A rare combination of synchronous quadruple neoplasms: a case report and literature review

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We report an exceptional combination of quadruple neoplasms composed of right-sided adenocarcinoma of the colon, renal cell carcinoma, teratoma of the ovary, uterine leiomyoma, and premalignant high-grade cervix dysplasia. These combinations were not reported before.

Keywords:
colon cancer, multiple primary tumors, quadruple

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Introduction

Multiple primary neoplasms (MPNs) are defined as occurrence of two or more malignancies in the same individual without any relationship between the tumors either simultaneously or with interval of time. The prevalence of MPNs is slowly increasing owing to prolonged survival of patients with cancer, with advances in diagnostic and therapeutic modalities [1].

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 [2].

Case presentation

A 71-year-old woman presented to the emergency department with right lower quadrant colicky abdominal pain and constipation for 2 months. The pain was localized, not radiated to periumbilical area or other abdominal regions. The patient has a history of 15 kg weight loss in the past 6 months, no history of bleeding per rectum, no family history of cancers, no fever, no history of autoimmune disease or inflammatory bowel disease, and no history of previous abdominal surgery. 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 organomegally, no ascites, and normal bowel sounds.

Investigations revealed red blood cells 3.82 mol/µl, hematocrit 28.5%, hemoglobin 8.8 g/dl, mean cell volume 73.2, no leukocytosis, normal platelet count, liver functions profile showing albumin 26 g/l, normal liver enzymes and normal kidney functions.

Computed tomography (abdomen) showed solid mass involving the ascending colon, cecum, and terminal ilium and causing obstruction to the appendix which is abnormally distended and fluid filled, giving picture of acute appendicitis. The mass was infiltrating surrounding fat and peritoneum with multiple regional lymphadenopathy. Three small ill-defined hypodense hepatic lesions are seen. All are subcentimeter in size, and these were suggestive of metastasis. Incidentally noted was a well-defined, solid, right renal mass measuring about 4 cm, most likely a malignancy, until proven otherwise, and also incidentally noted was a left adnexal well-defined fat-containing mass measuring ~7 cm (Figs 1 and 2).

Bone scan (technetium-99m) was done and showed homogenous uptake with no evidence of bone metastasis. Colonoscopy was done and showed fungating mass in ileocecal junction with biopsy taken. The patient underwent laparotomy where right hemicolectomy and primary anastomosis was done. The urologist performed right radical nephrectomy and the gynecologist did hysterectomy and bilateral salpingo-oophorectomy. Postoperative pathology showed four primary neoplasms and one premalignant condition as follows:

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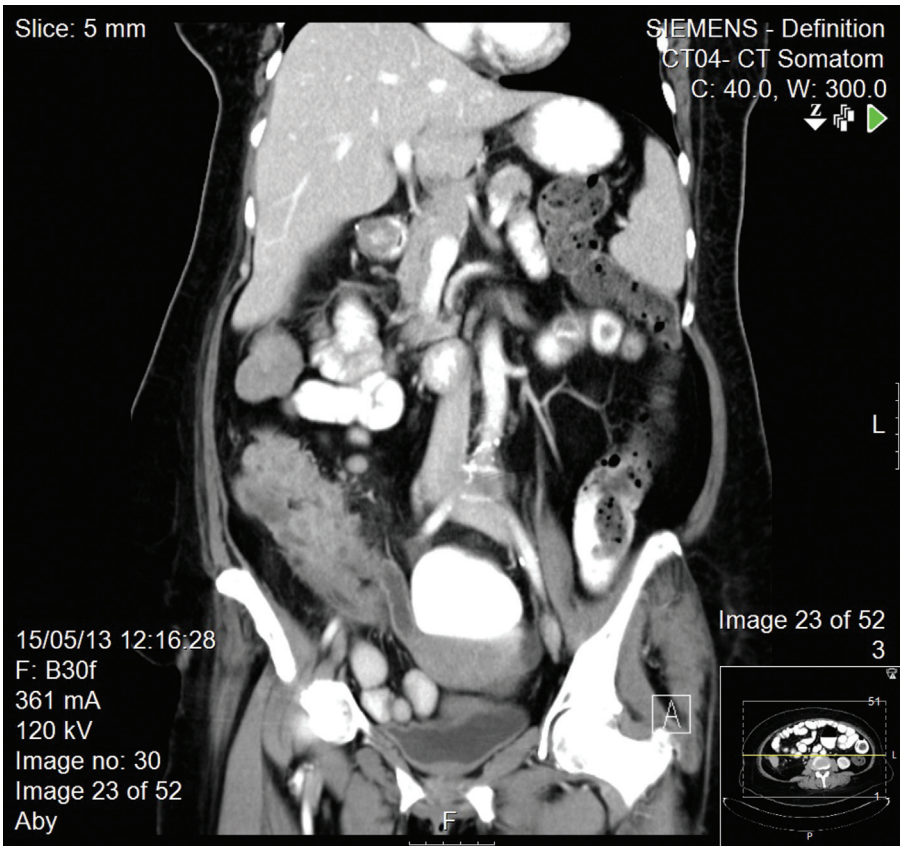
Figure 1



Computed tomography of the abdomen showing right ileocecal mass.

(1) 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. There was acute malignant appendicitis (Fig. 3).
(2) Chromophobe renal cell carcinoma measuring 3.5 cm. Margins were free. Normal adrenal (Fig. 4).
(3) Left ovarian teratoma with immature elements, WHO grade 2, containing skin and thyroid tissue (Fig. 5).
(4) Uterine leiomyoma of the myometrium (Fig. 6).
(5) Premalignant high-grade squamous dysplasia of the cervix CIN-2.

Discussion

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

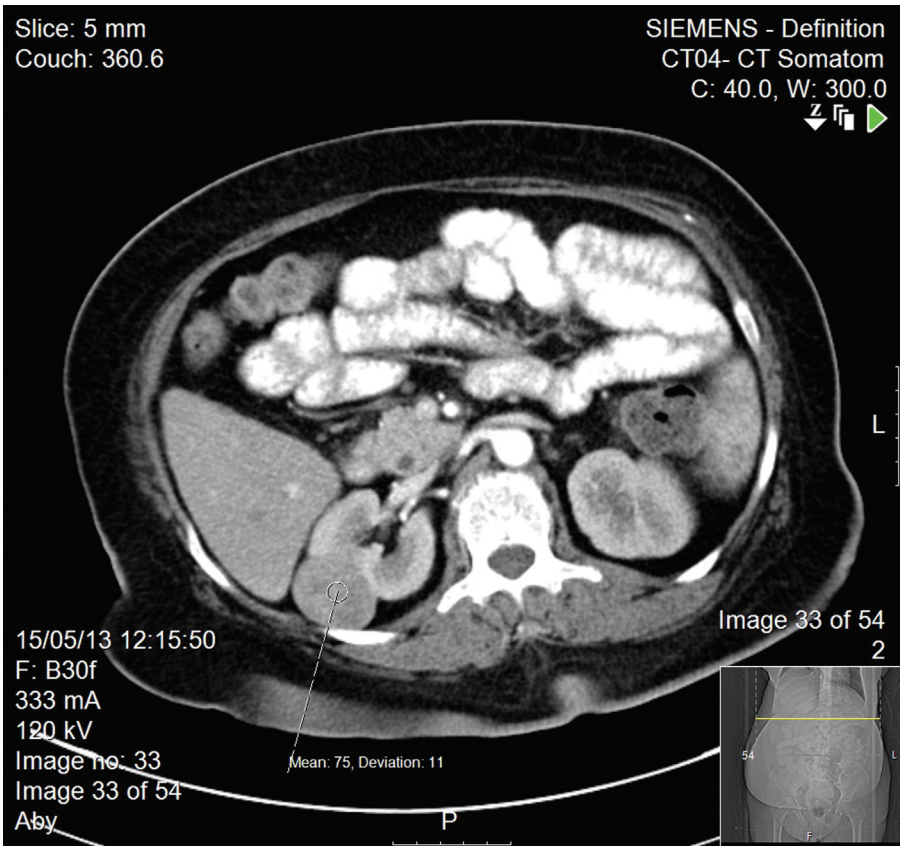
In 1932, Warren and Gates [5] proposed the first definition of multiple primary cancer stating that (a) each tumor must be malignant by histology, (b) each tumor must be anatomically distinct, and (c) the second tumor should not be a recurrence or metastasis of the first one. A synchronous cancer is defined as any cancer that occurs within 6 months of the first one, whereas a metachronous cancer is one that occurs at least 6 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 (3.8%) cases of colorectal multiple primary malignant tumors in different parts of the colon and 11 (1.3%) cases of colorectal primary malignant tumor associated with extracolonic primary malignant tumor [9]. Cancer survivors have a 20% greater risk for developing a second primary malignancy than the general population [10].

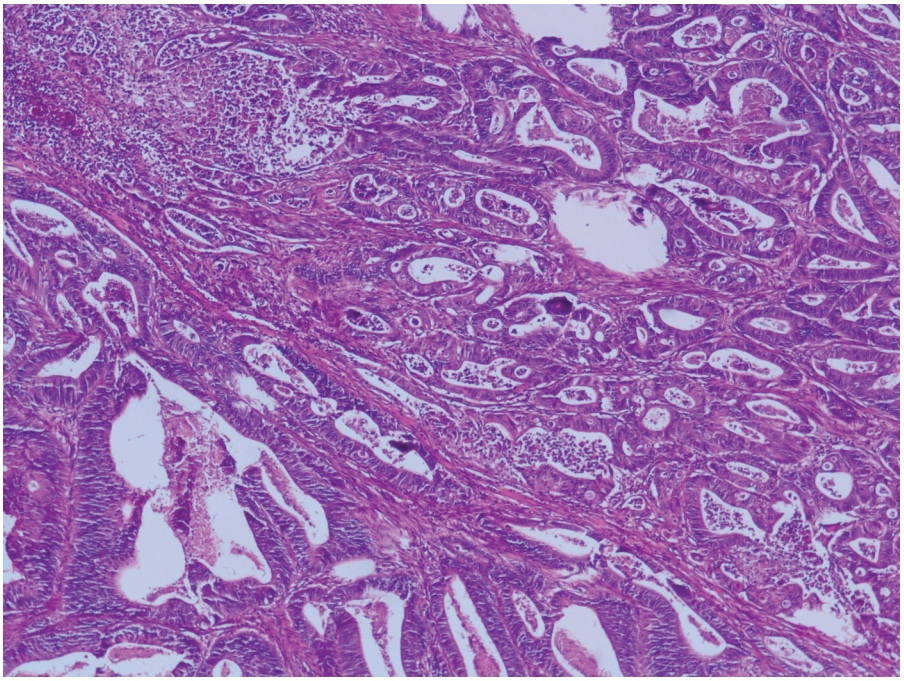
A review of the recent literature indicates that MPNs appear more frequently in the upper digestive tract, respiratory system, head and neck region, or urogenital

Figure 2



Computed tomography of the abdomen showing right kidney mass.

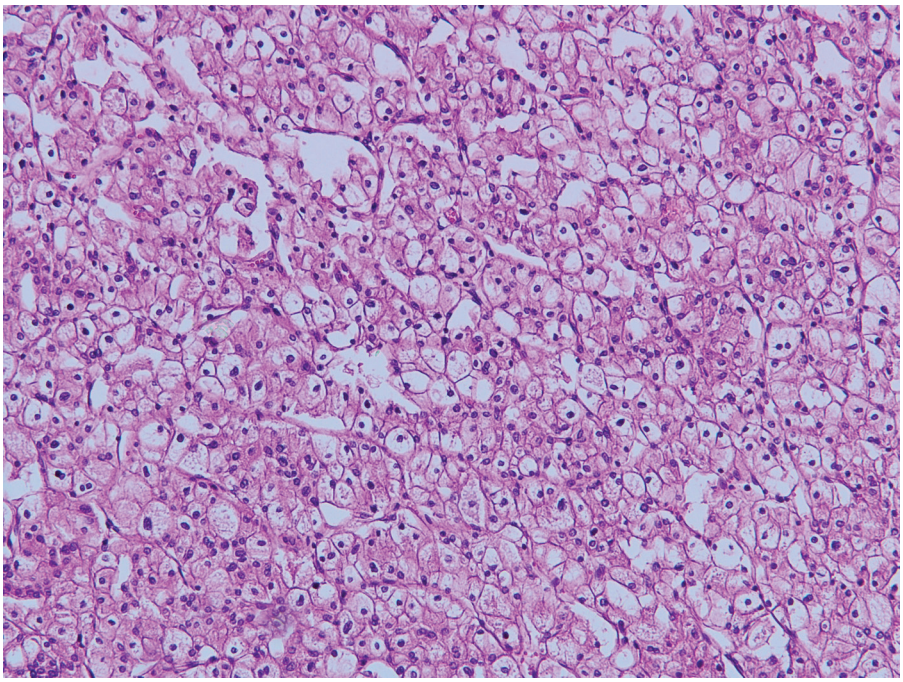
Figure 3



Histopathology showing adenocarcinoma of the colon.

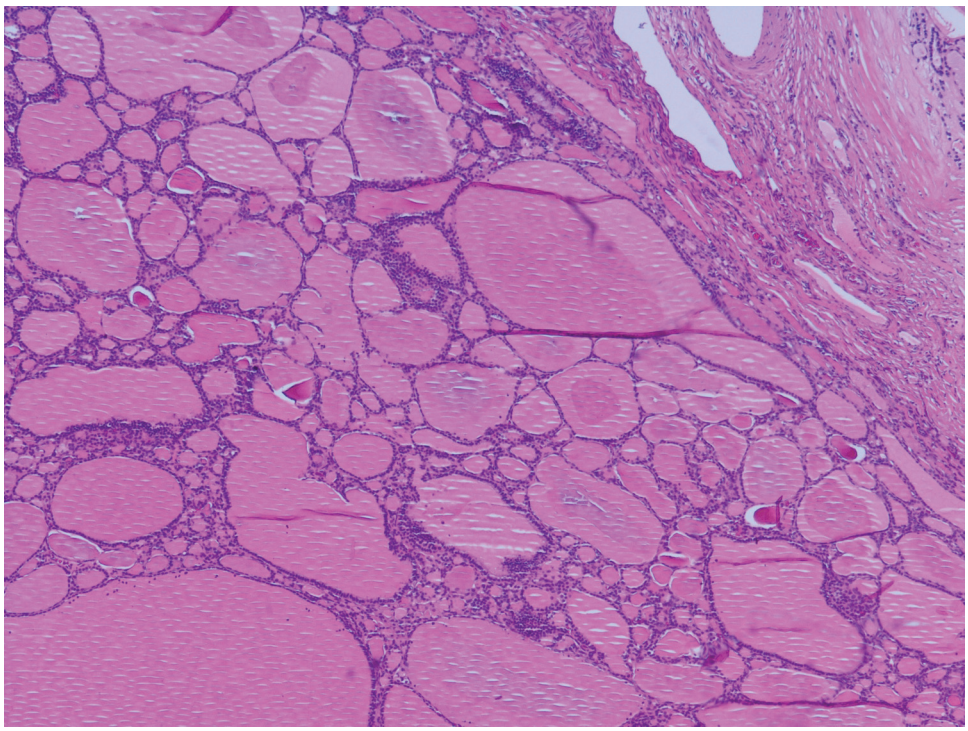
system; the reported incidence ranges from 2 to 10% [11]. Tianzhu He and colleagues [12] report a case of double primary cancer, combined of primary rectal carcinoma with renal cell carcinoma [13].

Figure 4



Histopathology showing renal cell carcinoma.

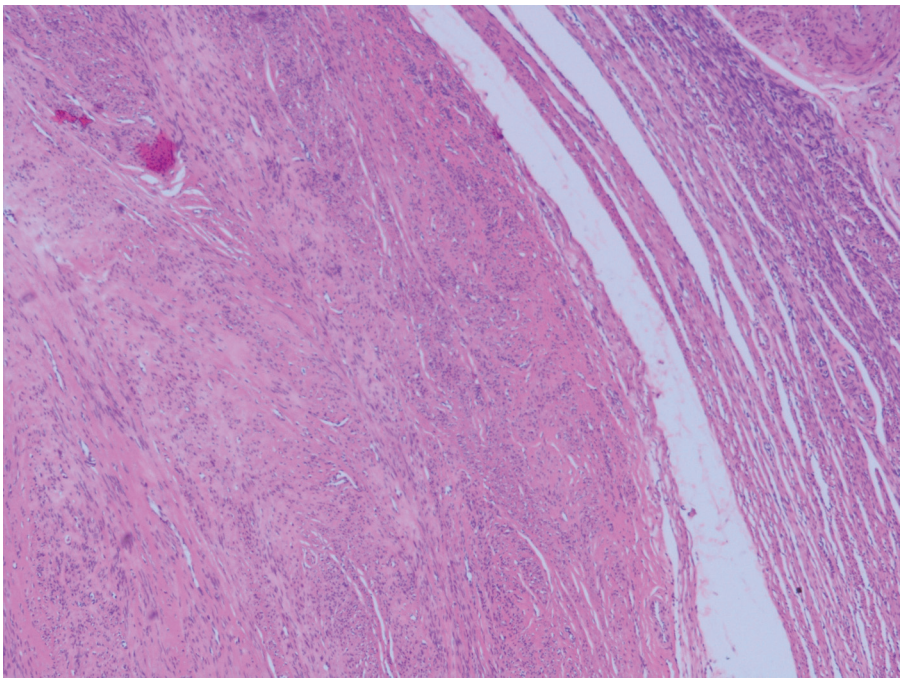
Figure 5



Histopathology showing ovarian teratoma with thyroid tissue.

A review of the literature revealed no similar combination case of synchronous cancers with ovarian teratoma, uterine leiomyoma, and cervical dysplasia. Table 1 shows 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 MPNs surgical resection [14]. Genetic factors, treatment exposure, alcohol abuse, and environmental effect are among the etiological

Figure 6



Histopathology showing uterine leiomyoma.

Table 1 Extracolonic primary malignancies reported in recent literature

First	Second	Third	Fourth	Fifth	Sixth	References
Large B-cell lymphoma	Colon					Yang *et al.* [16]
Colon	Breast					Nitipir *et al.* [17]
Kidney	Colon					Li *et al.* [18]
Stomach	Colon					Mederos *et al.* [19]
Colon	Kidney (urothelial)	Mesothelioma				Huang *et al.* [20]
Prostate	Lung	Colon				Feng *et al.* [21]
Lung	Colon					Kurishima *et al.* [22]
Endometrium	Colon					Lee *et al.* [23]
Colon	Kidney					Babu *et al.* [13]
Lung	Colon					Shuayb and Reza [24]
Prostate	Rectum					Watanabe *et al.* [25]
Colon	Mentle cell lymphoma					Yu *et al.* [26]
Colon	Non-Hodgkin lymphoma					Pachajoa *et al.* [27]
Prostate	Colon					Paola *et al.* [28]
Colon	Thyroid	Kidney				Peng *et al.* [29]
Colon	Glottis	Esophagus				Martin *et al.* [30]
Fallopian tube	Breast	Colon				Martin [30]
Colon	Bladder					Imagami *et al.* [31]
Esophagus	Stomach	Colon	Prostate	Colon		Arakawa *et al.* [32]
Stomach	Prostate	Colon	Bladder	Facial skin	Pancreas	Muto *et al.* [33]
Breast	Colon	Kidney				Parekh *et al.* [34]

factors of MPNs. It is reported that radiotherapy associates with 8% MPCs, and the remaining are correlated with lifestyle behaviors and smoking [15]. 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.

Our case has two primary malignant neoplasms in the right colon and 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 was that she survived 2

years after successful adjuvant management, with a myocardial infarction as an immediate cause of death.

Conclusion

Clinician should not only think of recurrence or metastatic lesion in presentation or during follow-up period but also occurrence of secondary or higher primary lesions in cancer survivors.

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Conflicts of interest

There are no conflicts of interest.

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