Double primary cancers registered in a tertiary care hospital: review of two cases

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Abstract: In our centre, among 1965 registered cancer patients between May 2011 and December 2013, we report three cases with multiple primary malignant neoplasms. One of them was excluded due to lack of data, and so we present the remaining two cases. The first case is an 82-year-old female patient with colon and thyroid cancer and the second case is a 61-year-old female patient with colon and breast cancer. Both cases were metachronous and discovered accidentally during the regular follow up, and managed with a curative intent. Conclusion: It is important for the clinicians to keep in mind that individuals with cancer are at increased risk for subsequent primary malignancies, which must be differentiated from recurrent or metastatic disease.

Keywords: Synchronous/metachronous • Primary malignancy • Multiple primary malignancies

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Introduction

Multiple primary malignant neoplasms (MPNMs) are defined as two or more malignancies in a single individual without any relationship between cancers [1]. It is not very rare, and has a marked increase in incidence in the past few years, possibly explained by the greater awareness, improved diagnostic techniques and facilities [2-5]. This entity was first described by Billroth at the end of the 19th century [6]. One of the earliest statistical analyses of MPNMs was carried out by Bugher in 1934 [7]. In our report, we present two cases with double primary tumours; one is a patient with colon cancer and a metachronous thyroid cancer and the other is a patient with colon cancer and a metachronous breast cancer.

Case Report (1)

An 82-year-old female patient was referred to our centre (King Abdullah Medical Center; Holy Capital) as a case of acute abdomen on 8 December 2012 for further investigation and management.

Her condition had started 2 months before with constipation of gradual onset and progressive course associated with nausea and vomiting, which finally resulted in a complete obstruction.

She had a history of diabetes mellitus type II and was on oral hypoglycaemic medications; she was subjected to an open cholecystectomy procedure more than 10 years ago due to gall stones. She had no relevant family history. On physical examination, her abdomen was distended and tender on palpation. There was a palpable mass in the left iliac region, and bowel sounds were not audible. On laboratory testing, she had a serum chemistry panel and complete blood count within normal limits. Computed tomography scan of the upper and lower abdomen revealed a colorectal mass causing complete intestinal obstruction (ileus). Urgent laparotomy was performed with resection of the colonic mass and diverting colostomy. The histology examination revealed (Figure 1):

- Moderately differentiated adenocarcinoma
- Tumour size 3 cm
- Tumour invades through the muscularis propria into the pericolic fat

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Figure 1. Adenocarcinoma of recto sigmoid, magnification 2.52×, H & E.

Figure 3. Thyroid carcinoma, nuclear grooves and inclusion, magnification 63×, H & E.

Figure 2. Post-contrast computed tomography showed left thyroid nodule.

- One lymph node was positive out of seven resected
- Lymphovascular invasion: not identified
- Perineural invasion: not identified.

The patient had a smooth recovery and was discharged 10 days after the operation. Post-operation evaluation and staging by computed tomography scan of the chest, abdomen and pelvis revealed no evidence of tumour residual or distant spread; at this time, she was started on capecitabine as adjuvant treatment and completed eight cycles without any significant adverse events. Three months later, computed tomography scan of the chest, abdomen and pelvis as part of her follow up revealed a left thyroid nodule measuring 2.6 cm × 1.2 cm with multiples cystic areas inside (Figure 2).

Fine needle aspiration cytology of the nodule revealed papillary carcinoma; at this time, she was transferred to the Head and Neck clinic for further management. Total thyroidectomy was performed and the histology examination revealed (Figure 3) the following:

- Left thyroid lobe: papillary carcinoma, follicular variant with negative surgical margins and no lymphovascular invasion
- Right thyroid lobe and isthmus: multinodular goiter.

Whole body iodine scan showed residual functioning thyroid tissue in the right lobe bed and regional lymph nodes without evidence of distant metastasis. She subsequently received an ablative dose of radioactive iodine 131 with 30 mCi. Currently, she is under follow up in the outpatient clinic with L-thyroxin therapy and calcium tablet supplementation.

Case Report (2)

A 61-year-old female colon cancer patient was transferred to our oncology centre in November 2011 for further management. Her condition had started 2 months before with intermittent diarrhoea, alternating with rectal bleeding, and associated with abdominal pain and weight loss. The patient was referred as an emergency to the nearest hospital with a possible situation of obstructive ileus, with vomiting and abdominal distension. Clinical examination revealed a distended, tender abdomen and inaudible bowel sounds.

Computed tomography scan of the upper and lower abdomen revealed a malignant stricture in the sigmoid colon with proximal colonic dilatation. In routine blood tests no abnormal findings were revealed. Urgent

Figure 4. Post-contrast computed tomography abdomen revealed malignant stricture sigmoid colon with proximal colonic dilatation.

Figure 5. Adenocarcinoma of colon, magnification 2.52 $\times$, H & E.

laparotomy had to be performed with right hemicolectomy and end-to-end anastomosis. The histology examination revealed adenocarcinoma of the colon (Figure 4).

The computed tomography of the abdomen revealing the relevant mass is shown in Figure 5. The histopathology report showed:

- Moderately differentiated adenocarcinoma infiltrating the entire thickness of the wall and adjacent pericolic fat
- Presence of perivascular and perineural invasion
- Negative surgical margins
- Three out six lymph nodes positive for metastasis.

Figure 6. Mammogram revealed ill-defined speculated soft tissue mass.

Post-operative re-assessment showed no local recurrence or metastatic spread. Being a stage III colon cancer patient, she subsequently received adjuvant chemotherapy with six cycles of FOLFOX. Since the completion of adjuvant chemotherapy, she was under regular follow up in our oncology centre. Six months after the end of adjuvant chemotherapy, a small right breast mass (2 cm $\times$ 2 cm) was clinically discovered accidentally. Bilateral mammogram and complementary breast ultrasonography revealed a small right breast mass (1.5 cm $\times$ 1.5 cm) with microcalcification, which was highly suspicious for malignancy (Figure 6).

Right breast lumpectomy with right axillary sentinel lymph node dissection was performed and the histology revealed the following (Figure 7):

- Invasive ductal carcinoma
- Grade II
- Tumour size 1.0 cm $\times$ 0.6 cm
- Negative surgical margins
- Negative lymphovascular and perineural invasion
- All lymph nodes were free of disease (0/5)
- Estrogen Receptor (ER) and Progesterone Receptor (PR) were positive and (human epidermal growth factor receptor 2) HER-2 was negative (score 0).

The patient was diagnosed as having breast cancer stage I (intermediate risk) and subsequently received four cycles of adjuvant chemotherapy with anthracycline and cyclophosphamide, followed by adjuvant radiotherapy and adjuvant hormonal therapy. Thereafter, she continued to be under regular follow up in the outpatient clinic of our oncology centre.

Figure 7. Invasive ductal carcinoma of breast, magnification 6.3×, H & E.

Discussion

MPMNs may be synchronous or metachronous neoplasias, depending on the interval between the respective diagnosis. Synchronous malignancies are second neoplasias occurring simultaneously or within 6 months after the first malignancy, while metachronous multiple malignancies are secondary neoplasias developed more than 6 months after from the first malignancy [8].

Three diagnostic criteria have been proposed for MPMNs: 1) each tumour must present definite features of malignancy, 2) each must be distinct and 3) the chance of one being a metastasis of the other must be excluded [9].

MPMNs are classified into four types: 1) multicentric, if the two distinct carcinoma arise in the same organ or tissue; 2) systemic, if they arise on anatomically or functionally allied organs of the same system; 3) paired organs, as in the breasts; and 4) random, if they occur as a co-incidental or accidental association in unrelated sites [10].

The frequency rate ranges between 0.7% and 14.5% [11, 12]. This wide range is misleading and questionable as no acceptable average rate can be quoted. There are a number of factors responsible for this wide range including the following:

- The majority of published data on MPMNs are case reports that are difficult to assemble into a meaningful frequency rate [13, 14].
- It is not clear in many of the reports whether the mentioned ranges refer to the number of patients with MPMNs as a whole, or to synchronous, metachronous or both [15, 16].

- Most reports lack unified definition of MPMNs, synchronous and metachronous lesions [17, 18].

Probable aetiology and mechanisms of multiple primary cancers include genes, environmental factors, treatment effects or combinations of the above mentioned. When researchers focus on genes as causal mechanisms, they often concentrate on cases diagnosed earlier in life in young individuals [19].

Although, for example, bladder and prostate cancer can coexist in the same individual rather frequently [20–22], the combination of colon cancer and either thyroid cancer or breast cancer are uncommon. In the two cases described here, there was no apparent family history and no predisposing factors or either malignancy.

The prognosis of patients with MPMs can be determined independently by the stage of each malignancy. Surgery is the treatment of choice for metachronous multiple primary malignancies if curative resection of each malignant tumour can be performed [23]. In the cases presented here, metachronous malignancies were discovered accidentally during regular follow up. In both cases, they were in early stages that gave us the chance for curative treatment. A large population base is needed in order to perform meaningful research on multiple primary cancers; such a population base will require extensive collaboration between cancer registries.

Conclusion

A cancer diagnosis should not exclude the existence of another concomitant malignancy, especially in patients older than 60 years of age.

Consent

Written informed consent was obtained from the patients for publication of this case report and any accompanying images. A copy of the written consent is available for review from the Editor-in-Chief of this journal.

Conflict of Interest

The authors certify that there is no actual or potential conflict of interest in relation with this article.

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