CASE REPORT

Malignant melanoma of cervix

Mayank Gupta

Department of General Pathology, Christian Medical College, Vellore, Tamil Nadu, India

Correspondence to

Dr Mayank Gupta,
gupta.mayank103@gmail.com

Accepted 14 November 2016

SUMMARY

A 68-year-old woman presented with symptoms of bleeding per vaginum. On examination, a growth was seen in the cervix, clinically considered to be squamous cell carcinoma. The growth was confined to the cervix and did not involve the parametria. However, on biopsy it was diagnosed as malignant melanoma. She underwent surgery elsewhere and was advised chemotherapy as these tumours are aggressive; however, she refused chemotherapy. She has been on regular follow-up and has an ongoing survival and disease-free period of more than 5 years. Primary cervical malignant melanomas are very rare as compared with vulval and vaginal counterparts and should be considered in the histological differential diagnosis of poorly differentiated malignant neoplasms involving cervix. Moreover, it is important to rule out metastasis from common primary sites such as skin, oesophagus, uveal tract and anorectal region before considering diagnosis of primary cervical melanoma.

BACKGROUND

Malignant melanoma involving the female genital tract accounts for 3% of all melanomas in women.

Vulva is the most common site of melanoma in the female genital tract and comprises of 5–10% of all vulval cancer. Vaginal melanoma accounts for <0.3% cases.¹ Primary cervical melanomas, as compared with vulval and vaginal counterparts, are very rare and few cases have been reported previously.^{2–7} We report an interesting case of primary malignant melanoma of cervix which has not recurred or spread for more than 5 years after surgery without undergoing chemotherapy. Histological differential diagnosis and criteria for diagnosing primary cervical melanoma are discussed.

CASE PRESENTATION

68-year-old postmenopausal woman presented with symptoms of bleeding per vaginum. On examination, vulva and vagina were normal. A non-pigmented polypoid growth was seen in the posterior lip of the cervix, clinically considered to be Federation of International Gynecologists and Obstetricians (FIGO) stage-Ib2 squamous cell carcinoma. However, histopathological examination showed a tumour arranged in sheets composed of round to polygonal cells displaying markedly pleomorphic vesicular nuclei, coarse chromatin, prominent nucleoli and eosinophilic cytoplasm (figure 1A–C). Tumour cells with bizarre nuclei were also present and mitotic figures were seen (figure 1D). Overlying mature ectocervical epithelium was evident on one aspect with junctional activity

(figure 2A). Melanin pigment was not evident. On immunohistochemistry (IHC), tumour cells were negative for cytokeratin (figure 2B) and diffusely positive for melan-A (figure 2C) and Human Melanoma Black 45 (HMB-45) (figure 2D). The tumour was negative for CD20, CD3, CD30, Leukocyte Common Antigen (LCA), synaptophysin and chromogranin. Thus, the case was signed out as malignant melanoma involving the cervix. A complete dermatological, ophthalmological and gastroenterological workup was non-contributory and the tumour was considered as primary tumour of the cervix. MRI of pelvis and abdomen revealed a tumour in the posterior wall of cervix with no involvement of bilateral parametria. Enlarged lymph nodes were seen along the right common iliac and internal iliac vessels (figure 3). Uterus, bilateral adnexae, urinary bladder and all intra-abdominal organs were normal. CT of the thorax and MRI of the brain were unremarkable. Positron emission tomography scan showed an intense uptake in the cervical growth without abnormal uptake in bilateral parametria, lymph nodes along right common iliac and internal iliac vessels or at any other sites in the body. Radical hysterectomy, bilateral salpingo-oophorectomy and lymphadenectomy with subsequent chemotherapy (five cycles of doxorubicin and ifosfamide) were advised. The patient underwent surgery at a different hospital and the specimen was reported as malignant melanoma confined to cervix (pT1b2) with no lymphovascular invasion. Uterus, bilateral adnexae and lymph nodes were free of tumour, as per the available histopathology report. As the surgery was performed in a different hospital, the author consulted the surgical team of that hospital and discussed the case. The surgeon informed that the growth was confined to the cervix. Uterus, bilateral adnexae, bilateral parametria, peritoneum, omentum, abdominal organs and rest of the pelvic organs were unremarkable. Few lymph nodes along the iliac vessels were slightly enlarged. Initially, the slides and blocks of the specimen were not available for review; later the slides and blocks were reviewed and the findings were consistent with the available histopathology report. The patient has been on regular follow-up (regular clinical examination and radiological investigations) and has disease-free survival for more than 5 years. She refused chemotherapy as she had observed serious side effects of chemotherapeutic drugs in one of her close friend who had breast cancer.

DISCUSSION

Primary malignant melanoma is among the least common of the malignant tumours that arise in the

CrossMark

To cite: Gupta M. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2016-217970

Figure 1 H&E stain: (A) tumour arranged in sheets, 4× magnification; (B) tumour, 10× magnification; (C) pleomorphic tumour cells with prominent nucleoli, 20× magnification; (D) tumour cell with bizarre nuclei in centre, 40× magnification.

cervix. All cases have been reported in adults and about one-half of the patients presented with the tumour extending beyond cervix.⁸ Abnormal vaginal bleeding has been the common presenting symptom and these tumours are grossly seen as fungating or polypoid, pigmented masses.¹ However, they may be non-pigmented and resemble usual cervical squamous cell carcinoma, similar to our case. As no pigment was evident, poorly differentiated squamous cell carcinoma (PDSCC), large cell neuroendocrine carcinoma (LCNC) and high-grade non-Hodgkin's lymphoma were the possible differential diagnosis on histology. PDSCC can resemble melanoma on routine histology as tumour cells in PDSCC may be arranged in sheets. Moreover, intercellular bridges and keratinisation are not seen in PDSCC. Presence of overlying ectocervical epithelium displaying full thickness dysplasia along with infiltrating tumour suggests a diagnosis of PDSCC but the ectocervical epithelium may or may not be seen in the biopsy. In our case, ectocervical epithelium was seen on one aspect with no features of dysplasia. Although junctional activity was present, IHC was necessary for exact characterisation. Diffuse expression of

Figure 2 (A) Tumour (red star) with overlying ectocervical epithelium displaying junctional activity (black arrow), H&E stain, 10× magnification; (B) tumour cells are negative for cytokeratin; however, overlying epithelium is positive, IHC, 10× magnification; (C) tumour cells diffusely positive for melan-A, IHC, 10× magnification; (D) tumour cells diffusely positive for HMB-45, IHC, 10× magnification. IHC, immunohistochemistry.

Figure 3 MRI of pelvis shows well-defined lobulated lesion involving posterior wall of cervix, reaching up to the body of uterus. The lesion appears mildly hyperintense on T2 and Short tau (T1) inversion recovery images. The lesion measures 55×44 mm. Fat planes with adjacent structure are maintained (A, white arrow). Multiple enlarged lymph nodes along right common iliac and internal iliac vessels (B, yellow arrow).

HMB-45 and melan-A along with negative expression of pancytokeratin in tumour cells confirmed the diagnosis of melanoma, ruling out PDSCC. LCNC was ruled out, as tumour cells were negative for synaptophysin and chromogranin. Negative expression of CD20, CD3, CD30 and LCA ruled out high-grade non-Hodgkin's lymphoma.

Cervical melanomas are believed to originate from melanocytic cells present in the uterine cervix.² The presence of these cells in the cervix has been previously confirmed by Osamura *et al.*⁹ Apart from melanoma, melanocytic cells in cervix can give rise to blue nevus and benign lentiginos.² Primary cervical melanomas are very rare and before considering this diagnosis, it is important to rule out metastasis to cervix from common primary sites such as skin, uveal tract, oesophagus and anorectal region.² Also in the absence of junctional activity on histology, the possibility of metastasis should be considered.¹

Following criteria were suggested by Morris and Taylor for the diagnosis of primary cervical melanoma: (1) absence of melanoma elsewhere in the body; (2) presence of junctional change in the cervix; (3) presence of melanin pigment in the normal cervical epithelium and (4) metastasis according to the pattern of cervical carcinoma. Out of the four criteria only the first two criteria were present in our case.¹⁰

As very few cases of cervical melanoma have been reported, standard consensus for its treatment is not available. Radical hysterectomy along with regional lymphadenectomy and/or vaginectomy is usually performed.¹¹ Chemotherapy protocols which are recommended for skin melanoma are prescribed for advanced and recurrent cervical malignant melanoma.¹² These tumours are resistant to radiotherapy (RT); however, RT is recommended for advanced disease, parametrial involvement, pelvic lymph node involvement, palliative treatment of recurrence, unsatisfactory surgical margins and residual tumour.¹³

Cervical melanoma has a very poor prognosis with only 25% survival rate for cases with even stage-I disease.^{3 8} The 5-year survival for stage I, stage II and stage III–IV is 18.8%, 11.1% and 0%, respectively.⁸ As far as our case is concerned, although the tumour was confined to the cervix with no lymphovascular invasion and no involvement of uterus, adnexae, parametria and lymph nodes, chemotherapy was advised considering the aggressive nature of the tumour. However, the patient did not undergo chemotherapy and fortunately her follow-up has been unremarkable for more than 5 years. Previously, one case of cervical melanoma (FIGO stage IIa1) having more than 3 years of survival has been reported and in that case also no chemotherapy was given.¹³

Thus, this case highlights criteria, histopathological features, histological differential diagnosis and fortunately unusual 5-year disease-free survival of a rare and aggressive primary cervical malignancy.

Learning points

- It is important to rule out metastasis to cervix from common primary sites such as skin, uveal tract, oesophagus and anorectal region before considering diagnosis of a rare primary cervical malignant melanoma.
- There are four criteria for diagnosing primary cervical malignant melanoma: (1) absence of melanoma elsewhere in the body, (2) presence of junctional change in the ectocervix, (3) presence of melanin pigment in the normal cervical epithelium and (4) metastasis according to the pattern of cervical carcinoma.
- Histological differential diagnosis of cervical melanoma includes poorly differentiated squamous cell carcinoma, large cell neuroendocrine carcinoma and a high-grade non-Hodgkin's lymphoma, which can be excluded by immunohistochemistry.
- Primary cervical melanoma has a very poor prognosis; however, some of these tumours may not have an adverse outcome in the absence of local spread, lymphovascular invasion and metastasis.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Nucci MR, Carcangiu ML, Ferry JA. Melanocytic tumors. In: Kurman RJ, Carcangiu ML, Herrington S, Young RH, eds. *World Health Organisation classification of tumours of female reproductive organs*. 4th edn. Lyon: IARC, 2014:204.
- 2 Liu Z, Wang H, Zhang X, et al. Primary malignant melanoma of the cervix: a case report. *Oncol Lett* 2014;8:2661–3.
- 3 Clark KC, Butz WR, Hapke MR. Primary malignant melanoma of the uterine cervix: case report with world literature review. *Int J Gynecol Pathol* 1999;18:265–73.
- 4 Pusceddu S, Bajetta E, Buzzoni R, et al. Primary uterine cervix melanoma resembling malignant peripheral nerve sheath tumor: a case report. *Int J Gynecol Pathol* 2008;27:596–600.
- 5 Santoso JT, Kucera PR, Ray J. Primary malignant melanoma of the uterine cervix: two case reports and a century's review. *Obstet Gynecol Surv* 1990;45:733–40.
- 6 Cantuaria G, Angioli R, Nahmias J, et al. Primary malignant melanoma of the uterine cervix: case report and review of the literature. *Gynecol Oncol* 1999;75:170–4.
- 7 Kristiansen SB, Anderson R, Cohen DM. Primary malignant melanoma of the cervix and review of the literature. *Gynecol Oncol* 1992;47:398–403.
- 8 Pusceddu S, Bajetta E, Carcangiu ML, et al. A literature overview of primary cervical malignant melanoma: an exceedingly rare cancer. *Crit Rev Oncol Hematol* 2012;81:185–95.
- 9 Osamura RY, Watanabe K, Oh M. Melanin-containing cells in the uterine cervix: histochemical and electron-microscopic studies of two cases. *Am J Clin Pathol* 1980;74:239–42.
- 10 Morris HJ, Taylor HB. Melanomas of the vagina. *Am J Clin Pathol* 1966;46:420–6.
- 11 Mousavi AS, Fakor F, Nazari Z, et al. Primary malignant melanoma of the uterine cervix: case report and review of the literature. *J Low Genit Tract Dis* 2006;10:258–63.
- 12 Piura B. Management of primary melanoma of the female urogenital tract. *Lancet Oncol* 2008;9:973–81.
- 13 Myriokefalitaki E, Babbal B, Smith M, et al. Primary malignant melanoma of uterine cervix FIGO IIa1: a case report with 40 months ongoing survival and literature review. *Gynecol Oncol Case Rep* 2013;5:52–4.

Copyright 2016 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow