Case Report

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Pathology Section

Synchronous Primary Endometrial Carcinoma and Metastatic Malignant Melanoma in Cervical Lymph Node

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ABSTRACT

The occurrence of dual malignancies is not rare but concurrent occurrence of two malignancies with different histogenesis and different anatomical sites is not known. In the studies which have been conducted so far, none of them has shown the simultaneous occurrence of metastatic malignant melanoma and primary endometrial carcinoma. We report herein a case of a 42-year-old female diagnosed with metastatic malignant melanoma in cervical lymph node with unknown developing primary endometrial carcinoma within two months. No foci of primary malignant melanoma were found in uterus. Dual primary malignancy is being suggested by the presence of two malignancies in a patient with different morphological picture on histopathological examination, at anatomically distinct sites. Malignant melanoma and endometrial carcinoma, being a rare combination, prompted us to report the case.

Keywords: Dual, Malignancy, Metastasis

CASE REPORT

A 42-year-old female presented with enlarged palpable left cervical lymph node for the last four months. FNAC of the cervical lymph node suggested the possibility of neoplastic pathology possibly malignant melanoma [Table/Fig-1].

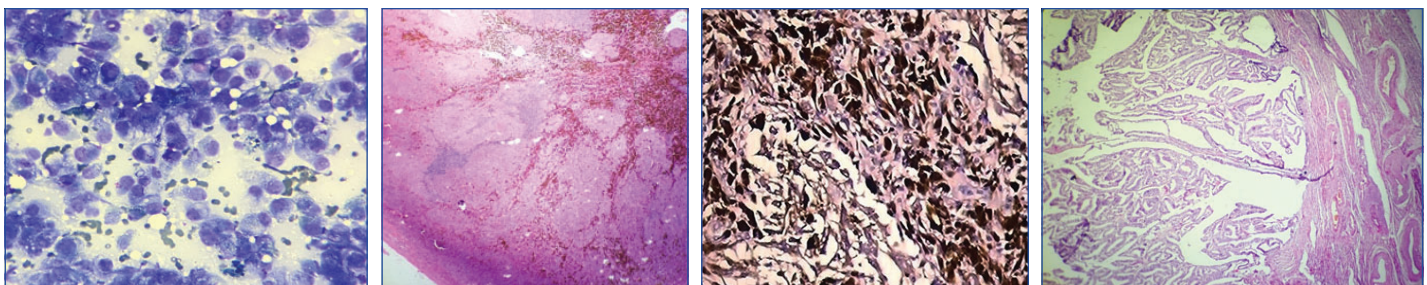
Excision biopsy was performed and histopathological examination of the lymph node showed metastatic deposits of malignant melanoma [Table/Fig-2]. Sections examined showed the presence of tumour cells in diffuse sheet in a background of lymphoid tissue. Individual tumour cells were large with eccentrically located nuclei, showing variable anisonucleosis, prominent nucleoli, intranuclear inclusions at places, had abundant amount of cytoplasm containing melanin pigment. Immunohistochemistry showed strong positivity for Melan-A and HMB-45 with focal positivity for CK [Table/Fig-3]. These findings were more consistent with the diagnosis of metastatic malignant melanoma.

Following biopsy report, patient underwent PET scan which showed no metabolically active lesions in neck region or any distant metastasis. Focal Fludeoxyglucose (^{18}F) (FDG) uptake was noted in the endometrial cavity of the uterus. Patient was advised endometrial biopsy for further evaluation but she did not turn for follow up.

Within a period of two months, patient again presented to Gynaecology Department with the chief complaints of per vaginal bleeding since 15 days. Endometrial biopsy was then taken and histopathological examination revealed features suggestive of adenocarcinoma. Total abdominal hysterectomy with salpingo-oophorectomy and pelvic lymph node dissection was performed. Diagnosis of endometrial carcinoma was confirmed on histopathological examination. Sections examined from endometrial growth showed a tumour arranged in the form of glandular pattern with little intervening stroma [Table/Fig-4]. Individual tumour cells were moderately pleomorphic with hyperchromatic nuclei, coarse chromatin, prominent nucleoli and moderate amount of cytoplasm. Tumour was extending from fundus to lower uterine segment with invasion of less than 50% myometrial thickness. Pelvic lymph nodes showed no evidence of any carcinomatous deposits (FIGO –IA). No focus of primary malignant melanoma was found in uterus. After Total Abdominal Hysterectomy (TAH) with Bilateral Salpingo-oophorectomy (BSO), excision of the cervical lymph node was planned. Skin consultation showed no lesions on oral mucosa or skin suggesting the possibility of melanoma. Patient was referred to the Department of Oncology for further management but the patient did not turn for follow up. This case was not associated with any syndrome, it was an incidental finding.

DISCUSSION

First case of multiple primary malignancies in a single patient was reported by Billroth in 1879 [1]. Since then, this phenomenon is being seen at increasing rates. This is attributable to the



[Table/Fig-1]: FNAC smears from cervical lymph node shows tumour cells with abundant fragile cytoplasm, at places containing melanin pigment with eccentrically located, pleomorphic nuclei. (MGG; 40X). **[Table/Fig-2]:** Photomicrograph showing metastatic deposits of malignant melanoma in cervical lymph node (H&E 10X). **[Table/Fig-3]:** Tumour cells showing strong positivity for HMB-45 on Immunohistochemistry (IHC, 40X). **[Table/Fig-4]**: Photomicrograph showing moderately differentiated endometrioid carcinoma (H&E 10X).

increased life expectancy of cancer survivors, which is the result of advancements in cancer therapeutics and more comprehensive screening protocols in cancer patients. Based on the type of study (antemortem or postmortem), incidence of multiple primary malignancies ranged from 0.734-11.3% [2-4]. Ocurrence of two synchronous malignant neoplasms with different histogenesis (endometrial carcinoma with concurrent malignant melanoma) is extremely rare. Only one case has been reported in the past with synchronous primary endometrial carcinoma and metastatic malignant melanoma arising from ovarian cystic teratoma [5]. But concurrent occurrence of endometrial carcinoma and metastatic malignant melanoma at different anatomical sites is not known to occur which is the unique feature in this case. A review of English literature shows no such case report till date. This is the first and only case of such kind reported so far.

Multiple malignancies in a single patient may occur in a single organ or may involve multiple and anatomically different organs. In our case uterus and cervical lymph nodes were the involved sites. Multiple primary tumours have been categorized into two by NAACCR (North American Association of Central Cancer Registries): (1) Synchronous – occurrence of tumours at the same time; and (2) Metachronous - occurrence of tumours one after the other at an interval of more than two months [6]. In 1932, Warren S and Gates D proposed criteria which assisted in differentiating between a true primary malignancy and a metastatic malignancy. According to this criteria: 1) each tumour should present a definite picture of malignancy; 2) each tumour should be histologically distinct; 3) the possibility that one is a metastasis of the other must be excluded [1]. The functional changes associated with the occurrence of multiple primary malignancies have been attributed to: 1) Common carcinogens exposed to multiple epithelial surfaces, exemplified by the phenomenon of field cancerization in head and neck tumours; 2) Late side effect of treatment used to treat first tumour; 3) Genetic predisposition; 4) Microsatellite instability [7,8]. Other probable mechanisms for the multiple primary cancers are: the immune system of patients and the intensive exposure to carcinogens including chemo- and/or radiotherapy used in the treatment of tumours. Second tumours induced by prior radiation or chemotherapy usually manifest after a latent period of 15-20 year [9]. In a study by Hulikal N et al., most of the synchronously diagnosed second tumours were incidentally diagnosed during the staging evaluation of the primary tumour, as in our case [10].

Aydiner A, conducted a 10 year period study on 26,255 cancer patients and observed that 271 (1%) patients had multiple primary malignant tumours, out of which 92 were synchronous tumours [4]. Another study by Bagri PK et al., showed the incidence of multiple primary malignancies to be 0.18% (41 cases out of total 23,260 cancer cases) among which eight cases were synchronous (19.5%). The study results showed that the most common site of primary tumour was head and neck (14 cases; 34.15%) followed by gynaecological cancers (9 cases; 21.95%), breast (7 cases; 17.07%), lung cancer (2 cases; 4.9%), oesophageal cancer (3 cases; 7.3%) and then other tumours (6 cases; 14.6%). The most common sites of second malignancy were found to be breast and gastrointestinal tract (each 9 cases; 21.95%) followed by lung (7 cases; 17.07%) and gynaecological cancers (5 cases; 12.20%) [10].

The occurrence of dual primary malignancies is not rare. But the concurrent occurrence of two malignancies with different histogenesis and different anatomical sites is not known. Review of literature shows no reports of concurrent primary endometrial carcinoma and metastatic malignant melanoma in cervical lymph nodes with unknown primary. This is the first and the only case where primary endometrial carcinoma developed synchronously in a patient with metastatic melanoma in lymph nodes with an unknown primary. In this case, primary endometrial carcinoma and malignant melanoma were two distinct malignancies as proven by clinical and histopathological examination. Neither of the two malignancies were a metastasis of the other.

CONCLUSION

Conclusion drawn from this case is that before labeling a lesion as metastatic (a lesion that is anatomically away from the primary malignancy), a detailed evaluation of the case is necessary. Otherwise, the possibility of a synchronous primary malignancy may be missed.

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