Primary malignant melanoma of uterine cervix in a young female - Report of a rare case

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Abstract
Malignant melanoma (MM) of gynaecological tract represents about 2% cases of all melanomas. Most of the gynaecologic tract melanomas are reported in vulva and vagina. Malignant melanoma of uterine cervix is extremely rare and about 78 cases are mentioned in literature. Primary Malignant melanoma of cervix usually occurs in sixth decade of life and has poor prognosis. We report a case of primary malignant melanoma diagnosed in a young woman of 28 years. Initial diagnosis of malignant melanoma was made on the basis of morphological features revealed in the cervical biopsy obtained from a polypoidal cervical growth. Cervix as the primary site of occurrence of malignant melanoma was confirmed after extensive clinical and radiological evaluation. Radical hysterectomy was the initial treatment. Histopathogical diagnosis was substantiated in this patient with the help of immunohistochemical markers.

Keywords: Primary malignant melanoma, Cervix, Diagnosis, Histopathological features.

Introduction

Less than 2% cases of malignant melanoma (MM) occur in female genital tract and majority of cases occur in vulva or vagina.[1] Cervix is the least common site in female genital tract to harbour malignant melanoma. Primary malignant melanoma of uterine cervix is thus a rare disease that chiefly occurs in post menopausal women and has poor prognosis.[2] Early diagnosis of cervical melanoma and its differentiation from squamous cell carcinoma of cervix is essential as the therapeutic approach is different for the two neoplasms.[3] MM especially amelanotic should be suspected in poorly differentiated cervical tumours and confirmed with the help of Immunohistochemical markers. A case of primary MM of cervix diagnosed in a young premenopausal female from the region is reported.

Case: 28 years old female presented to outpatient clinic of Gynaecology and Obstetrics department with the complaints of blackish foul smelling discharge and bleeding per vagina since last six months. She did not have abdominal pain or any menstrual complaint. She was detected to be hypothyroid four years back and is taking regular Thyroxin supplement. The young woman was married at 21 years of age. She had one abortion and two LSCS deliveries. Her last child birth occurred two years back.

On general examination the patient appeared to be thin built, conscious with stable vitals. Her systemic examination did not reveal any abnormality. On per speculum examination a polypoidal growth of size about 3x2cm was seen arising from anterior lip of cervix from 9 o'clock to 2 o'clock position with no involvement of the vagina or vulva. The growth was bluish black in colour, with irregular external surface and bled on touch. Cervical biopsy was taken and sent for histopathological examination.

H and E stained sections showed focally ulcerated cervical stratified squamous epithelium and presence of a few pigment containing tumour cells in the upper layers of cervical epithelium. A pigmented tumour mass was seen in subepithelial location (Fig. 1). Tumour cells were polygonal, round and spindle shaped, with moderate eosinophilic cytoplasm, vesicular nuclei and prominent nucleoli. There was heavy intracytoplasmic coarse brown black pigment deposition that obscured the cellular details at places. Infiltration of lymphocytes, plasma cells and melanophages was seen in the adjacent area (Fig. 1). Special stain Masson Fontana confirmed the pigment in the tumour cells to be melanin. With these characteristic morphological features, diagnosis of malignant melanoma was given. Complete clinical, radiological and ocular examination of the patient was advised to rule out extension from nearby sites or metastatic deposits from distant sites.

There was no pigmented lesion anywhere on sun exposed body parts. No cutaneous or mucosal pigmented lesion was found on thorough clinical examination of the patient. Her proctosigmoidoscopy, cystoscopy, chest radiograph and fundoscopy examination were normal without evidence of any pigmented lesion. An abdominal ultrasound, performed preoperatively, showed normal liver, spleen, kidneys, bowel, and retroperitoneal structures.

Pre operative MRI revealed ill defined lesion of size 3.6 x2.7cm limited to anterior lip of cervix. The fat planes were maintained with no parametrial involvement. Urinary bladder and rectum were free.

The patient underwent modified radical hysterectomy on the basis of biopsy diagnosis. As the vagina and vulva were not seen to be involved on

examination or MRI, they were not included in the surgical intervention. The specimen consisted of uterus with cervix, left and right fallopian tubes and left ovary accompanied by separately removed right and left internal iliac and right external iliac group of lymph nodes Gross examination of hysterectomy specimen revealed a blue-black irregular, firm growth of size 3x2cm limited to the cervix (Fig 2,3). Extensive sectioning was done. Sections from the ectocervix showed melanocytic cell proliferation in the squamous epithelium and basal layer. Nodular aggregates of pigmented tumour cells were also seen beneath the cervical epithelium in subepithelial stroma. Sections from the tumour showed similar cellular features of MM as seen in biopsy. Lymphovascular invasion was not present. The final diagnosis was primary malignant melanoma of cervix, FIGO stage III-B (clinically < 4cm pT1b1N1).

Sections from endocervix (Fig. 4), endometrium, myometrium did not show presence of tumour. Both fallopian tubes and left ovary was free of tumour. One out of two left internal iliac lymph nodes showed evidence of tumour metastasis (Fig. 5). IHC study was performed that showed positivity for S 100, HMB 45 (Fig. 4, inset) that confirmed the diagnosis of MM.

Post operative recovery of the patient was uneventful. Patient received 25 fractions of External beam Radiotherapy and is under regular clinical follow up. Poor prognosis due to her advanced disease is explained to the close relatives.

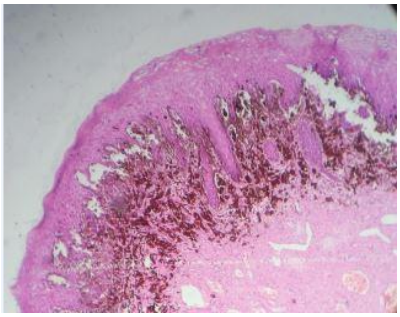

Fig. 1: Tissue section – proliferation of melanin containing tumor cells in the cervical epithelium and subepithelialstroma (H & E,x100)

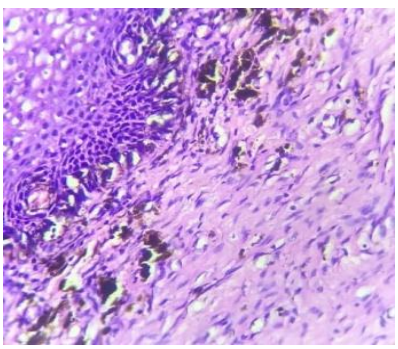

Fig. 2: Tissue section-Pleomorphic tumor cells with intracellular melanin (H&E,x400)

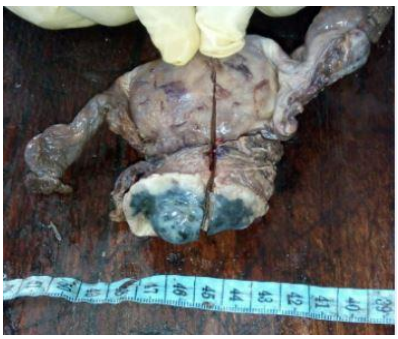

Fig. 3: Specimen of uterus showing blue-black growth at cervical os

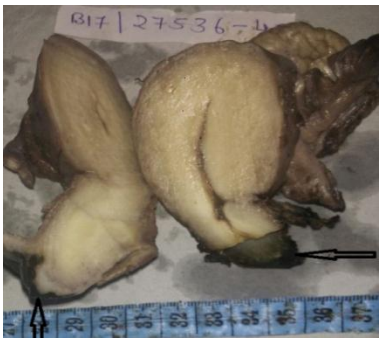

Fig. 4: Bisected uterus showing black coloured growth at anterior lip of cervix

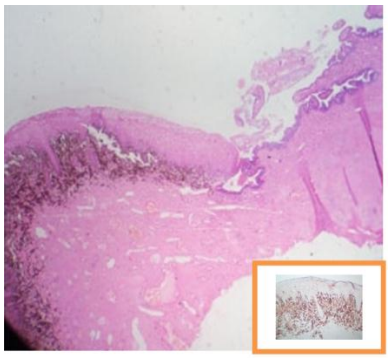

Fig. 5: Tissue section- melanoma cells limited to ectocervix and uninvolved endocervix (H&E, ×100) Inset- strong reactivity for HMB 45 in tumor cells (HMB 45, 400x)

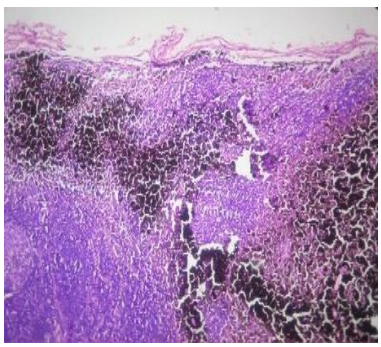

Fig. 6: Lymph node showing metastatic deposits of melanoma cells with abundant melanin pigment (H&E, ×100)

Discussion

Malignant melanoma (MM) is a tumour of melanocytic cells, that arises in skin and mucous membranes. The tumour can be pigmented or nonpigmented i.e. amelnotic. Mucosal MMs account for 0.03% of all cancers.[4] They are known to occur in oral and anogenital mucosal surfaces, esophagus, meninges and eye.[5] In female genital tract, occurrence of MMs is more frequent in vulva or vagina than in cervix.

Benign as well as malignant melanocytic lesios can arise in the cervical epithelium. Occurrence of MM in cervix was accepted after demonstration of melanocytes in cervix by cid[6] for the first time in 1959. With about 78 cases of primary malignant melanoma described in the literature, etio-pathogenesis of cervical MM is not studied in details and specific risk factors like those for cutaneous melanomas, are not identified for cervical melanoma.[7]

Diagnosis of primary MM of cervix is considered when most of the criteria given by Morris and Tailor[8] are fulfilled. The Clinical and histopathological diagnostic criteria include-

1. The presence of melanin in the normal cervical epithelium,
2. The absence of melanoma elsewhere in the body,
3. Demonstration of junctional changes in the cervix and
4. Metastases according to the pattern of cervical carcinoma

CT or MRI can help to determine the disease extension and MRI can distinguish melanoma from other tumours by a distinct pattern due to presence of melanin in the tumor.[4,9]

MM of uterine cervix usually occurs in postmenopausal women, between 60 to 70 years of age.[10] Occurrence in premenopausal young woman like our patient adds to rarity of the case.

Presentation and spread of MM is reported to be similar to that for carcinoma cervix. Clinically patients present with vaginal bleeding or discharge that may be blackish in colour. Abdominal pain, postcoital bleeding, dyspareunia are the other symptoms.[11]

Melanoma may be suspected on visualisation of a blue black growth by the alert gynecologist during per speculum examination. Morphological diagnosis of melanoma is made on the basis of characteristic gross and microscopic features with presence of brown black intra and extracellular melanin pigment. Microscopic identification of melanoma is based on presence of junctional activity i.e. intraepithelial component, presence of melanin pigment in the tumour cells and macrophages, cytological aytpia, invasion of the surrounding tissues and collection of lymphocytes at the tumour periphery. The cells may be spindle, epitheloid or small. Prominent nucleoli are seen in at least some nuclei.[12] With presence of coarse granular brown black pigment in the tumour cells cytological diagnosis is possible on cervical scrape (Pap) smear or FNAC smear examination from the cervical growth.[11,13]

In amelanotic tumours with little or no pigment, diagnosis has to be suspected on the basis of cellular features and confirmed with the help of IHC markers like HMB-45, S100 or Melan A. HMB-45 positivity in conjunction with negativity for epithelial markers and suggestive histomorphology is specific for melanoma[3]. When the tumour is amelanotic with little or no pigment, diagnosis of MM should be considered in differential diagnosis of a poorly differentiated cervical malignancy that also include MPNST, lymphoma, carcinoma and sarcoma.[12,14]

Staging of primary cutaneous melanoma is based on the thickness of primary lesion, and the same system should prove clinically relevant for primary cervical MM according to Clark et al.[9] At present most of the authors follow FIGO staging system as it correlates better with patient survival.[15]

Cervical MM remains localized initially and spreads to vagina, vulva and pelvic wall in advanced stages. Spread to rectum, urinary bladder and urethral tube occurs commonly and pattern of lymphatic metastasis is usually similar to that of carcinoma cervix.[16]

Available literature about primary mm of cervix is mostly in the form of single case reports and a few recent case series.[16-20] At present there is no consensus on the treatment of cervical melanoma. Recommended therapeutic regimens for cervical melanoma include radical hysterectomy with pelvic lymph node dissection followed by radiation therapy, either intracavitary or external beam radiation or both. Various Chemotherapeutic agents have been used in advanced cases.[2] Immuotherpy in combination with chemotherapy is tried and found effective.[3]

Prognosis of patients with primary MM of uterine cervix is unpredictable and generally poor as it is diagnosed in advanced stages.[19,20] Early diagnosis of cervical melanoma and its differentiation from squamous cell carcinoma of cervix becomes essential due to differences in therapy and prognosis of the two neoplasms.[9]

Conclusion

Malignant melanoma should be considered in differential diagnosis of poorly differentiated malignancy on histopathological examination of a cervical mass that is pigmented or otherwise. Microscopic diagnosis in biopsy or cytology smear can be confirmed by study of selected IHC markers. Diagnosis of primary malignant melanoma of cervix also needs extensive clinical and radiological investigative work up. Early diagnosis of cervical melanoma and its differentiation from squamous cell carcinoma of cervix is essential as the therapeutic approach and prognosis is different for the two neoplasms.

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