

Gastric Carcinoma Diagnosed Incidentally on Cervical Biopsy in A Young Female

Mahendra Kumar¹, Naushad Shah¹, Jaya Mishra^{1*}, Ritesh Kumar², Subrat Panda³

¹Department of Pathology, North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences, Shillong, India

²Department of Radiotherapy, North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences, Shillong, India

³Department of Obstetrics & Gynecology, North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences, Shillong, India

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ABSTRACT

Gastric carcinoma usually metastasizes to liver, peritoneum, lymphnodes, ovary, lung and brain. But gastric malignancy metastasizing to cervix is extremely rare and even rarest in young patients. Reaching to the primary site of hidden gastric malignancy on a cervical biopsy was very interesting in present case. Distinction of primary cervical malignancy to metastasis is very important for clinical and pathological point of view which helps in the diagnosis, staging, treatment and prognosis of the patient. Here we are documenting a case of gastric malignancy which presented as cervical mass and bilateral ovarian enlargement in a 22 years old female.

***Corresponding author:**

Dr. Jaya Mishra, Associate Professor, Department of Pathology, North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences, Mawdiangdiang, Shillong, 789018, Meghalaya, India

Phone: +91 - 96824331357

E-mail: jayamishraxyz@gmail.com



Introduction

Metastatic cervical carcinomas are generally originate from intrapelvic organs, however, they may receive metastasis from extrapelvic organs rarely.^[1,2] In scientific literature, the most common organ which metastasizes to cervix is ovary followed by gastro-intestinal tract (GI tract), uterine tube and breast.^[3,4,5] Metastatic ovarian adenocarcinoma (Krukenberg tumour, KT) are uncommon which originates in the stomach in the vast majority of cases, however may come from other organs such as intestine, breast, gallbladder, uterine cervix or appendix also. ^[6] Prognosis of KT is extremely poor as compared with primary ovarian cancer(s).^[7] Its management is further complicated by simultaneous involvement of other organ such as cervix in present case. Here we are documenting an incidentally diagnosed case of gastric carcinoma presented with cervical growth and KT in young female.

Case Report

A 22-years-old married woman was referred from a local hospital to Gynaecology OPD of our Institute with chief complaints of progressive enlargement of abdomen along with dragging pain in lower abdomen and difficulty in breathing for last 3 weeks. Bowel habit was normal. Menstrual history and other gynecological history were non contributory and did not suggest pregnancy and other gynecological disorders. General physical examination revealed mild pallor with Hb of 7 gm/dl, however, there were no icterus or lymphadenopathy. Abdominal examination showed markedly enlarged abdomen with tense ascities and

it was difficult to access any organ or mass per abdomen. Per vaginal examination revealed growth in posterior lip of cervix measuring 1.5×2cm. Biopsy from cervical mass was taken and sent for histopathological examination. Cervical pap smear was not prepared. Bilateral adnexa and uterus could not be accessed properly due to tense ascitis. Her laboratory investigation was significant for CEA of 10.07 ng/mL (reference range: <3ng/mL), however AFP (<2ng/mL) and β -HCG (5.17mIU/mL) were within normal range. Cytological evaluation of ascetic fluid showed scanty cellularity and few scattered cells of suspicious nature. Further, radiological investigations (Ultrasonography and CT-scan) revealed enlarged ovaries measuring 4.9×3.9×4.6cm and 6.2×4.4×5.2cm with solid-cystic component. These findings suggested the possibility of bilateral ovarian neoplasm on radiology.

Histological examination of cervical biopsy showed frank epithelial malignancy which occupied most of the sub epithelial region (FIGURE-1A) and causing disarrays of lining cervical epithelium with focal ulceration, leading to confusion between primary cervical carcinoma and metastasis (FIGURE-1B). The tumor cells were arranged mainly in sheets, showing moderate pleomorphism, round vesicular nuclei and moderate amount of clear to amphophilic cytoplasm (Figure-1b). At places tumor cells had eccentric nuclei and moderate amounts of clear cytoplasm simulating signet ring- like cells (Figure- 2). In the light of radiological findings, a diagnosis of cervical malignancy with a possibility of metastasis from ovary

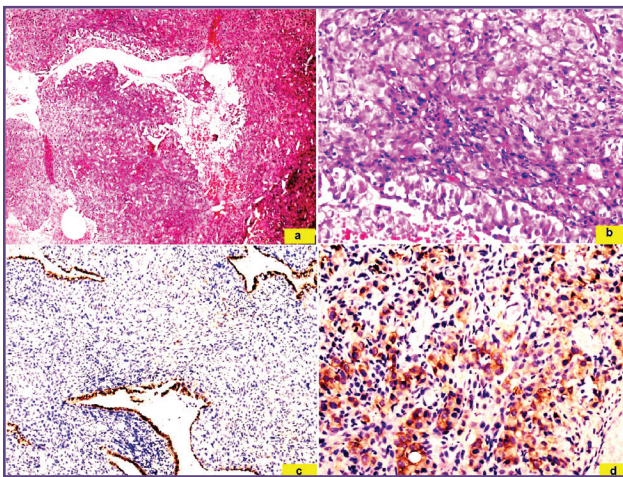


Fig. 1: Panel of microphotographs from cervical biopsy shows a diffuse tumor (1a, H&E, x10) along with disarray of lining epithelium (1b, H&E, x20). IHC shows CK-20 positivity (1d, x20) & CK-7 negativity (1c, x10) in tumor cells. Unremarkable cervical lining epithelium shows positivity for CK-7 (1c, x10).

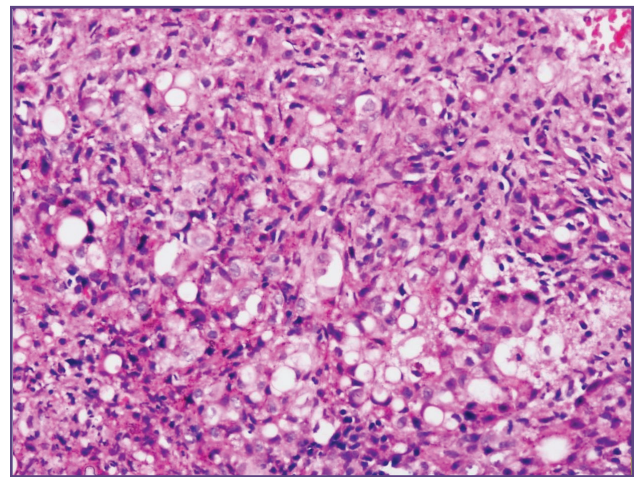


Fig. 2: Higher magnification of cervical biopsy highlights signet ring morphology of tumor cells focally (H&E, x40).

was considered. Vice-versa, primary cervical carcinoma metastasizing to bilateral ovaries was also considered which is very rare. Presence of few signet like cells had raised a possibility of bilateral ovarian metastasis along with cervical involvement by unknown primary. So, search for primary other than ovary was advised.

Further, upper GI endoscopy had detected a large ulcerated growth at lesser curvature of the body of stomach. Endoscopic biopsy was advised from the same which subsequently revealed moderately differentiated adenocarcinoma of stomach. These tumor cells had almost similar morphology as the tumor cells of cervical biopsy (Figure-3a & 3b). All the diagnostic puzzles fell into place when immunohistochemistry (IHC) panel was performed on both the biopsied specimens (i.e., the cervical and the stomach). The tumor cells were positive for CK-20 (FIGURE 1D & 3C) and negative for CK-7 (Figure 1c & 3d) confirming the GI origin of the adenocarcinoma. In addition to these markers, tumor were also negative for ER, PR, WT-1, TTF-1, synaptophysin and chromogranin, which rule out possibility of other metastatic tumor site (breast, ovary, lung and peritoneum) & neuroendocrine nature of tumor. Patient was so sick that further intervention like FNAC and biopsy from ovarian mass could not be performed.

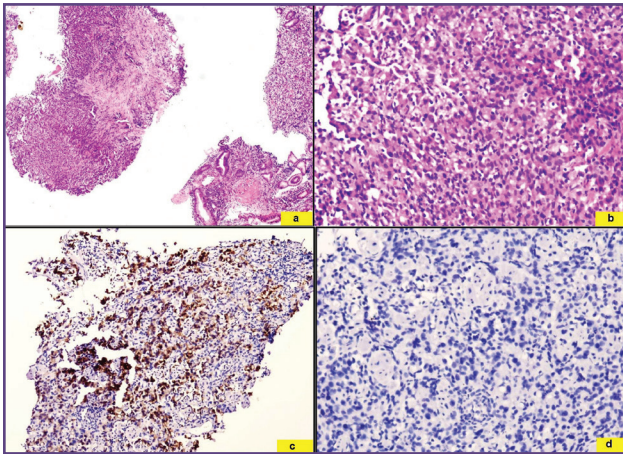


Fig. 3: Panel of microphotographs of gastric biopsy shows a diffuse tumor (3a, H&E, x4) and high power of same (2b, H&E, x20) highlights minimally pleomorphic tumor cells having moderate amount of eosinophilic to amphophilic cytoplasm. IHC shows CK-20 positivity (3c, x10) and CK-7 negativity (3d, x20) in tumor cells.

Correlating clinical, radiological, biochemical and histological findings, final diagnosis of adenocarcinoma of stomach with metastasis to bilateral ovaries (Krukenberg tumor) and cervix was made.

Patient was referred to Oncology & Palliative care unit and offered for systemic palliative chemotherapy but she

denied for the same due to socio-economic reasons and left the hospital against medical advice.

Discussion

Uterine cervix is an uncommon site for metastatic tumor.^[3,4] The most common malignancy spreading to the cervix is the endometrial carcinoma which involves through direct extension and typically involves the endocervical glands with or without stromal involvement. The common primary sites of malignancies which metastasize to cervix are ovary, gastrointestinal tract, uterine tube, breast and peritoneum in descending order of frequency.^[3,8] Loco-regional characteristics which may explain the low incidence of cervical metastases include - small organ size, reduced blood flow and distal location, as well as the organ's abundant content of fibrous tissue. All these characteristics make the uterine cervix a medium that is scarcely favorable for the propagation of malignant cells.^[9]

On the other hand, ovaries are the frequent targets for metastasis for malignant tumors. Metastasis altogether accounts for 10-30% of all the malignant ovarian tumors.^[10] Primary sites of malignancy may be either gynecological or non gynecological organs. Non gynecological tumors which metastasize to the ovaries are stomach, breast and colon followed by others.^[10] Woodruff and Novak defined the KT as arising in the ovarian stroma and having characteristic mucin-filled signet-ring cells.^[11] "Krukenberg tumor" is occasionally used as a synonym for metastatic ovarian tumors from various organs. In general KT is rare in Western countries and accounts for 3-4% of metastatic ovarian tumors.^[12] On the other hand, the incidence of KT in Japan is rather high because of the high incidence of gastric cancer.^[13,14]

Simultaneous involvement of both cervix and ovaries are extremely unusual and very rare in young age.

Average age of presentation is 45 & 43 years for overall KT and patient with cervical metastasis respectively.^[3,15] Average age is slightly lower in gastric primary tumor as compared to other primary sites in both KT and patients with cervical metastasis.^[3,15] In the present case patient was 22 year old which was quite young for cervical metastasis along with KT. Clinically, most of the either kind of patients present with abdominal swelling and pain in abdomen as in our case. Some of the patient may have endocrine manifestation such as virilization, hirsutism and vaginal bleeding (estrogenic effect) and very few may be asymptomatic.^[3,15] Few patients may have an already known primary tumor and associated symptoms before the diagnosis of metastasis to ovary. A large study has demonstrated that primary tumor was identified only

in about 50% cases even after extensive search and 32% of that had diagnosis of primary tumor before ovarian metastasis.^[15] Herein patient had abdominal swelling, mild pain and severe ascitis, however did not have any major gynecological symptoms/complains like vaginal bleeding. On colposcopic examination, there was a growth on the posterior vaginal wall from which the biopsy was taken.

Common histological features of metastatic carcinoma within the cervix include predominant involvement of the deep stroma, absence of surface involvement and of an in situ component, prominent lymphovascular permeation and entrapment of normal endocervical glands.^[4] In contrast to these features, herein biopsy showed superficial stromal infiltration as well as disarray and focal ulceration of lining endocervical epithelium which was very unusual and rare for cervical metastasis. Similar pattern of infiltration has been discussed in a case series of six cases of cervical metastasis.^[4] This kind of superficial pattern of involvement raised the possibility of primary cervical carcinoma metastasizing to bilateral ovaries. However in view of few signet rings like cells and bilateral ovarian enlargement possibility of a primary adenocarcinoma outside the genital tract was considered and further investigation revealed tumor with similar morphology in the stomach. To resolve the confusion between primary versus secondary origin of the cervical tumor, IHC was performed and tumor was positive for CK20 and negative for CK 7 which favored the possibility of GI origin of the tumor. Other IHC markers which can be used to rule out other metastatic sites / tumors are ER, PR, WT-1, p53, p16, TTF-1, HMB-45, CEA and thyroglobulin. There are various morphological features which may help to discriminate between primary and secondary nature of tumor in cervix. Primary cervical tumors are characterized by dysplastic epithelium with or without ulceration, in situ epithelial lesions, superficial stromal invasion and absence of prominent lymphovascular permeation. On the other hand secondary cervical malignancy usually lacks these features and there is mainly deep stromal involvement, lymphovascular involvement, entrapment of normal endocervical glands and single cell infiltration with signet ring morphology (specially in gastric signet ring carcinoma).

Isolated dissemination to the uterine cervix is more common among patients with ovarian and colorectal cancer compared with those of gastric or breast cancer. In the majority of patients with gastric, breast and ovarian cancer, disease spread to other pelvic or extrapelvic organs. Regarding survival, gastric and colorectal primaries have poorer survival as compared to primary tumor from breast and ovaries.^[15] In present case primary tumor was in stomach and has disseminated to the ovaries and

cervix leading to poor expected survival of the patient. Considering advance stage of tumor, patient was offered for palliative systemic chemotherapy. But patient left the hospital against the medical advice and lost to follow up.

This case emphasizes that systematic work-up for known primary tumor sites is important in suspected cases of metastatic gynecological tumor.

Conclusion

To conclude, cervical metastasis along with bilateral ovarian involvement is uncommon in gastric carcinoma and extremely rare in young female. Clinician should keep the rare possibility of cervical metastasis from gastric primary in their differential diagnosis. It is important for the pathologist to be aware of the possibility of cervical metastasis to avoid an erroneous diagnosis of a primary cervical adenocarcinoma. The detailed histopathological features of the lesion and judicious use of immunohistochemical techniques allow us to determine the true origin of the metastatic tumor.

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Competing Interests

None declared.

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