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DUAL MALIGNANCIES: - A CASE REPORT OF A SYNCHRONOUS PRIMARY BREAST AND CERVIX MALIGNANCIES WITH A REVIEW OF THE LITERATURE

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ABSTRACT
The work was created in collaboration with the following authors. Author **EB** saw the patient and performed the surgery. Author **OBA** designed the study, and wrote the first draft of the manuscript. Authors **UIV** and **AM** managed the literature searches, while authors **UC** and **ONO** edited the manuscript.

INTRODUCTION
Multiple primary malignancies (MPM) are rare. Its frequency among all cases of malignancies has been reported to be 1-3%.[1,2] Nemeth et al, in their work on MPM found dual malignancies in 3-5 % of their patients, triple tumors in only 0.5% and quadruple tumors in 0.3%.[3] In 1934, Bugher,[4] carried out one of the earliest statistical analysis of double primary malignancies, deriving an equation for the probability of death from cancer during a specified period of age with a coincidental second malignancy. The phenomenon of MPM has been identified with increasing frequency, in part to the increase in life expectancy of cancer survival, a boon of advancements in cancer therapeutics and to the more comprehensive screening protocols used in cancer patients.[5] We report a rare combination of the occurrence of dual malignancy of the breast and cervix.

CASE REPORT
A 45 –year old, para8^{+3}, (all alive), patient was admitted for an evaluation of a lump in the right breast that had been present for a 5-month duration, as well as abnormal vaginal bleeding accompanied by a foul-smelling watery vaginal discharge of a 2-month duration. The breast lump was painlessness, not associated with any form of discharge. Her last delivery was about 13 years prior to presentation. She does not have a family history of breast or gynecological cancers, nor does she smokes but consumes alcohol occasionally. She gave a positive history of 4 years usage of 3 monthly injectable contraceptives. Menarche was at 12 years.

Further examination revealed a left peri-areolar mass, 1cm by 1cm, cystic, tender and mobile with dirty brown discharges. There was no axillary lymph node enlargement. A working diagnosis of the left breast mass was conducted in which she was worked up with PCV, ESR, FBS (which all lacked abnormal results) for an excisional biopsy of the left breast mass. In addition, speculum examination showed a hemorrhagic looking cervix, irregular looking inferior lip with bleeding on contact and necrotic part which sloughed during examination. All other examination yielded essentially normal results. Cystic and Carcinoma of the uterine cervix was made. Tissue obtained during the speculum examination was also sent for histopathology examination

The surgical pathology report came as moderately well differentiated squamous cell carcinoma of the cervix (Fig 1) and papillary carcinoma of the breast (fig 2)

Based on this, a diagnosis of a synchronizes dual primary cancer of breast and cervix was made. She was given the best supportive care and referred to a tertiary centre for further management.

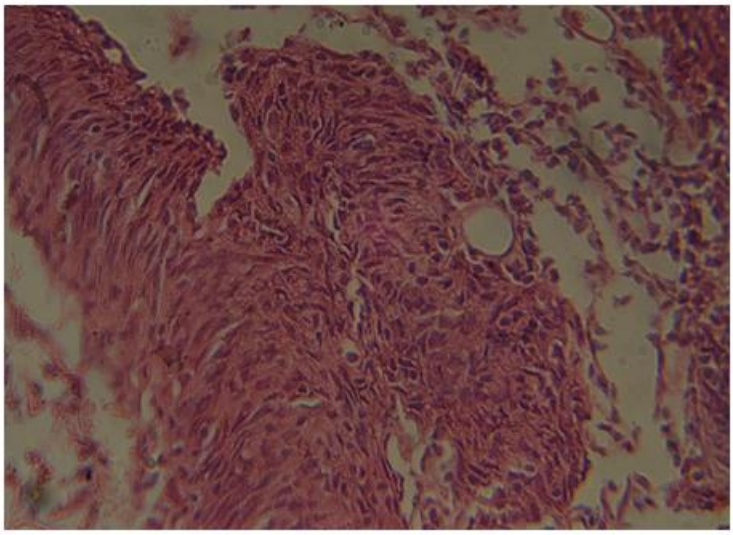

Fig. 1: Moderately well differentiated squamous cell carcinoma (cervix) X40.

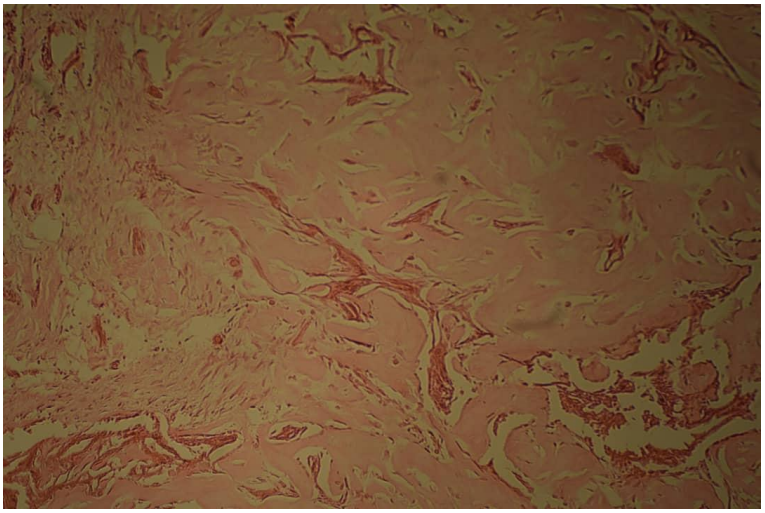

Fig. 2: Papillary carcinoma (Left Breast) X10.

DISCUSSION

The first reported case of multiple primary malignancies in a single patient was by Billroth.[6] in 1879. Double primary malignancies could be divided into synchronous or metachronous malignancies depending on the interval between formal diagnosis.[7] The former were second tumors occurring either simultaneously, or within 6 months of the first malignancy while the metachronous malignancies were secondary tumors that had developed after 6 months or more after the first malignancy.[8,9]

The main difficulty in making a diagnosis of MPM is the ability to differentiate it from metastasis in which Warren and Gates,[6] established criteria for this. The diagnoses of a MPM should fulfill the following:

- Each tumor should be histologically distinct
- There should be at least 2 cm of normal mucosa between the tumors. If the tumors are in the same location, they should be separated in time by at least five years.
- The possibility of one being the metastases of the other must be excluded.

The Surveillance Epidemiology and End Results (SEER) program database gave the incidence of MPM from 1%, initial liver primary to as high 16% initial bladder primary.[10] If the initial primary is the breast, the percentage of patients expected to develop multiple primaries is 10% and for lung 4%.[10] A report from an Indian Regional Cancer Institute reported that most common sites of primary tumors were head and neck cancers followed by gynecological cancer, breast cancer, lung cancer, esophageal cancer and then other sites.[8] In 12.20% of cases seen at the Indian centre, there were association of breast cervix and in 14.63%, there were association of lung-head and neck cancers.

Though the pathophysiology and mechanism involved in the occurrence of multiple primary malignancies are not fully understood, several factors and other complex have been implicated.[2] These include environmental factors (tobacco and alcohol abuse, occupation and pollution),

genetic predisposition, previous medical treatment (radio or chemotherapy), gender-specific factors, hormonal factors, and interaction of these factors. Other proposed causal factors include progressive ozone depletion and effect of ionizing radiation, increased use of organ transplants, genetic manipulation, and immunomodulators.[11]

The index case fulfilled the Warren and Gates criteria.[6] for a synchronous multiple malignancies. The two tumors are histological distinct, (papillary carcinoma of the breast and moderately well differentiated squamous cell carcinoma of the cervix). They are most metastasis of one or the other and are separated by at least 2 cm of normal. The malignancies have been occurring either simultaneously or within 6 months after the first malignancy.[8]

Though multiple metachronous primary malignancies are becoming increasingly frequent, however, multiple synchronous primary malignancies are still unusual.[12,13,14] The synchronous occurrence of carcinoma of the uterine cervix and the breast is still a rarity.[12,15] We are aware of other reported cases of dual malignancies in Nigeria.[16,17] but this index case is the first involving the breast and the cervix.

The possibility of multiple primary malignancies existence should always be considered during pretreatment evaluation,[8] and the prognosis of its patients should be determined independent by the stage of each malignancy with the most aggressive and advanced cancer being addressed first.

CONCLUSION

Prognosis of patients with dual synchronies cancers may depend on the underlying genetic detects. The proper investigation of these patients might uncover predisposing genetic abnormalities that might benefit their families. The possible presence of multiple primary malignancies should always be considered during pretreatment evaluation and screening should be gear toward early detection of associated tumors.

CONFLICTS OF INTEREST

None.

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