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

Primäres malignes Vaginalmelanom – Kasuistik und Literaturübersicht

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- vaginal tumour
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- Vaginaltumor
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Abstract
With fewer than 250 cases published worldwide, primary vaginal melanoma is an extremely rare malignantly 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 seltener Tumor der Vagina. Oft wird 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.

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 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. Coloscopy 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-iliacal metastasis and para-aortal lymph node metastases. The interdisciplinary tumour board concluded that multivisceral resection was indicated.

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...
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 resected 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...
squamous cell carcinomas. Between 5–10% are clear cell adeno-
carcinomas, 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 com-
mon symptom of vaginal melanoma is vaginal bleeding, followed
by dyspareunia [11,14]. The 5-year survival rate for this very ag-
gressive, 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 dif-
fERENCE 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 signif-
ificantly 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 tu-
mours, the survival benefit of surgery was even more pro-
nounced (25 vs. 9 months; p = 0.006) [9]. Nevertheless, due to
the limited number of cases in the literature, there are no stand-
thard 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 colpec-
tomy or evisceration) offered a superior outcome compared to
“wide local excision” or radiation with regard to the 2-year sur-
Vival rate [15]. Other authors did not find any significant differ-
ces 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 re-
ported 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 patients with cutaneous melano-
ma and lymph node metastasis [1]. Analogous to cutaneous mel-
anoma, dacarbazine or interleukin-2 are used in the palliative
therapy 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 con-
trast 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 tu-
mours and when resection margins are positive [6,7]. Therapy
consists of intracavitary brachytherapy with 2–5 applications of
cesium-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 prog-
Wnosis. To date, tumour size is the only prognostic factor, and com-
plete surgical resection is the therapy of choice. The data is insuf-
ficient 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.

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Conflict of Interest

None.

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