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Case Report

Pathology Section

Synchronous Primary Carcinoma of Cervix and Ovary- A Rare Case Report

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ABSTRACT

Synchronous malignancies of female genital tract account for less than 3% of all genital tract neoplasms. Amongst synchronous tumours, ovarian with endometrial carcinoma accounts for 51.7% while ovarian with cervix accounts for less than 10% of them. Unusually, they have a favourable prognosis with five years survival rate being 73.3%. Authors hereby, present a case of 51-years-old female presented with bleeding per vagina and on examination cervical mass was detected. The cervical mass biopsy confirmed cribriform adenocarcinoma of cervix. Uterus and cervix could not be removed as it was FIGO (The International Federation of Gynecology and Obstetrics) stage III B (inoperable) thus was managed on chemotherapy and radiotherapy. A month later she presented with bilateral ovarian masses for which she had undergone bilateral oophorectomy and omentectomy. Histopathology confirmed moderately differentiated mucinous cystadenocarcinoma of bilateral ovaries. Thus a case of synchronous carcinoma of cervix and ovary was concluded. She tolerated all managements successfully.

Keywords: Cervical neoplasms, Mucinous cystadenocarcinoma, Ovarian neoplasms, Primary malignancy

CASE REPORT

A 51-year-old (gravid 2, parity 2, abortus 0) female came with irregular bleeding per vagina and history of pain in abdomen on and off since two months. There was no history of diabetes, hypertension, tuberculosis, asthma, epilepsy, drug allergy or surgical history.

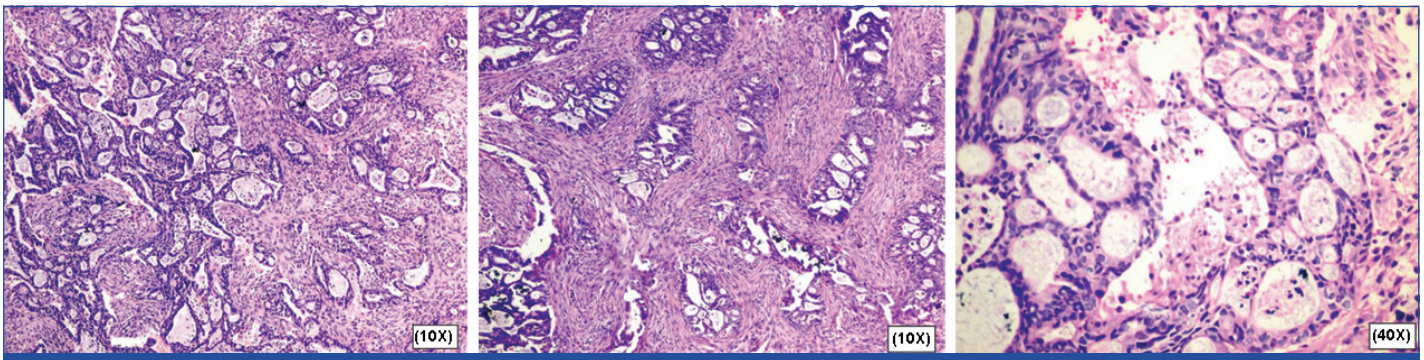
On examination, the respiratory, cardiovascular and central nervous systems were unremarkable. Her CA-125 (cancer antigen 125) levels were 18.4 U/mL (normal is <35 U/mL). Per speculum examination showed a growth at cervix measuring 4.8×4.5 cm, extending on upper 1/3rd of vagina and bleeding on palpation. Magnetic Resonance Imaging (MRI) showed large polypoidal heterogeneously enhancing T2 hyperintense mass involving cervix and extending to lower uterine body and upper half of vagina inferiorly. There was extension into bilateral parametria and invasion of posterior wall of bladder with resultant uterovesical fistula with right uterovesical junction and terminal ureter involvement. Bilateral ovaries were solid-cystic and enlarged.

Histopathological examination of cervical growth biopsy revealed cribriform adenocarcinoma of cervix showing stromal infiltration in the form of glandular confluence with cribriform architecture. Histopathology diagnosis was established as adenocarcinoma of cervix with cribriform pattern [Table/Fig-1-3]. Immunohistochemistry (IHC) was advised to differentiate between primary cervical carcinoma and ovarian carcinoma metastasis. IHCs showed positivity for Cytokeratin 7 (CK7), Paired-box gene 8 (PAX8), Carcinoembryonic Antigen (CEA), Caudal-type homeobox 2 (CDX2) and negative for Cytokeratin 20 (CK20), Wilms' tumor gene (WT1); thus confirmed the cervical origin of the tumour. The tumour extended into bilateral parametria, posterior wall of bladder and ureter rendered it to be inoperable. Thus, chemotherapy and radiotherapy with further routine investigations were advised.

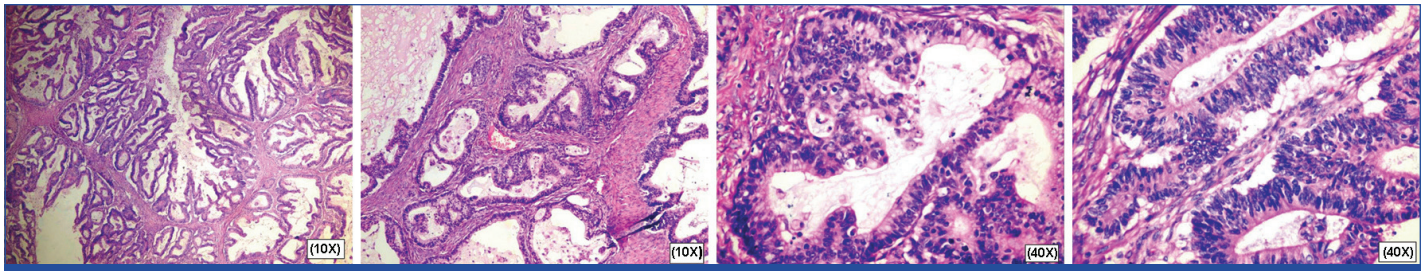
On follow-up; per abdomen examination revealed a palpable mass occupying both iliac, lumbar and umbilical areas arising from pelvis which was solid-cystic on sonography. She was diagnosed radiologically to have bilateral ovarian tumours.

Bilateral salpingo-oophorectomy and infracolic omentectomy was performed. Intraoperative findings included ascites of 1.5 litres with bilateral, irregular and solid cystic ovarian tumours. Right and left ovary measured 15×15×8 cm and 16×15×10 cm, respectively. Also, right and left ovary weighed 700 grams and 1260 grams, respectively. Lower cervix was adherent to the posterior bladder wall. Parametrium was involved up to lateral pelvic wall and para-aortic lymph nodes were palpable (FIGO stage IV A) [1]. Postoperative period was uneventful.

Histopathology revealed moderately differentiated mucinous cystadenocarcinoma of bilateral ovaries exhibiting complex glandular architecture separated by fibrovascular stroma. Glands showed intestinal type lining with pseudostratification, nuclear atypia, and stromal invasion. Histopathology diagnosis was established as moderately differentiated bilateral mucinous cystadenocarcinoma



[Table/Fig-1]: Glandular confluence with cribriform pattern of cervical adenocarcinoma (10X, H&E Stained). **[Table/Fig-2]:** Cervical adenocarcinoma with stromal invasion (10x, H&E Stained). **[Table/Fig-3]:** Cribriform pattern of cervical adenocarcinoma. (40X, H&E Stained). (Images from left to right)



[Table/Fig-4]: Complex glandular architecture separated by fibrovascular stroma. (10X, H&E Stained). **[Table/Fig-5]:** Stromal invasion by neoplastic glands. (10X, H&E Stained). **[Table/Fig-6]:** Intestinal type glands lined by dysplastic epithelium. (40X, H&E Stained). **[Table/Fig-7]:** Dysplastic glands showing nuclear atypia and pseudo-stratification. (40X, H&E Stained). (Images from left to right)

[Table/Fig-4-7]. IHC was advised to differentiate between primary ovarian carcinoma and cervical carcinoma metastasis and performed at a higher centre. IHC on ovarian tumour showed positivity for CK, CEA, CDX2, CK20 and negative for CA-125 and WT1; thus confirmed the ovarian origin of the tumour. Fallopian tubes and ascitic fluid were free of tumour. Infracolicomentum was also free of tumour.

Postoperative palliative chemotherapy with radiotherapy was given and patient underwent suprapubic cystostomy for passage of urine. Patient had undergone regular follow-up for two years.

DISCUSSION

Simultaneously occurring primary genital tract malignancies can be synchronous as in our case [2]. Synchronous malignancies of cervix and ovaries are rare and only few cases are studied in literature [3]. The most commonly encountered association consists of ovarian and endometrial cancers which accounts for 50-70% of all synchronous female genital tract tumours. As for the association between ovarian and cervical cancers only isolated cases have been reported so far [4]. Surveillance Epidemiology and End Results (SEER) programme defines synchronous cancers, as cancers of the endometrium and ovary diagnosed within two months of each other which in the present case was within one month interval. The patients with synchronous cancers experienced much better survival than those with single ovarian cancers in each stage strata. Synchronous cases may have a lead-time advantage over single ovarian cases because endometrial tumours more often present with gynaecologic-related symptoms that occur sooner and prompting clinical examination and treatment. Age adjusted hazard ratios showed a 67% reduced risk of death [5]. After additionally adjusting for stage, the risk reduction for synchronous cancers was reduced to 53% (hazard ratio 0.47, 95% CI 0.42-0.53) [5]. Overall, ovarian cancer survival rates are low because the disease tends to be diagnosed at late stages, whereas endometrial cancer tends to be diagnosed at an earlier stage, resulting in better survival [5].

While the aetiology remains unclear, it has been postulated that when simultaneously subjected to carcinogen, embryologically similar tissues of female genital tract may develop synchronous neoplasm. Others suggested that metaplasia may occur in similar histological epithelium of genital tract and peritoneum [6,7]. Certain risk factors associated with these synchronous cases include nulliparity, obesity, unopposed oestrogen use, late menopause, diabetes causing increasing chances of disease whereas plasma levels of beta-carotene, lycopene, folate, Vit-B12 are protective. Certain genes viz., p53, p21, CCND1, ERCC1 and Her2neu association is seen [8,9]. Earlier reported cases of synchronous ovarian and cervical carcinoma are elaborated in [Table/Fig-8] [3,4,7,8,10,11].

Warren S and Gates O established three criteria for the diagnosis of multiple malignant primaries: 1) Each tumour must present a definite picture of malignancy; 2) Each tumour must be distinct; and 3) The possibility of one tumour being a metastasis of the other must be excluded [12]. This case meets all three criteria. Human Papillomavirus-Deoxyribonucleic Acid (HPV-DNA) positive staining indicates metastatic involvement of ovary by cervical malignancy [10,13,14]. Synchronous genital malignancies cause more clinical problem as compared to singly occurring once; hence such cases tend to be detected at an earlier stage [3]. Based on case reports, patients which presented with single malignancy symptoms had difficulty to predict the possibility of synchronous malignancy [3,10]. In the present case, the patient had symptoms of cervical malignancy whereas ovarian malignancy was diagnosed after thorough investigations. Histopathological examination becomes confirmatory for diagnosis and the prognosis depends on malignancies being metastatic or synchronous. The latter group has a better prognosis [3,10,14].

Authors	Year	Age in years	Ovarian carcinoma	Cervical carcinoma
Huang YD et al., [10]	2006	30	Endometrioid ovarian carcinoma	Mucinous adenocarcinoma
Srivastava K and Zahra F [3]	2009	55	Serous cystadenocarcinoma	Squamous cell carcinomas
Kambi DP et al., [7]	2013	55	Papillary cystadenocarcinoma	Adenosquamous carcinoma
Sakarya DK et al., [8]	2015	65	Endometrioid adenocarcinoma	Endometrioid adenocarcinoma
Bacalbasa N et al., [11]	2020	53	Serous ovarian adenocarcinoma	Moderately differentiated adenocarcinoma
Nadarajan L and Nusee Z [4]	2021	63	High grade serous carcinoma of ovary	Squamous cell carcinoma of cervix
Present case	2023	51	Mucinous cystadenocarcinoma	Adenocarcinoma with cribriform pattern

[Table/Fig-8]: Earlier reported cases of synchronous ovarian and cervical carcinoma [3,4,7,8,10,11].

Surgical management should be offered in all such cases as it greatly aids in diagnosis and staging for the reported tumours followed by adjuvant chemotherapy [15]. This leads to improving overall survival and long term follow-up of such patients should be maintained to determine prognosis.

CONCLUSION(S)

Thus, synchronous primary ovarian malignancy and cervical malignancy are rare. It requires proper staging and histopathological subtyping for diagnosis and improving prognosis, although their prognosis is better when compared with cases of single primaries. However, the difference in our case report was that the cervical malignancy was advanced involving the urinary bladder, ureter and bilateral parametria.

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