Case Report

Multiple Primary Tumors

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Abstract

Multiple primary tumors occur in clinical practice causing diagnostic dilemma. It is not very common, but the incidence has increased gradually since it was first described very many years ago. However, in spite of its increasing incidence, the presence of such primary malignancies in the breast and colon has been rare and far between, as against its presence in breast and lungs, both breasts, colon and stomach, two colonic sites, and endometrium and ovaries. It could be due to genetic disorders such as Li-Fraumeni syndrome in which case the affected individuals develop multiple cancers in childhood or early adulthood. This is, however, very rare. It could be due to metastasis of one cancer to another site. The challenge is making a correct diagnosis and giving the appropriate management. Erroneously handling one as a metastasis of the other and instituting management as such would be inappropriate. It is necessary to make proper clinical and histopathological diagnosis and to institute proper management. We report the case of a woman who had primary cancers involving rare organ combinations of the breast and ascending colon.

Keywords: *Carcinoid, colorectal cancer, metachronous, synchronous*

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Introduction

Multiple primary cancers occurring in more than one site are not a rarity. This could be synchronous or metachronous, occurring at the same time or at different times, respectively. It is said to occur in the endometrium and ovary in 5% of women with endometrial and 10% of women with ovarian cancer,[1] 3.4% in patients with gastric cancer, with the most common other primary cancer being colorectal, (20.4%).[2] Samadder *et al*. found 0.71% and 1.60% of synchronous and metachronous colorectal cancer (CRC), respectively, in patients with CRC.[3] The presence of multiple primary cancers was first reported about 100 years ago.[4] Since then, the frequency of occurrence has gradually increased.

It is necessary to distinguish between the occurrence of two primary cancers and one being a metastatic cancer of the other. This differentiation is necessary for proper management of the patient, especially in terms of staging, type of surgery, chemotherapy to be given, and the eventual prognosis. Resolving this dilemma has been difficult, prompting many authors to describe many molecular tests for resolution. However, there is no consensus on the best method to achieve this. Diagnostic criteria proposed by Ulbright and Roth[5] were revised by Scully.[6]

This is a case report of a patient with synchronous primary cancers of the breast and colon.

Case Report

The patient is a 62-year-old homemaker who presented with an 18-month history of left breast swelling and a 6-month history of abdominal mass. The painless breast swelling started out as a "pimple," but it gradually increased in size. No swelling in the armpit. She applied local balm to no avail. Two months after the onset of breast swelling, she noticed a change in bowel habit, with the passage of mucoid nonbloody watery stool about four times a day. This was accompanied by occasional colicky lower abdominal pain. There was associated weight loss, nausea but

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no vomiting; 2 months later, she noticed a swelling in the right lower abdomen which gradually increased in size.

A year after onset of breast swelling, she sought orthodox medical help, and after investigations, which included a breast computed tomography, and reported as Birads 4, She was told that she would need a mastectomy but she objected.

She did not seek further medical help until the abdominal swelling became obvious and very painful.

She attained menarche at 18 years, had her first full term pregnancy at age 22, breastfed all her five children for 1 year each, and reached menopause at 40.

There were no history of use of oral contraceptive drugs and no family history of breast cancer or other cancers. She never smoked or drank alcohol.

Examination revealed an elderly woman, mildly pale, anicteric. There was a 10 cm × 8 cm mass in the upper outer quadrant of the left breast, hard, fixed to skin but not to underlying structures. There were matted ipsilateral axillary nodes.

There was a palpable 12 cm × 10 cm mass in the right iliac fossa, hard, fixed to the skin, and posterior abdominal wall.

Fine-needle aspiration cytology of the breast mass was C5. Abdominopelvic ultrasound scan revealed a right iliac fossa mass and Hepatic metastasis. Chest X-ray and electrocardiogram results were normal. Her packed cell volume was 22.6%, white blood cell was 13100, erythrocyte sedimentation rate was 55 mm/h. Electrolytes were normal. She was transfused with 2 pints of blood and was prepared for surgery. She had both modified radical mastectomy and exploratory laparotomy in which a right hemicolectomy was done [Figure 1]. Intraoperative findings were a 10 cm × 8 cm tumor in the ascending colon, involving the serosa and was fixed to the posterior abdominal wall. No other part of the gastrointestinal tract was involved with tumor. Matted nodes were seen along the right colic artery to its origin. There were also matted ipsilateral axillary nodes. She had an uneventful recovery.

Histopathology [Figure 2] showed invasive ductal carcinoma with involvement of the lymph nodes. It was estrogen receptor negative, progesterone receptor negative, and human epidermal receptor 2 negative, that is, the cancer is triple negative.

The cut section of the colonic specimen [Figure 3] showed normal cecum and a tumor in the ascending colon from the mucosa involving the wall (muscular layer) of the colon. Histopathology [Figure 4] showed

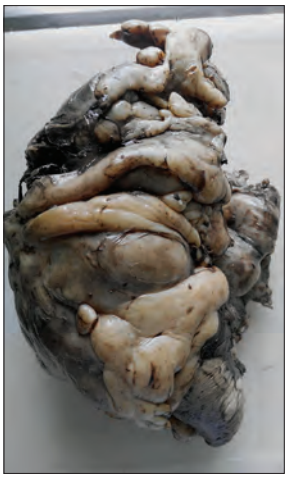

Figure 1: Right hemicolectomy specimen

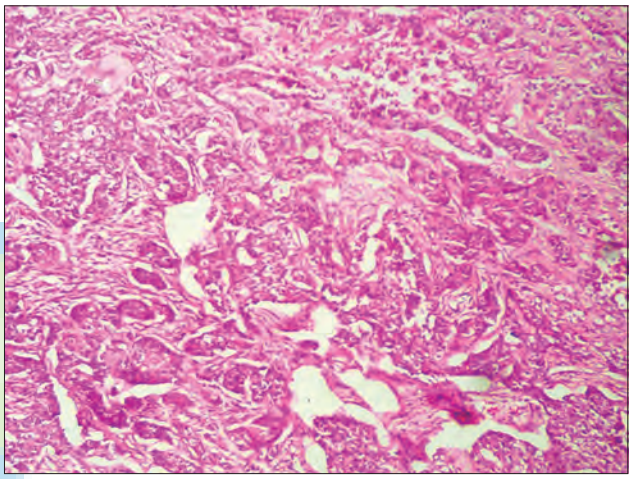

Figure 2: Photomicrograph of invasive ductal carcinoma of the breast pleomorphic neoplastic ductal cells with hyperchromatic to vesicular nuclei

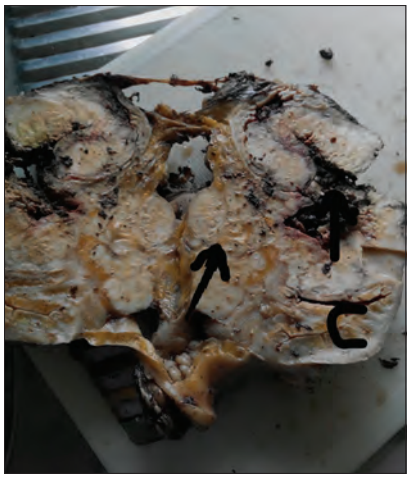

Figure 3: Cut section of the surgical specimen showing the normal caecum (C) and tumor in the ascending colon and lymph nodes

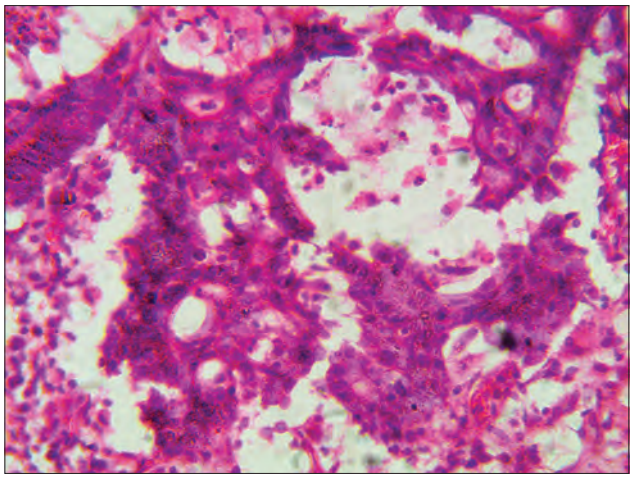

Figure 4: Photomicrograph of the ascending colon showing well-differentiated neuroendocrine neoplasm

solid nests and sheets of uniform round- to oval-shaped cells with central monomorphic nuclei showing finely stippled chromatin and scanty cytoplasm and faint red cytoplasmic granules with infiltration of the muscular layer of the colon. The tumor cells are strongly positive to chromagranin and AE1/AE3. Features are those of carcinoid tumor of the colon.

She was eventually referred to the oncologists for chemotherapy and radiotherapy.

Discussion

The possibility of the presence double cancers in patients is not always considered but it is very necessary to know and be aware that other cancers can occur in addition to any cancer, especially CRC, either as a synchronous or metachronous cancer. In a series, it was found that in 1.65% of cases, CRC was accompanied by other cancers,[7] of which 35.2% each were breast cancers and gastric cancers. Others included lung, skin, thyroid, cervical, ovarian, and urinary bladder cancers. Multiple primary cancers constitute about 5.5%–8.5% of all cancer cases.[8]

It is apt to differentiate a synchronous primary from a metachronous primary and also from a metastatic spread. This is difficult to do based on clinical findings[9] alone and no consensus[10] on the definition of these terms has been reached. However, synchronous cancers could be defined as two histologically distinct, simultaneously detected malignancies or two histologically distinct malignancies diagnosed during the same hospital admission[11] or two histologically distinct malignancies, arising in the same site, following each other in sequence of <2 months.[4,12] To decide whether a second cancer is a primary or a metastasis is also very difficult. This has necessitated the use of Warren and Gates criteria:[13]

1. Each tumor must have a definite picture of malignancy
2. Each tumor should be histologically distinct
3. The possibility that one is a metastasis of the other must be excluded.

The two tumors in this case have distinct pictures of malignancy and are both histologically distinct. It is therefore difficult to identify one as a metastasis of the other. Breast metastasis from nonmammary primary cancer like the colon is rare, accounting for <2%[14] of all breast cancers, ditto for colon metastasis from noncolonic primary cancer.

The presence of multiple primary cancers is more common in similar organs or organs of the same system,[15] but it is very rare in different organs or different systems such as the breast and colon or breast and lung. Hence, in this case, double primary cancers is the more likely diagnosis rather than one being a metastasis of the other, given that they are histologically distinct (invasive ductal carcinoma in the breast and carcinoid tumor in the ascending colon) and separate (breast and colon). Chromagranin stain was not done for the breast specimen because carcinoid tumors are rare in the breast and the histology type of the breast tumor was invasive ductal. Moreover, spread of breast cancer to the ascending colon is extremely rare. This tallies with NAACCR definition that "multiple lesions of different histologic types occurring in different sites are considered as separate primaries whether occurring simultaneously or at different times."[16]

Carcinoid tumors are mainly found in the gastrointestinal tract, occurring in the appendix, ileum, rectum stomach, and colon in decreasing order.[17] Majority are small lesions, <1 cm, and can be treated with local excision endoscopically and/or transanally, while larger ones (above 2 cm) require surgical resection. Patients may present with classical carcinoid symptoms of flushing and diarrhea. When these occur in the presence of hepatic metastasis, it is carcinoid syndrome. In addition to flushing and gut hypermotility, patients could present with abdominal pain, weight loss, intestinal obstruction, constipation, and lower gastrointestinal bleeding. While patients with carcinoid tumor may be asymptomatic, midgut carcinoids are likely to be symptomatic at diagnosis. They present late due to the liquid content of the right side of the colon and its capacity to expand compared to the rigid left side. They are therefore more likely to have metastatic disease at presentation.[18] Our patient had bouts of diarrhea before she noticed the presence of a right lower abdominal swelling. There was spread to regional lymph nodes at surgery and she had hepatic metastasis.

A differential diagnosis of this condition is Li-Fraumeni syndrome, a genetic disorder. However, it was not considered here because it is very rare, patients usually have multiple childhood or early adulthood tumors. Bone cancer is usually one of the cancers in this syndrome. None of these was present in this patient.

In addition to oncologic resection, adjuvant chemotherapy is mandatory in metastatic disease.

This rare occurrence of two primary tumors in the breast and colon necessitated this case report. It is necessary to take patients through proper evaluation so that a second primary tumor will not be missed or misdiagnosed as a metastasis.

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Conflicts of interest

There are no conflicts of interest.

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