

Primary Malignant Vaginal Melanoma – Case Report and Review of the Literature

Primäres malignes Vaginalmelanom – Kasuistik und Literaturübersicht

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Key words

- vaginal tumour
- malignant melanoma
- multivisceral resection

Schlüsselwörter

- Vaginaltumor
- malignes Melanom
- multiviszerele Resektion

Abstract

With fewer than 250 cases published worldwide, primary vaginal melanoma is an extremely rare malignant entity which is mostly diagnosed in advanced stages. The estimated incidence of vaginal melanoma is 0.026/100 000 women per year. The poor prognosis for advanced tumour stages and different therapies used in very limited numbers of patients require precise preoperative staging and a planned interdisciplinary therapeutic approach.

Zusammenfassung

Das primäre Melanom der Vagina ist mit weltweit weniger als 250 publizierten Fällen ein äußerst seltenes Malignom und wird meist erst im fortgeschrittenen Stadium diagnostiziert. Die Inzidenz des vaginalen Melanoms wird auf 0,026/100 000 Frauen pro Jahr geschätzt. Die schlechte Prognose bei oftmals später Diagnosestellung sowie die verschiedenen Therapieansätze bei sehr geringen Fallzahlen erfordern ein exaktes präoperatives Staging und eine interdisziplinäre Therapieplanung.

History and Clinical Findings

A 44-year-old patient presented to the gynaecological outpatient clinic of our hospital due to dragging pain in the lower abdomen and vaginal bleeding after intercourse. The patient had undergone a vaginal hysterectomy for multiple uterine myomas 5 years previously. She had no history of other operations or secondary illnesses. She had not had regular gynaecological check-ups for the last 5 years. The subsequent clinical examination found a granulomatous tumour at the cranial end of the vagina.

computer tomography confirmed the findings and additionally demonstrated non-specific wall thickening in the sigma with a diameter of 23 × 15 mm. Thoracic X-ray and thoracic CT were unremarkable. Colonoscopy showed no pathological findings. Anorectal endosonography, however, demonstrated a tumour with a diameter of 4 cm, located directly ventral and adjacent to the wall of the rectum. Dermatological and ophthalmological examinations were unremarkable. For the final clinical diagnosis, full-body PET-CT was done and showed, in addition to the known malignant melanoma in the area at the end of the vagina (diameter in this case: 9 × 7.2 cm), bilateral pararectal metastases, left-sided para-iliac metastasis and para-aortal lymph node metastases. The interdisciplinary tumour board concluded that multivisceral resection was indicated.

Diagnostic Investigation

Biopsy samples indicated an infiltrating nodular melanoma. Further diagnostic investigations were done to determine whether it was a primary tumour or metastasis. Magnetic resonance tomography (MRT) showed a large nodular lesion at the stump of the vagina with a diameter of 5 × 4.5 × 9 cm in close proximity to the rectum, sigma and bladder (○ Fig. 1). Several regional lymph nodes were suspicious but there was no infiltration of the pelvic wall (○ Fig. 2). Additional

Therapy

A double-J catheter was inserted for urological management in preparation for the resection. Subsequently we performed an en bloc tumour resection with partial resection of the vagina, deep anterior resection of the sigma and rectum

received 13. 3. 2012

revised 2. 4. 2012

accepted 16. 4. 2012

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DOI <http://dx.doi.org/10.1055/s-0032-1315006>
Geburtsh Frauenheilk 2012; 72: 740–743 © Georg Thieme Verlag KG Stuttgart · New York · ISSN 0016-5751

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Fig. 1 Vaginal tumour at the cranial end of the vagina (MRT).

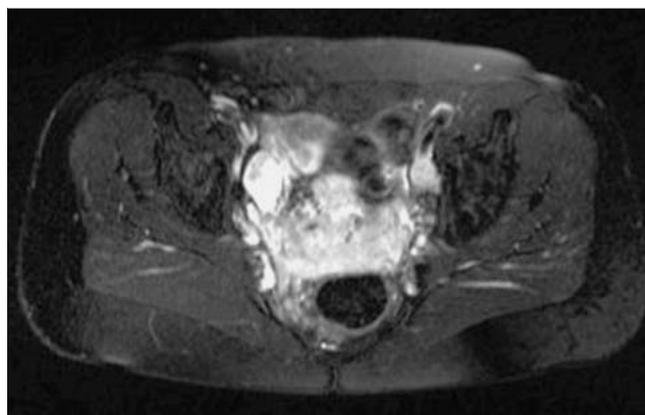


Fig. 2 Vaginal tumour with lymph node infiltration (MRT).

and partial resection of the bladder roof. In addition, left-sided adnexa extirpation was done, together with bilateral iliacal and para-aortal lymphadenectomy, appendectomy and creation of a protective cecostomy. The postoperative course was without complications and the patient was closely monitored. The final gynaecological examination showed a non-inflamed 6 cm vaginal remnant. The patient refused the recommended adjuvant palliative therapy with dacarbazine. The patient died only 4 months after the operation.

Histology

The final histological examination showed an ulcerated, nodular, vaginal melanoma measuring 85 mm at its widest point with a resection margin of at least 35 mm. Examination of the 22-cm re-

sected tissue adherent to the sigma and rectum showed tumour infiltration extending into the subserous adipose tissue with a still intact colonic mucosa. Metastases were noted in the left- and right-sided lymph nodes of the obturator fossa, in the left para-aortal lymph nodes and in the pericolic and perirectal lymph nodes. In addition, a small nodular melanoma infiltrating the tip of the mesenteriolum of the appendix was found.

Microscopically, the tumour consisted of giant, mainly epithelioid cells, distinct polymorphic hyperchromatic cells, numerous atypical mitoses and a few giant tumour nuclei. Dark brown pigmentation was noted in the tumour cells in some sections (Fig. 3 and 4). Using Chung et al.'s classification, the tumour was classified as level IV (invasion > 3 mm), pN1 (34/61) pM1 L1 V0 R0.

Discussion

As vaginal melanomas are very rare, most published studies consist of case reports, with only a few case series with limited numbers of patients. Most (90–95%) malignant vaginal lesions are

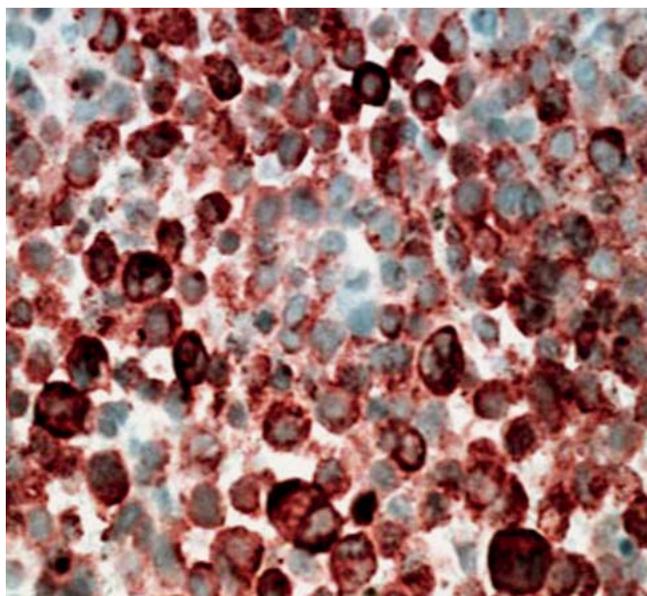


Fig. 3 Immunohistology using melanoma monoclonal antibody, clone HMB45.

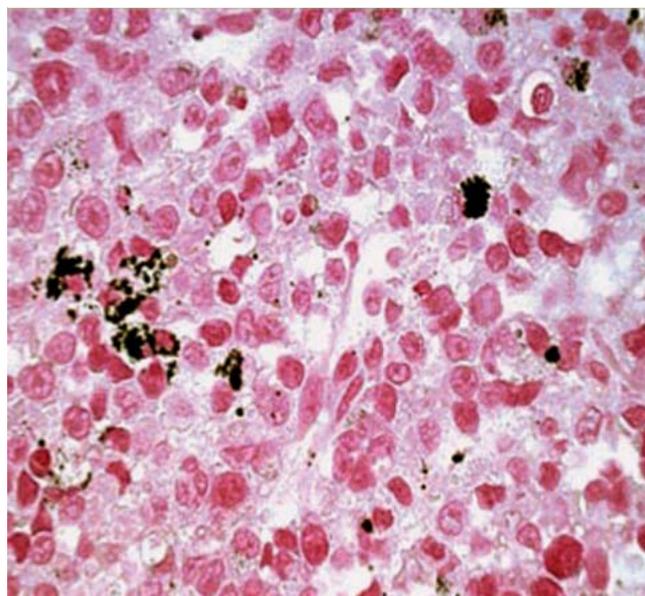


Fig. 4 Detection of tumour cells using Masson-Fontana stain.

squamous cell carcinomas. Between 5–10% are clear cell adenocarcinomas, and less than 3% are malignant melanomas. In women, 1.6% of melanomas are located in the genital tract [3,16], most of them around the vulva (70%), followed by vaginal (21%) and cervical (19%) locations. Vaginal melanoma metastases are even rarer with only 5 cases reported in the literature to date [5]. It has been suggested that vaginal melanomas arise from melanocytes, which are present in the vagina in around 3% of women [4]. Most vaginal melanomas are diagnosed in the 6th or 7th decade of life in postmenopausal women [5]. The most common symptom of vaginal melanoma is vaginal bleeding, followed by dyspareunia [11, 14]. The 5-year survival rate for this very aggressive, rapidly growing tumour is very poor, and is reported to be 0–25% irrespective of the chosen therapy [10,16]. Vaginal melanomas are usually only detected in advanced stages. Around 50% of patients already have lymph node metastasis at diagnosis, and 20% have distant metastasis [11].

In the study by Miner et al. (n=35), typical prognosis-relevant factors such as age, depth of invasion, pigmentation, ulceration and even adjuvant therapy were not found to be correlated with patient outcome. Even the microscopic assessment of positive and negative resection margins did not show any significant difference in recurrence-free survival times [7].

Meta-analyses by Reid et al. and Buchanan et al. also showed no correlation between the depth of tumour invasion and patient survival [2,12]. Tumour size is considered the only prognostic factor. Thus patients with a tumour size of < 3 cm survived significantly longer than patients with tumour sizes of > 3 cm (12 months vs. 41 months) [2,12]. Another series with 14 patients confirmed the correlation between tumour size and prognosis. Thus, 3 of 7 patients with a tumour < 3 cm survived more than 5 years while none of the patients with a tumour > 3 cm survived longer than 5 years [10]. The median survival rate after diagnosis is approximately 20 months [7].

Primary surgery is considered the method of choice and appears to be superior to primary radiation (25 vs. 13 months; p=0.039). After excluding very advanced, surgically non-resectable tumours, the survival benefit of surgery was even more pronounced (25 vs. 9 months; p=0.006) [9]. Nevertheless, due to the limited number of cases in the literature, there are no standard therapy recommendations. Various surgical procedures have been described, including “wide local excision”, colpectomy, radical resection with total abdominal hysterectomy, bilateral salpingo-oophorectomy, and evisceration. Only Van Nordstrand et al. reported in their study that radical surgery (total colpectomy or evisceration) offered a superior outcome compared to “wide local excision” or radiation with regard to the 2-year survival rate [15]. Other authors did not find any significant differences in survival rates with different surgical procedures [7,12]. Due to the poor prognosis of vaginal melanoma, the aim must be to obtain local excision with a tumour-free resection margin. Sentinel lymph node biopsy, an established method to determine the lymph node status of cutaneous melanomas, has been reported as an alternative to complete lymphadenectomy which is associated with a high morbidity [9] [8].

There are no consistent recommendations with regard to the benefits of adjuvant chemotherapy. Pegylated interferon alpha-2b can prolong survival times in patient with cutaneous melanoma and lymph node metastasis [1]. Analogous to cutaneous melanoma, dacarbazine or interleukin-2 are used in the palliative treatment of vaginal melanomas. The lack of studies means that it is not clear whether adjuvant chemotherapy prolongs recur-

rence-free survival in patients with vaginal melanoma. In contrast to malignant cutaneous melanomas, c-kit mutations have been detected immunohistologically in mucosal melanomas in approx. 20% of cases. There are several case reports of successful “off label” therapies using c-kit blockers (e.g. imatinib, sunitinib) when c-kit mutations were present [13].

Radiotherapy is usually used to treat primary non-resectable tumours and when resection margins are positive [6,7]. Therapy consists of intracavitary brachytherapy with 2–5 applications of caesium-137 (0.7–20 Gy per dose) [11]. Due to the limited data, which is exclusively retrospective, it is not possible to make any assertions regarding the value of adjuvant radiotherapy.

Conclusion

Vaginal melanoma is a very rare tumour entity with a poor prognosis. To date, tumour size is the only prognostic factor, and complete surgical resection is the therapy of choice. The data is insufficient to assess the value of sentinel lymph node biopsy and adjuvant radio- or chemotherapy. Because this tumour entity is almost asymptomatic, it demonstrates the importance of regular preventive medical check-ups as the prognosis is extremely poor once symptoms become manifest.

Acknowledgement

We would like to thank Prof. Dr. Eckhard Koepcke, Rostock, for his advice and Dr. Annegret Radtke for providing the histological images.

Conflict of Interest

None.

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