Triple horror: A rare case of triple metachronous malignancy

Sir,

Herein, we present an exceptional case of a premenopausal female who got initially treated for carcinoma of the right breast but subsequently developed malignant spindle-cell tumors of the right lung and tongue metachronously. To the best of our knowledge, such a combination of multiple primary malignancy (MPM) has never been reported earlier in the literature. MPM is defined as the existence of two or more malignancies, synchronous or metachronous, in different organs unrelated to each other.[1] The incidence of MPM has increased over the past years secondary to the long-term survival of cancer patients due to improvements in the early detection and adequate treatment of malignancy. Despite its low incidence, the association of dual malignancies in a single patient has been widely reported in the literature, whereas only a few cases of triple malignancies have been described.

The index case is a 27-year-old female who developed carcinoma of the right breast in 2013. She was clinically staged as T4b N2 M0 after detailed workup. The tumor was positive for the estrogen receptor and human epidermal growth factor receptor 2 and negative for progesterone receptor on immunohistochemistry. She received neoadjuvant chemotherapy with four cycles of docetaxel and epirubicin (DE) followed by right modified radical mastectomy. Postoperative histopathological examination revealed a tumor of 3 cm × 2 cm × 1 cm involving overlying dermis with ulceration of epidermis and close to deep resected margin (<1 mm). Twelve axillary lymph nodes were identified, of which four were involved with soft-tissue tumor deposits [Figure 1a]. She further received adjuvant chemotherapy with two more cycles of DE and radiotherapy of dose 50 Gy in 25 fractions over 5 weeks to the right chest wall, axilla, and supraclavicular region till September 2013. She was started on hormone therapy with tamoxifen and kept on follow-up. After a disease-free interval of 2 years, she developed metastases to multiple skeletal sites and brain. Then, she received palliative radiotherapy to the whole brain (20 Gy/5 fractions over 1 week), vertebral, and pelvic bone metastases (8 Gy/1 fraction) in November 2015. She was started on palliative systemic therapy with lapatinib and capecitabine. Follow-up contrast-enhanced computed tomography scan of the neck, chest, abdomen, and pelvis and contrast-enhanced magnetic resonance imaging of the brain were done in June 2016 which showed metastatic lesions in the brain, both lungs, bone, bilateral adnexae, and a well-defined mass (7.2 cm × 6.4 cm) in the right upper lobe of the lung with broad base toward costal pleura and medially abutting the superior vena cava [Figure 2]. Biopsy from this right upper lobe lung mass was done which showed a malignant spindle-cell tumor immunopositive for vimentin, desmin, MIC2, and EMA (focal weak) while negative for spinal muscular atrophy (SMA), CD34, myogenin, Bcl2, calretinin, and cytokeratin (CK) [Figure 1b]. Hence, she was placed on the second-line palliative chemotherapy with lapatinib and vinorelbine and also received palliative radiotherapy to the right lung mass (20 Gy/5 fractions over 1 week). After 7 months into treatment, in December 2016, she noticed a swelling in the right lateral border of the tongue. A biopsy from this lesion was done, which revealed features of malignant spindle-cell tumor [Figure 1c]. The tumor cells were positive for vimentin and SMA (focal) while negative for CK, EMA, p40, and desmin. Meanwhile, she developed dyspnea for which supportive management was initiated, but eventually, she succumbed to respiratory failure.

Synchronous cancer occur simultaneously or within an interval of 6 months, whereas metachronous cancer follow in sequence and occur >6 months apart, each of which must be distinct with no possibility of one being the metastasis of the other.[2] In the study by Bittorf *et al.*, 57 (0.1%) of 52 398 included patients had a minimum of three primary malignancies.[3] The frequently observed combination of MPM is that of colorectal carcinomas with urogenital or gynecological tumors. Management of MPM is tricky and depends on whether malignancies are appearing simultaneously or metachronous. In synchronous setting, improving the general condition of the patient holds utmost importance followed by radical treatment of each primary, if possible, otherwise, the patient may be administered palliative therapies, including chemotherapy

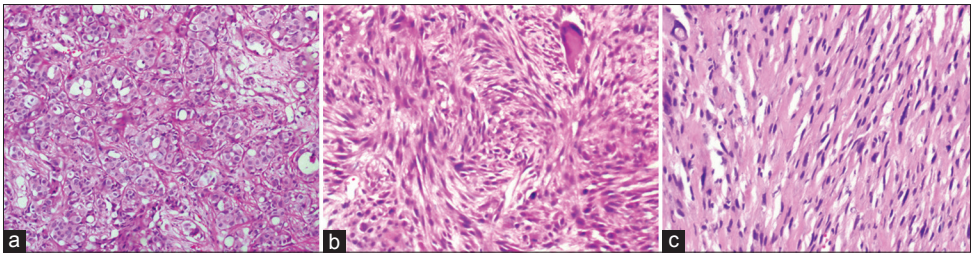

Figure 1: Histopathological examination showing (a) invasive ductal carcinoma, (b) features of malignant spindle-cell tumor in the lung, (c) features of malignant spindle-cell tumor in the tongue

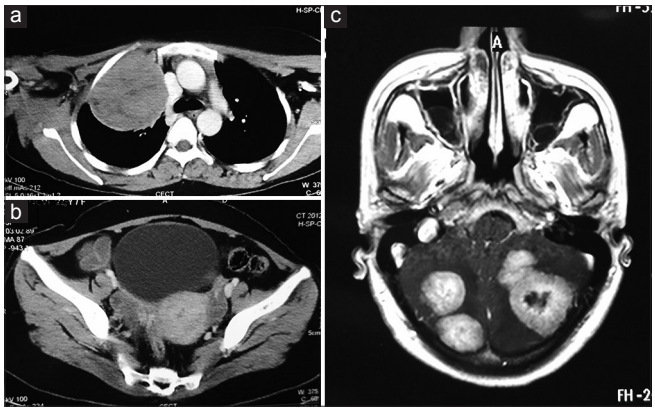

Figure 2: (a) Contrast-enhanced computed tomography scan showing well-defined mass in the right upper lobe of the lung with broad base toward costal pleura and medially abutting the superior vena cava; (b) Contrast-enhanced computed tomography scan showing bilateral adnexae metastases; (c) Contrast-enhanced magnetic resonance imaging of the brain showing metastatic lesions

and radiotherapy or best supportive care option can be hold as last resort. In metachronous MPM setting, it is usually easier to manage if the patient complies, as radical treatment can be offered for each malignancy without much complication.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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