Case Report

Synchronous malignancies of ovary, fallopian tube and cervix-
A rare case

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Abstract
Multiple primary tumours may either be synchronous or metachronous tumours, depending on the timing of
diagnosis of the different primary tumours. Synchronous gynecological tumors are rare and are frequently double
primaries involving ovary and endometrium. Triple synchronous primary malignancies are even rarer and carry a
diagnostic and therapeutic challenge to a pathologist and oncologist, respectively. Theories on etiopathogenesis are
presented. This case is presented for its rarity and interesting pathogenesis.

We are presenting a rare case of triple synchronous primary malignancies originating in the uterine cervix,
fallopian tube and ovary. An elderly female of 55yrs underwent panhysterectomy for Squamous cell carcinoma cervix,
diagnosed on pap smear and tubo-ovarian mass, picked up on ultrasound examination. On histopathologic examination a
diagnosis of Primary papillary cystadenocarcinoma ovary and fallopian tube with synchronous adenosquamous
carcinoma cervix was made. Multiple primary neoplasms of female genital tract is a well-recognized yet rare occurrence.
Field cancerization is a concept that was suggested by Slaughter et al.7 in 1953 which suggests that when the body is
exposed to carcinogens, other organs besides the organ with cancer are also exposed to the carcinogen and carry a high
risk of cancer. Although the presented case is probably an incidental event, the pathogenesis of the neoplastic process
affecting the tissues with common embryological origin needs further research and evaluation. It is important to
distinguish multiple primary neoplasms from metastatic disease because of the fact that overall survival as well as
treatment would vary considerably.

Keywords: synchronous tumors, cervical cancer, ovarian carcinoma

1. Introduction
Patients suffering from primary genital malignancies are sometimes co-afflicted with other primary cancers.
Synchronous multiple tumours of female genital tract are relatively rare comprising only 1-6% of genital neoplasms1,2. The
incidence of synchronous primary malignancies of the female genital tract is 0.63%. Out of these the commonest is the
dermatoid carcinoma of the ovary and endometrium (40%) which carries a favourable prognosis because of earlier
detection and low grade malignancy. Other reports of synchronous malignancies of ovary and cervix have similar
histopathology so the possibility of these being metastatic lesions can be ruled out only after thorough histopathological
study of the surgical specimens3. Cases of triple synchronous primaries are extremely rare, with only 13 cases being
reported till date and all these cases are involving cervix, endometrium and ovary\textsuperscript{4,5}, and a single quadruple case of synchronous primaries in the ovary, fallopian tube, endometrium and cervix\textsuperscript{5}. To the best of our knowledge, this is the first case of triple synchronous cervical, fallopian tube and ovarian carcinomas.

2. Case history

55 yrs old female presented with postmenopausal bleeding, pain abdomen since 2 months. Past history and family history was insignificant. On systemic examination, there was abdominal distension. Pervaginal inspection showed a cervical growth which bleeds on touch. There was right sided forniceal tenderness with a palpable pelvic mass. USG abdomen was reported that both right sided ovary and fallopian tube were enlarged, the ovary showing a cystic mass, while the tube showed a solid lesion. Pap smear was reported as squamous cell carcinoma. Subsequently cervical biopsy was carried out which confirmed Invasive nonkeratinizing squamous cell carcinoma of cervix. A pre-operative diagnosis of cervical carcinoma with tubo-ovarian mass was made. The patient underwent panhysterectomy.

2.1 Gross

Pan hysterectomy specimen revealed an irregular grey white exophytic growth in the cervix without any apparent involvement of lower uterine segment. Right sided ovary showed an uniloculated cyst 4x3cms across, with tiny papillary excrescences on the inner surface. The middle third of the right fallopian appeared dilated, the cut section showing a hard irregular grey white nodule.

2.2 Microscopy

Cervix showed infiltrating tumour cells arranged in both glandular and squamoid patterns. Both ovary and fallopian tube showed tumour cells in branching papillary fronds.

Figure 1: a. Pan hysterectomy specimen. An irregular grey white growth in the cervix, a grey white nodule in the fallopian tube and a cystic mass with papillary excrescences in the ovary. b,c. 10x, 40x H&E. Section from cervix showing infiltrating tumour cells arranged in both glandular and squamoid patterns.
2.3 Final Diagnosis

Primary papillary cystadenocarcinoma ovary and fallopian tube with synchronous adenosquamous carcinoma cervix.

3. Discussion

In a patient with primary gynecological malignancy, synchronous malignancies elsewhere in the body have to be ruled out as their incidence is 4.3%\textsuperscript{3}. The mechanism of multiple primary cancers is not fully known, but many hypotheses have been suggested, such as family history, immunologic and genetic defects, prolonged exposure to carcinogens, radiation and chemotherapy for the primary cancer. While the etiology and pathogenesis of these tumours remain unclear, it has been proposed that embryologically similar tissues, when simultaneously subjected to either hormonal influences or carcinogens may develop synchronous neoplasms in genetically susceptible individuals\textsuperscript{1}. Slaughter et al (1953) coined the term ‘field cancerization’ for the mucosa of head and neck region undergoing genetic transformation directly proportional to the intensity and duration of carcinogen exposure, making it more susceptible to develop many foci of premalignant lesions and malignant transformation. This concept has been extended to be applied for female genital tract, wherein repeated exposure of the mucosa of the female genital tract to multiple risk factors leads to the development of multicentric disease\textsuperscript{6}. It is suggested that cancers developing in different sites originate from histologically similar epithelium. This "secondary mullerian system" concept attempts to explain the etiology of synchronous primaries in female genital tract.
The cervical and ovarian carcinomas were of different histopathology- adenosquamous carcinoma cervix and cystadenocarcinoma ovary. Thus it both were considered as primaries. Whereas fallopian tube and ovary, both showed similar histopathology- papillary cystadenocarcinoma. However metastases to fallopian tube from ovarian carcinoma was ruled out considering the facts that there was no direct extension of the ovarian tumour to the tube, there being a gap of about 1.5 cms; there was no serosal involvement, the lesion arising as a discrete nodule from the tubal wall projecting into the lumen, distending the lumen. These findings favour primary in the fallopian tube over ovarian metastases.

4. Conclusion
Although rare, the possibility of triple synchronous primary malignancies should be considered when evaluating gynecologic malignancies. Patients with multiple primary cancers have a high frequency of microsatellite instability (MSI), arguing that MSI affects the pathogenesis of some multiple primary cancers. Identifying all the components in synchronous tumours and distinguishing them from metastatic disease become important as each of them have to be staged and treated appropriately. Overall survival and treatment would vary considerably. Multiple primary neoplasms do not have worse prognosis in terms of survival than single ones. There have been several papers investigating the use of genetic markers, such as loss of heterozygosity, for definitively diagnosing tumors as synchronous primaries rather than one being a metastasis of the other, but none of these has specifically addressed whether there is a common predisposing genetic event leading to the development of synchronous neoplasms. Validity of immunohistochemical and cloning studies is also not clear. Centralised Registration of such cases with standardized protocol is required in view of expected increase in incidence due to increase in life expectancy.

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