CASE REPORT

The Unfortunate Case of Triple Primary Malignancies

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ABSTRACT

We herein report a rare case of triple primary malignancies in a single patient. A 51-year-old Burmese lady without a family history of malignancies or known genetic predisposition developed three primary malignancies involving breast, colon and uterus within two years. She was first diagnosed with left metaplastic breast cancer (pT2N0M0) in 2018 and underwent a mastectomy and axillary clearance. She then presented to us with intestinal obstruction and per vaginal bleeding. A CECT abdomen and pelvis was performed and proceeded with emergency right hemicolectomy for obstructed hepatic flexure tumour. The histopathology of the right hemicolectomy specimen revealed mixed neuroendocrine and non-neuroendocrine neoplasm (MiNEN). Endometrial pipelle sampling showed endometroid carcinoma. A multidisciplinary team approach is crucial in managing patients with multiple primary malignancies in order to achieve the best onchological outcomes.
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Keywords: Triple malignancy, Synchronous tumor, Sporadic cancers, Mixed neuroendocrine and non-neuroendocrine neoplasm (MiNEN)

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INTRODUCTION

Multiple primary malignancies were described as a tumour with a different histologic pattern and location of origin and produced its metastasis besides excluding the possibility of metastasis of one another. The rarity increases with the number of primary tumours, as triple primary malignancy prevalence accounts for 0.5% (1). The pathophysiology remains enigmatic and attributable to multifactorial cause such as oncogenic predisposition, smoking, diet and genetic inheritance. We want to report a case of triple primary malignancies in the absence of specific genetic or familial predilection.

CASE REPORT

A 51-year-old Burmese lady with underlying diabetes mellitus was diagnosed with left metaplastic breast carcinoma (pT2N0M0) in 2018. She underwent left mastectomy with axillary clearance and is currently in remission. She was then started on tamoxifen 20mg/day following her hormonal status. During this admission, she presented with symptoms of intestinal obstruction for three days with concurrent history of per vaginal bleeding since a year ago. Otherwise, neither abnormal bowel symptom nor constitutional symptom was recognized. Clinically, the abdomen was distended with no signs of peritonism. A friable fungating mass was seen per vaginally with contact bleeding, and endometrial pipelle sampling was sent for examination. Her full blood counts showed microcytic hypochromic anaemia with marked leukocytosis, whereby other biochemical tests were within normal limits. A segmental small bowel dilatation on the abdominal x-ray, with subsequent contrasted-enhanced computed tomography of the abdomen and pelvis, showed colonic mural thickening at hepatic flexure, causing luminal narrowing with a transition zone of bowel dilatation apart from significant uterine wall thickening (Figure 1, 2 and 3). Subsequently, an emergency exploratory laparotomy and right hemicolectomy for obstructed hepatic flexure tumour were done. Intraoperatively noted a long segment of tumour extending from ascending colon up to hepatic flexure. There were no synchronous tumour or metastatic lesions. She developed septicemia postoperatively and was nursed in the ICU for several days. She recovered well and was discharged on postoperative day 16. Histopathology examination of right hemicolectomy specimen revealed 70% of poorly differentiated neuroendocrine neoplasm with 30% of moderately differentiated adenocarcinoma (MiNEN). There was no lymphovascular invasion, and the surgical margins were free from the tumour (pT3N0M0). Pipelle sampling showed grade 2 endometroid carcinoma. Two months after recovered from the abdominal surgery, she underwent total abdominal hysterectomy and bilateral salpingoophorectomy (TAHBSO) and the histopathology

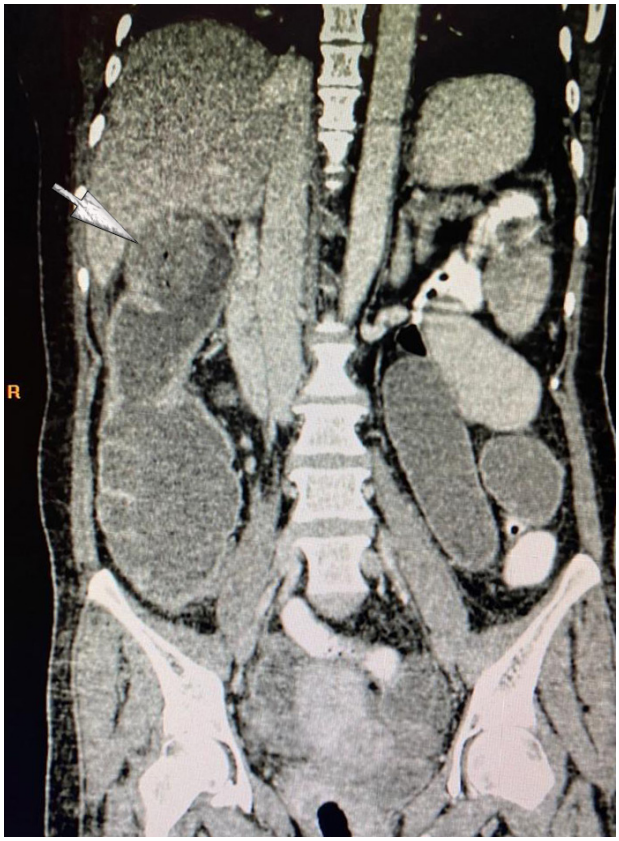

Figure 1: Coronal view of CECT abdomen and pelvis showing hepatic flexure obstructing tumour as pointed by the white arrow, with colonic dilatation proximal to the pathology

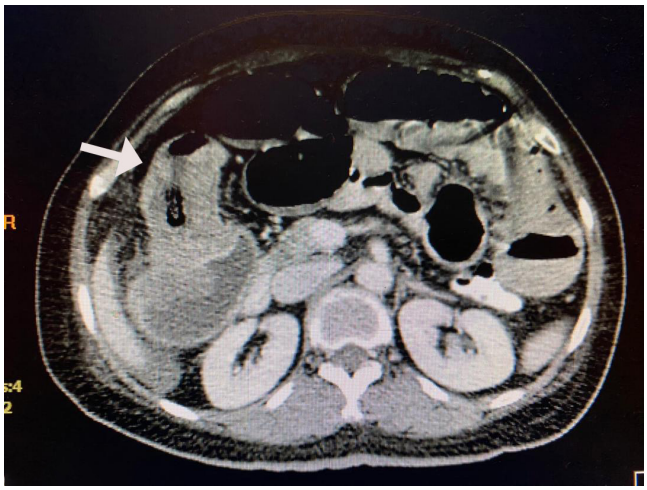

Figure 2: Axial view of CECT abdomen and pelvis with notable narrowing of lumen, thickening of mural as pointed by the white arrow

examination showed endometroid carcinoma (pT3N0, Figo stage IIIB). During the follow-up, the patient recovered well, and the oncology team has planned pelvic radiotherapy for the endometrial carcinoma. In view of multiple primary malignancies, we have suggested for her to undergo genetic evaluation, patient however refused due to financial constraints.

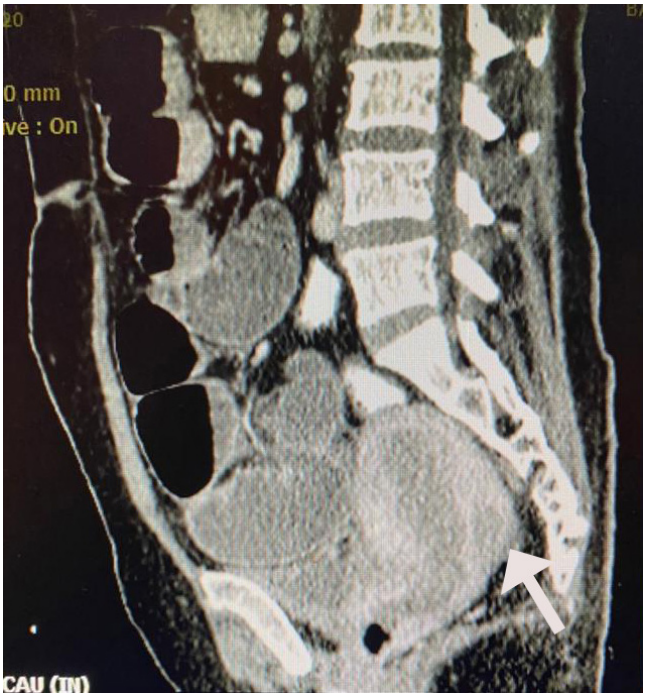

Figure 3: Sagittal view of abdomen and pelvis, showing thickened and irregular uterine wall as pointed by the white arrow

DISCUSSION

Two primary malignancies are reported between the range of 2-17% (1). The etiology is multifactorial and consist of environmental factors, hormonal factors, genetic predisposition, and treatment-related factors such as previous exposure to radiotherapy or chemotherapy predisposing an individual to develop future malignancies (2). Commonly, multiple malignancies are associated with inherited mutation, namely, Lynch syndrome, Li-Fraumeni, von Hippel Lindau syndrome and many more. They often have a strong family history of malignancies; therefore, genetic testing would be beneficial. However, our patient does not have any family history of malignancy, and due to financial constraints, genetic testing was not performed.

This patient has rare histologic subtypes of the colon and breast, MiNEN of the colon and metaplastic breast cancer, accounting for less than 1% of all colon and breast cancers. Based on the available data, it is associated with an aggressive tumour with a dismal prognosis (3). The histology of colon cancer was dominated by a high grade, poorly differentiated neuroendocrine tumour with a lesser degree of adenocarcinoma as the non-neuroendocrine component, 70% to 30%, respectively. Due to the rarity of this histology, there is generally a lack of consensus regarding its management. Current treatment strategies are based on multimodal and individualised approaches, as suggested by several retrospective studies (4).

The metaplastic subtype of breast cancer is associated with a poorer prognosis than its counterpart, infiltrating ductal adenocarcinoma subtype. Commonly it presented with large tumour size ironically sparing the respective node, as in our patient. Nevertheless, systemic therapy is less effective in this subtype; hence systemic chemotherapy was not offered in our patient. Adjuvant hormonal therapy with tamoxifen was initiated based on its receptor sensitivity which successfully provide remission until now. Chemoprevention therapy with tamoxifen is not without any adverse effects. It has been attributed to the occurrence of endometrial pathology, which subsequently predisposed to malignant transformation, namely endometrial carcinoma (5). As in our patient scenario, she has been on tamoxifen for two years. However, we are unsure whether tamoxifen chemoprevention therapy contributes to the development of endometrial cancer, as the duration of exposure is considered short.

To date, there is no consensus regarding the management of multiple primary malignancies, especially the rare histology counterpart. Therefore, if the individual cancer is feasible for curative treatment, radical therapy is indicated to provide the best survival outcome whenever possible. Although the management of this complex case is challenging in a district hospital due to various limitations, a multidisciplinary approach is eminent to ensure the best possible outcome for the patient.

CONCLUSION

In conclusion, more than two primary malignancies are considered a rare occurrence, compounded by a rare histology subtype, which entitles for subsequent DNA sequencing test to identify susceptible genetic coding and risk stratify the patient. Ideally, it may propagate into an individualized surveillance protocol for such patient, translated into earlier detection, intervention and subsequently, a better prognosis.

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