A Rare Combination of Synchronous Quadruple Primary Neoplasms: A Case Report and Literature Review

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Abstract
The prevalence of multiple primary neoplasms (MPNs) is slowly increasing due to prolonged survival of cancer patients with advances in diagnostic and therapeutic modalities. We report an exceptional combination of quadruple primary neoplasms composed of right sided adenocarcinoma of the colon, renal cell carcinoma, teratoma of the ovary, uterine leiomyoma and pre malignant high grade cervix dysplasia. These combinations were not reported before.

Keywords: Multiple primary tumors; Quadruple; Colon cancer

Introduction
Multiple Primary Neoplasms (MPNs) is defined as the occurrence of two or more malignancies in the same individual without any relationship between the tumors either simultaneously or with an interval of time. According to the cancer registries in the national Cancer Institute, cancer survivors had a 14% higher risk of developing a new malignancy than the general population [1,2].

Case Presentation
A 71-year-old female presented to the emergency department with right lower quadrant colicky abdominal pain and constipation for 2 months. The pain was localized not radiated to the periumbilical area or other abdominal regions. The patient has a history of 15 kg weight loss in the last 6 months. No history of bleeding per rectum, No family history of cancers, No fever, No history of autoimmune disease or inflammatory bowel disease. No history of previous abdominal surgery. The systemic review revealed on and off back pain. The patient is a known case of diabetes mellitus and hypertension for 10 years. Abdominal examination showed tenderness in right lower iliac fossa, No palpable masses or organomegaly, No ascites. Normal bowel sounds.

Investigations revealed red blood cells 3.82 M/ul. Hematocrit 28.5%. Hemoglobin 8.8 g/dl. Mean cell volume 73.2, no leukocytosis, normal platelets count. Liver functions profile showed albumin 26 g/L. Normal liver enzymes. Normal kidney functions.

Computed Tomography (CT-Abdomen) showed Solid mass involving the ascending colon, cecum, terminal ilium and causing obstruction to the appendix which is abnormally distended and fluid filled, giving a picture of acute appendicitis. The mass was infiltrating surrounding fat and peritoneum with regional lymphadenopathies. Three small ill-defined hypodense hepatic lesions are seen all are subcentimeter in size, these were suggestive of metastasis. An incidentally noted is left adnexal well-defined fat containing mass measuring about 7 cm (Figures 1 and 2).

Bone scan (Tc99m) was done and showed homogenous uptake with no evidence of bone metastasis. Colonoscopy was done and showed a fungating mass in ileocecal junction with biopsy taken. The patient underwent laparotomy where right hemicolecctomy and biopsy taken. The patient underwent laparotomy where right hemicolecctomy with the formation of stoma was done. The urologist performed right radical nephrectomy and the gynecologist did the hysterectomy and bilateral salpingo oophorectomy. Post-operative pathology showed 4 primary neoplasms and one premalignant condition.

- Invasive moderately differentiated adenocarcinoma of the right colon measuring 7 cm. Tumor invades through the muscularis propria into the fat reaching the serosal surface, margins were free. 3/29 lymph nodes are positive for metastasis. Acute malignant appendicitis (Figure 3)
- Chromophobe renal cell carcinoma measuring 3.5 cm. Margins were free. Normal adrenal (Figure 4)
- Left ovarian teratoma with immature elements, WHO grade 2 containing skin and thyroid tissue (Figure 5).
- Uterine Leiomyoma of the myometrium (Figure 6).

Figure 1: CT of the abdomen showing right ileocecal mass.

Figure 2: CT of the abdomen showing right ileocecal mass.
Discussion

Colorectal Cancer (CRC) is the third most common cancer in the world with more than 1.2 million new cases diagnosed each year [3]. It’s the most common malignant tumor in Saudi males [4].

In 1932, Warren and Gates [5] proposed the first definition of multiple primary cancer stating that: (a) each tumor must be malignant by histology; (b) each tumor must be anatomically distinct, and (c) the second tumor should not be a recurrence or metastasis of the first one. A synchronous cancer is defined as any cancer that occurs within six months of the first one whereas a metachronous cancer is one that occurs at least six months after the first cancer [6]. Our case presented with all four neoplasms and premalignant condition at the same time of presentation.

Second primary malignancy in males with renal cell carcinoma was found as high as 26.6% [7]. Most diagnosed synchronous double primary malignancies were lung cancer and head-neck cancers [8]. A review of 837 cases of colorectal carcinoma showed 32 cases (3.8%) of colorectal multiple primary malignant tumors in different parts of the colon and 11 cases (1.3%) of colorectal primary malignant tumor associated with extra colonic primary malignant tumor [9]. Cancer survivors have a 20% greater risk for developing a second primary malignancy than the general population [10].

A review of the recent literature indicates that MPNs appear more frequently in the upper digestive tract, respiratory system, head and neck region, or urogenital system; the reported incidence ranges from 2% to 10% [11]. Tianzhu He and colleagues report a case of double primary cancer combined of primary rectal carcinoma with renal cell carcinoma [12].

A review of the literature revealed no similar combination case of synchronous cancers with ovarian teratoma, uterine leiomyoma and cervical dysplasia. Table 1 showed extracolonic primary malignancies reported in recent literature. Metastatic disease has worse prognosis and survival rate than those with MPNs. There are many reports of successful multi Primary Neoplasms (MPNs) surgical resection [13]. Genetic factors, treatment exposure, alcohol abuse and environmental effect are among the etiological factors of MPNs. It is reported that radiotherapy associates with 8% MPCs, and the remaining are correlated with lifestyle behaviors and smoking [14]. Any other tumor should not be expected as a metastasis. Synchronous or metachronous tumors may exist. Assuming the second primary malignancy as...
metastasis will change the prognosis and the goal of treatment from curative to palliative [15-35].

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Table 1: Extracolonic primary malignancies reported in recent literature.

**Conclusion**

Our case has two primary malignant neoplasms in the right colon, right kidney, and a third premalignant dysplasia of the cervix. The patient had liver and spleen metastasis most likely from the colon cancer. It also has two benign tumors in the ovary and myometrium.

Surprisingly the ovarian teratoma contained thyroid tissue which can be a cause of occult hyperthyroidism. Unexpected event of our patient that she survived 2 years after successful adjuvant management with a myocardial infarction as an immediate cause of death. Clinician should not only think of recurrence or metastatic lesion in presentation or during follow up period, but also occurrence of second or higher primary lesions in cancer survivors.

**References**