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CASE REPORT

Round Cell Vaginal Malignant Melanoma
A rare entity

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سرطان الخلية المهبلية المدوّرة الميلانيني الخبيث
حالة نادرة

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الملخص: يصاب الجلد غالبا بالسرطان الميلانيني الخبيث، ولكن في حالات نادرة قد يصيب هذا السرطان أنسجة أخرى. ويُعد سرطان الميلانين في المهبل حالة نادرة، كما أنّ نوع الخلايا المدوّرة غير مألوف. على الرغم من تشخيص هذه الحالة سريريا بوصفها لحيمة إحْليليَّة، لكنها شُخصت بواسطة فحص الأنسجة المرَضيَّة المناعية وفحص الصبغ المناعي على أنها سرطان الخلية المهبلية المدوّرة المصبوغة الميلانيني الخبيث. رفضت المريضة إجراء عملية جراحية جذرية وأعطيت دورة كاملة من العلاج الإشعاعي لكنها توفيت بعد ذلك بعام. يكون مآل سرطان الميلانين المهبلي الخبيث سيئا للغاية حتى عندما تكون الآفة موضعية حين اكتشافها، ويتراوح معدل البقاء على قيد الحياة لمدة خمس سنوات بين 10–20% ، ويتأثر المآل حسب حجم الورم، حيث يكون أكثر سوءا عندما يكون حجم الورم ≥3سم. ولا يتأثر معدل البقاء بالعمر وعدد الخلايا ومرحلة ومكان الآفة.

مفتاح الكلمات: ميلانوما، مهبل، خباثة، صبغة ماسون فونتانا، صبغة مناعية نسيجية كيميائية، أورام خلية مدورة، تقرير حالة، الهند.

ABSTRACT: Malignant melanoma is predominantly a skin disease but in rare instances it may occur at other sites. A vaginal melanoma is a rare clinical entity and the round cell type is an uncommon variant. Although the present case was clinically diagnosed as a urethral caruncle, on histopathological examination and immunostaining it was diagnosed as a round cell pigmented malignant melanoma. The patient refused radical surgery and was given a full course radiotherapy treatment but died a year later. Malignant vaginal melanoma carries a very poor prognosis even when lesion is localised at the time of presentation. The five-year survival rate ranges from 10–20% with the prognosis being influenced by tumour size. A tumour size ≥3cm has a poor prognosis. Age, mitotic count, stage, and location of the lesion do not influence survival rates.

Keywords: Melanoma; Vagina; Malignancy; Fontana-Masson stain; Immunohistochemical staining; Round cell tumors; Case report; India.

Malignant melanoma is predominantly a skin disease but in rare instances it may occur at other sites, including the mucous membrane of vulva, vagina, lips, throat, oesophagus, or perianal region, as well as the eye (uvea or retina). Malignant melanoma of the vagina is a rare entity, first reported by Poronas in 1887.[1] It accounts for 2.6–2.8% of all primary malignant tumors of the vagina and 0.4–0.8 % of all malignant melanomas in females.[2] Being of black race is considered as an adverse prognostic factor for melanoma; however, the relative risk in white and black women was found to be equal.[3]

Vaginal melanoma is a highly malignant disease due to extensive lymphatic invasion. Additionally, its propensity for haematogenous spread due to early metastases is very common;[2] hence, it is associated with a worse prognosis. Regardless of the therapy chosen, results of treatment have been poor, with reported five-year survival rates ranging from 10–20%.[4,5]

We report the case of a malignant melanoma having an uncommon morphology arising at the vaginal introitus. The morphological details and salient features of the case are discussed.

Case Report

A 66-year-old postmenopausal female presented to the outpatient department with complaints of a

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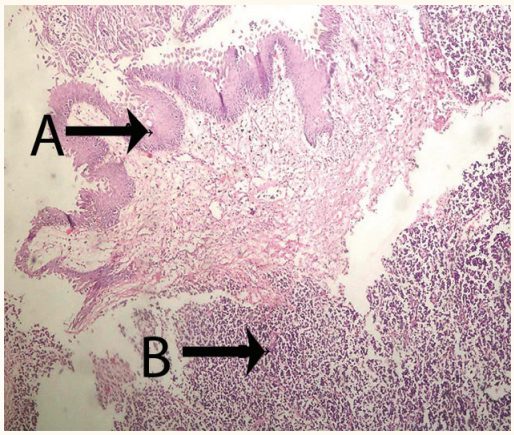

Figure 1: A photomicrograph showing ulcerated hyperplastic squamous epithelium (**A**). The deeper tissue shows a very infiltrative cellular tumour (**B**) with a diffuse pattern and a few clusters in some places (haematoxylin & eosin stain × 100).

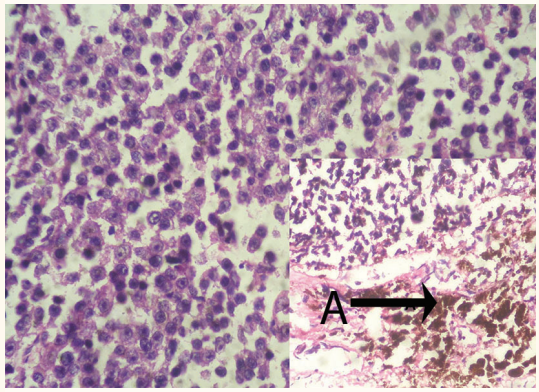

Figure 2: A photomicrograph showing tumour cells which are mostly tiny with a small amount of cytoplasm and rounded nuclei with a prominent nucleolus. The inset shows tumour cells containing dark brown pigment in the cytoplasm (**A**) (haematoxylin & eosin stain × 400; Inset × 200).

growth near the vaginal introitus and blood-stained discharge *per vaginum* for the previous 2 months. There were no urinary symptoms. A vaginal hysterectomy had been performed 6 years before for a third degree uterovaginal prolapse. On general examination, the vital signs were within normal limits and a systemic examination did not reveal any significant abnormal findings.

On local examination, a dark brown nodular swelling measuring 30 x 25 mm was noted in between the urethra and the vaginal introitus. The surface of the tumour was ulcerated and bled on touch. On cystoscopic examination, the bladder was normal but the posterior wall of the urethra was stretched; however, no ulceration was seen. On *per speculum* examination, the anterior vaginal wall showed hyperpigmentation. On the basis of a clinical examination, the provisional diagnosis was an urethral caruncle. An excision biopsy showed a firm, greyish-brown soft tissue piece measuring 30 x 25 x 15 mm. The cut surface showed dark brown areas towards the periphery. The depth of tumour invasion was >20 mm. Microscopic examination revealed an infiltrative cellular malignant tumour showing a diffuse pattern. The tumour cells were small and round with a small amount of pinkish cytoplasm, and rounded rather than uniform nuclei. Many nuclei showed prominent and large nucleoli. Mitotic figures were frequent. Occasionally, the cells and nuclei were oval and spindle shaped. A few multinucleate cells were also seen. In many places, the cells contained dark brown melanin pigment in the cytoplasm, which was confirmed histochemically by a Fontana-Masson ammoniated-silver nitrate stain. The tumour cells were positive for S100 and HMB-45 immunostaining. The overlying mucosa was ulcerated and infiltrated by tumour cells. Lymphovascular invasion was also seen. A diagnosis of malignant melanoma was made.

The patient refused radical surgical treatment; hence, radiotherapy was advised. The patient was referred to a radiotherapy centre where she received a full course of treatment. She lived for about one year but then died suddenly at home with complaints of sudden abdominal pain, possibly a complication of widespread metastatic disease.

Discussion

The present case is the first vaginal melanoma detected at our institution in 10 years. During this period, 6,080 malignancies were reported out of which 15 (0.24%) were malignant melanomas. In a comparative review constituting 84,836 cases of malignant melanomas occurring between 1985 and 1994 from the National Cancer Data Base at Memorial Sloan Kettering Cancer Hospital Centre in New York, 91.2% were cutaneous, 5.2% were ocular, and 1.3% were mucosal malignancies, while 2.2% had unknown primaries. It also revealed that in women, only 1.6% of melanomas were genital and only 21% of these, involved the vagina. The common presenting symptoms in 35 women treated for vaginal melanomas were vaginal bleeding in

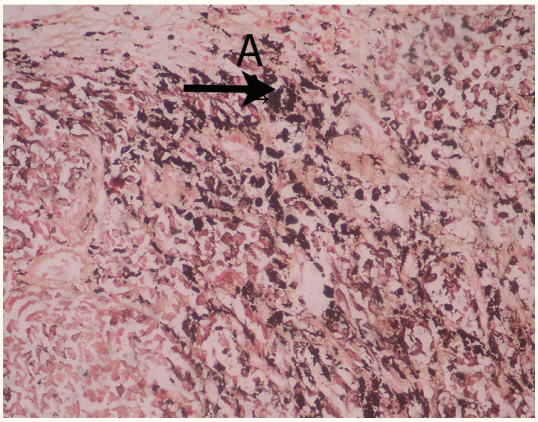

Figure 3: A photomicrograph showing melanin pigment in tumour cells (**A**). (Fontana-Masson silver stain × 200).

23 patients (66%), and pain in 1 patient (3%); the remaining 11 patients (31%) had no symptoms, with the disease being discovered during routine screening examinations.[4]

Our patient complained of a mass at the vaginal introitus and blood-stained discharge. The tumour was dark brown and ulcerated at the surface. As mentioned above, it was clinically misdiagnosed as an urethral caruncle.[6] Also, because of the epithelial ulceration, it may have been mistaken for a squamous cell carcinoma.[1] Although it was predominantly a small round cell tumour having a diffuse arrangement, the diagnosis was not a problem because of the presence of melanin pigment in the cytoplasm of the tumour cells. However, Scambia G. *et al.* reported that 6% of vaginal melanomas were amelanotic.[7] If this small round cell melanoma had been amelanotic, the differential diagnosis could have included lymphoma, peripheral neuroectodermal tumour (PNET), Merkel cell tumour, and rhabdomyosarcoma.[7] Amelanotic melanomas would require the help of immunohistochemical stains such as S100, HMB-45, vimentin, cytokeratin, leucocyte common antigen (LCA) and neuron-specific enolase (NSE) for diagnosis and to exclude other tumours. If the amelanotic melanoma had been a spindle-cell type then it would have had to be differentiated from malignant fibrohistiocytoma (MFH), a malignant peripheral nerve sheath tumour, and hemangiosarcoma.[8] Other differential diagnoses which could have been considered were metastatic deposits of poorly differentiated malignancy, vaginal hemangioma, or endometriosis.

Malignant vaginal melanoma carries a very poor prognosis even when the lesion is localised at the time of presentation. The five-year survival rate ranges from 10–20%, with prognosis influenced by tumour size. A tumour measuring ≥3 cm has a poor prognosis. Patient age, mitotic count, tumour stage, and lesion location do not influence survival.[9]

The disease is associated with a high risk of local recurrence, distant metastasis, and poor clinical outcome. A retrospective review of 37 cases of vaginal melanoma showed a survival rate of 19.1 months for Stage I disease. Other studies revealed that tumour size and nodal status were significant prognostic factors, whereas, tumour thickness was a weak predictor of survival. Several

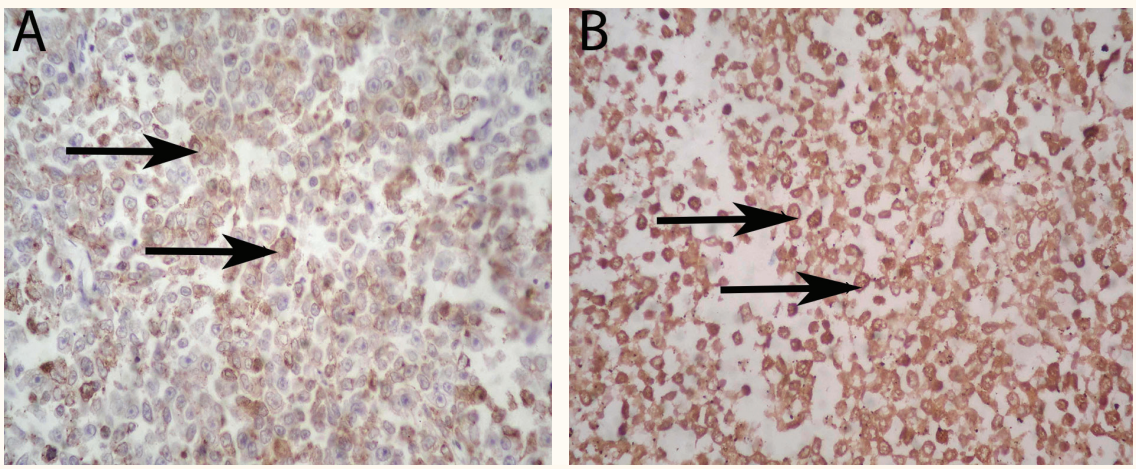

Figure 4: (**A**) Photomicrograph showing tumour cells' positivity for S-100 protein (polyclonal anti-S-100 immunostain using 3-Amino-9-Ethyl-l-Carbazole [AEC] chromogen, counterstain with Harris haematoxylin x 400). (**B**) Photomicrograph showing tumor cells positive for HMB-45. (HMB-45 antibody using 3,3'-Diaminobenzidine [DAB] chromogen, counter stain with Harris haematoxylin stain x 400).

types of treatment can be administered but none of them is considered a standard approach. There is no difference in survival between patients who have radical surgical procedures and those who have more conservative surgical procedures. Immunotherapy with interferon-alpha (IFN-alpha) has been demonstrated to reduce recurrence rates and offers a better chance of survival.[10]

Treatment modalities include surgical removal/extirpation, irradiation, and chemotherapy either singly or in combination with other treatments. In the present case, excision was done. Wide local excision with pelvic node dissection was advised but the patient refused this surgery; hence, radiotherapy was advised. Follow-up treatment was not available at our institution.

Conclusion

Vaginal melanoma is a rare clinical entity and the round cell type is an uncommon variant. Although the present case was clinically diagnosed as an urethral caruncle, histologically it was diagnosed as a round cell pigmented malignant melanoma. Immunostaining assisted in confirming the diagnosis.

References

1. Manlucu ED, Dickson H, Mahood L, Nath ME. Final diagnosis: Primary malignant melanoma of the vagina. From: path.upmc.edu/cases/case167/dx.html. Accessed: May 2012.
2. Park BJ, Yoon JH, Lee HY, Lee SH, Han KT, Ryu KS, et al. A case of primary malignant melanoma of the vagina. Korean J Obstet Gynecol 2003; 46:667–71.
3. 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 2004; 171:1225–30.
4. Miner TJ, Delgado R, Zeisler J, Busam K, Alektiar K, Barakat R, et al. Primary vaginal melanoma: A critical analysis of therapy. Ann Surg Oncol 2004; 11:34–9.
5. Ragnarsson-Olding B, Johansson H, Rutqvist LE, Ringborg U. Malignant melanoma of the vulva and vagina. Trends in incidence, age distribution, and long-term survival among 245 consecutive cases in Sweden, 1960–1984. Cancer 1993; 71:1893–7.
6. Ali S, Siddiqui E, Ojha H, Koneru S, Hock L. Malignant melanoma of the female urethra. From: www.ispub.com/ostia/index.php?xmlFilePath=journals/iju/vol2n1/melanoma.xml. Accessed: May 2012.
7. Scambia G, Benedetti Panici P, Baiocchi G, Coli A, Ferrone S, Natali PG, et al. A primary amelanotic melanoma of the vagina diagnosed by immunocytochemistry. Int J Gynaecol Obstet 1989; 29:159–64.
8. Şahande E, Dilek SA, Handan A, Abdullah T, Gulhan A. Amelanotic malignant melanoma of the vagina. Turk J Canc 2000; 30:126–30.
9. Chung A, Casey M, Flannery J, Woodruff JM, Lewis JL Jr., et al. Malignant melanoma of the vagina-report of 19 cases. Obstet Gynecol 1980; 55:720.
10. Lin LT, Liu CB, Chen SN, Chiang AJ, Liou WS, Yu KJ. Primary malignant melanoma of the vagina with repeated local recurrences and brain metastasis. J Chin Med Assoc 2011; 74:376–9.