm) are wide local excision with a safety distance of 1 cm and, with deeper lesions, an *en bloc* resection with safety distance of 2-3 cm with regional (inguino-femoral) lymphadenectomy (22). In intraoperative examinations the pathologist cannot safely distinguish invasive melanoma from melanoma *in situ*. Thus, it is advisable that maculous-lentiginous hyperpigmentated areas should be excised.

Although the duration of follow-up was shorter in those patients who underwent less radical surgery, the absence of recurrence in patients with lesions of a depth of 2 mm or less suggest that patients with superficial lesions may be spared the morbidity of radical resection. Patients with vulvar melanoma lesions deeper than 4 mm have a high risk of distant metastases that is unlikely to be significantly decreased, even with the use of radical vulvectomy and bilateral inguinofemoral lymphadenectomy.

Cases with primary melanomas close to the introitus, urethra or cervico-vaginal regions may require a radical vulvectomy (patients 5-7), a resection of the urethra (patient 7) or colpohysterectomy (patient 4) to have a safety distance. We could confirm that, despite radical surgery in cases of progressive tumor (patients 4, 5, 7 and 9), no difference in recurrence-free survival time and no decrease of metastatic risk was reached (Table II).

The diagnostic and therapeutic meaning of elective groin lymph node dissection ("sentinel node biopsy") is being evaluated in various studies. In view of the relative ease and minimal trauma, sentinel node biopsy could be a routine procedure in malignant melanoma of the vulva and vagina (23) as it is already established in surgical treatments of breast cancer and cutaneous malignant melanoma.

Patients with local recurrence of vulvar melanoma should undergo local excision and, in addition or alternatively, local radiation. At clinical stage IV (distant metastases), single or small numbers of metastases should be removed completely if possible, but no general recommendation for palliative mono-chemotherapy (DTIC) or for combined immunochemotherapy (no study) exists. The follow-up evaluation should be intensive in the first five years, as this is the time period when 90% of the metastases appear. The German Dermatological Society has recommended a gynecological examination every 3 months for up to 3 to 5 years, including inspection of the skin and mucous, palpation and lymph node sonography (24). In cases of locoregional metastases, chest X-ray and abdominal sonography biannually is recommended. Patients with distant metastases should undergo CT scan (abdomen, chest) and cerebral MRI.

Conclusion

Vulvar melanoma is an aggressive neoplasm, with a poorer prognosis than cutaneous melanoma. An extremely bad prognosis independent of primary treatment is shown by malignant melanoma of the vagina, uterine cervix and ovary.

Melanoma of the vulva has traditionally been treated with radical vulvectomy and bilateral inguinofemoral lymphadenectomy, regardless of lesion size, thickness, or depth of invasion (18). The initial surgical modality did not influence long-term survival, but affected disease-free survival significantly. The increased local recurrence rate is not attributed to surgical failure, but to the inherent abnormality of melanocytes (25). That is why the treatment of invasive vulvar melanoma has become more individualized during the past decade. Superficial lesions may need only wide local excision, thus avoiding the morbidity associated with more radical operation (26).

References

1 Ariel IM: Malignant melanoma of the female genital system: a report of 48 patients and review of the literature. J Surg Oncol *16(4)*: 371-83, 1981.

2 Weinstock MA: 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*: 1225, 1994.
3 Tasseron EW, van der Esch EP, Hart AA, Brutel de la Riviere G and Aartsen EJ: A clinicopathological study of 30 melanomas of the vulva. Gynecol Oncol *46(2)*: 170-5, 1992.
4 Kuhn W: Malinge Melanome der Vulva. *In*: Manual Maligne Melanome, 6. Auflage 2001, Tumorzentrum München (Hrsg. Prof. Dr. med. Volkenandt, Prof. Dr. med. G. Plewig)
5 Phillips GL, Bundy BN, Okagaki T, Kucera PR and Stehman FB: Malignant melanoma of the vulva treated by radical hemivulvectomy. A prospective study of the Gynecologic Oncology Group. Cancer *73(10)*: 2626-32, 1994.
6 Kaufmann R, Proebstle T and Sherry W (1995): Malignes Melanom. *In*: Zeller WJ, zur Hausen H (Hrsg) Onkologie. Ecomed, Erlangen.
7 TNM Klassifikation maligner Tumoren. 6. Aufl. Springer, Berlin Heidelber New York.
8 Clark WH, From L, Bernardina EA and Mihm MC: The histogenesis and biologic behavior of primary human malignant melanomas of the skin. Cancer Res *29*: 705-26, 1969.
9 Breslow A: Thickness, cross-sectional areas, and depth of invasion in the prognosis of cutaneous melanoma. Ann Surg *172*: 902-6, 1970.
10 Woolcott RJ, Henry RJW and Houghton CR: Malignant melanoma of the vulva. Australian experience. J Reprod Med *33*: 699-702, 1988.
11 Look KY, Roth LM and Sutton GP: Vulvar melanoma reconsidered. Cancer *72*: 143-6, 1993.
12 Balch CM, Soong S-J, Shaw HM, Urist MM and McCarthy WH: An analysis of prognostic factors in 8500 patients with cutaneous melanoma. *In*: Balch CM, Houghton AN, Milton GW, Sober AJ and Soong S-J: Cutaneous Melanoma. 2nd edition. Philadelphia: J. B. Lipincott 165-87, 1992.
13 Chung AF, Woodruff JM and Lewis JL: Malignant melanoma of the vulva. Obstet Gynecol *45*: 638-46, 1975.
14 Piura B, Egan M, Lopes A and Monaghan JM: Malignant melanoma of the vulva: a clinicopathologic study of 18 cases. J Surg Oncol *50(4)*: 234-40, 1992.
15 Rogers RS *et al*: Mucosal, genital and unusal clinical variants of melanoma. Mayo Clin Proc *72*: 362-366, 1997.
16 Buchanan DJ *et al*: Primary vaginal melanoma: Thirteen-year disease-free survival after wide excision and review of recent literature. Am J Obstet Gynecol *178*: 1177, 1998.
17 Makovitzky J, Schmitz C, Vogt-Weber B and Nizze H: Primary malignant melanoma of the cervix uteri: a case report of a rare tumor. Anticancer Res *23*: 1063-8, 2003.
18 Phillips G: Current management of vulvar melanoma. Oncology *4*: 61-4, 1990.
19 Rose PG, Piver MS, Tsukada Y *et al*: Conservative therapy for melanoma of the vulva. Am J Obstet Gynecol *159*: 52-5, 1988.
20 Bradgate MG, Rollason TP, McConkey CC and Powell J: Malignant melanoma of the vulva: a clinicopathological study of 50 woman. Br J Obstet Gynecol *97*: 124-33, 1990.
21 Scheistroen M, Trope C, Kaern J, Abeler VM, Pettersen EO and Kristensen GB: Malignant melanoma of the vulva FIGO stage I: Evaluation of prognostic factors in 43 patients with emphasis on DNA nondiploidy and surgical treatment. Gynec Oncol *61(2)*: 253-8, 1996.
22 Nakagawa S, Koga K, Kugu K, Tsutsumi O and Taketani Y: The evaluation of the sentinel node successfully conducted in a case of malignant melanoma of the vagina. Gynecol Oncol *86(3)*: 387-9, 2002.
23 AWMF: Dt. Krebsgesellschaft, Deutsche Gesellschaft für Gynäkologie und Geburtshilfe, Deutsche Dermatologische Gesellschaft: Kurzgefasste Interdisziplinäre Leitlinien 2002, 3. Auflage 2002.
24 Orfanos CE, Jung HG, Rassner G, Wolff HH and Garbe C: Stellungnahme und Empfehlungen der Kommission Malignes Melanom der Deutschen Dermatologischen Gesellschaft zur Diagnostik, Behandlung und Nachsorge des Malignen Melanoms der Haut – Stand 1993/94 Hautarzt *45*: 285-91, 1994.
25 Lotem M, Anteby S, Peretz T, Ingber A Avinoach I and Prus D: Mucosal melanoma of the female genital tract is a multifocal disorder. Gynecol Oncol *88(1)*: 45-50, 2003.
26 Davidson T, Kissin M and Westbury G: Vulvo-vaginal melanoms: should radical surgery be abandoned? Br J Obstet Gynaecol *94*: 473-6, 1987.
27 Dunton CJ, Kautzky M and Hanau C: Malignant melanoma of the vulva: a review. Obstet Gynecol Survey *50(10)*: 739-46, 1995.

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