Case Report

Herceptin responsive lung adenocarcinoma in the setting of bilateral synchronous lung primaries and breast carcinoma

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Abstract:

The incidence of human epidermal growth factor receptor 2 (Her-2) mutations in lung adenocarcinoma is approximately 3%; however, its significance in the management of these lung cancers remains under investigation. We describe an incidental but unique opportunity to evaluate the response to treatment with herceptin in a patient with bilateral synchronous lung primaries in conjunction with breast carcinoma. Interval imaging following surgical resection of the squamous cell carcinoma while on herceptin treatment delineated the radiological regression of the Her-2 positive lung adenocarcinoma. We feel that this case highlights the potential role for herceptin treatment in Her-2 positive lung adenocarcinomas and demonstrates the importance of screening for these mutations.

Key words:

Breast carcinoma, herceptin, herceptin responsive adenocarcinoma, synchronous lung primaries

The management of non-small cell lung cancer (NSCLC) continues to evolve; however, surgical resection remains the mainstay of treatment for operable tumors. Stereotactic ablative radiotherapy offers a potential alternative in patients who are unfit or otherwise decline surgical resection; however, molecular-targeted therapy represents a more individualized approach to cancer management.

Molecular-targeted therapies have demonstrated significant benefit in many cancers, such as breast, gastric, and colon cancer. A key feature is mutation testing and in lung cancer that is dependent on the histologic subtype. Among NSCLC, adenocarcinoma in particular has demonstrated a number of genetic mutations susceptible to targeted therapy. These therapies enable additional survival potential in inoperable patients or those that develop metastatic disease.

Adenocarcinomas with human epidermal growth factor receptor 2 (Her-2) mutations have previously demonstrated unimpressive responses to herceptin therapy; however, the documented case report and trials were all associated with chemotherapy and were trialed among inoperable patients.[1,2] Consequently, we report our experience of the response to treatment with herceptin alone in a surgical candidate with bilateral synchronous lung primaries in conjunction with breast carcinoma.

Case Report

A 70-year-old female ex-smoker was diagnosed with bilateral synchronous lung primaries during staging of a right-sided breast carcinoma. Computed tomography (CT) of the thorax revealed a 1.5 cm spiculated left upper lobe mass and a 1.2 cm right upper lobe nodule. Positron-emitted tomography (PET)-CT demonstrated no evidence of mediastinal or hilar lymphadenopathy [Figure 1a and b]. Core biopsies of the lung confirmed a left upper lobe squamous cell carcinoma positive for cytokeratin (CK) 5/6 and P63. The right upper lobe nodule was an adenocarcinoma that was thyroid transcription factor 1 (TTF-1), napsin, and CK-7 positive and CK-20 negative. The core biopsy of the breast demonstrated an infiltrating Grade II ductal carcinoma that was estrogen

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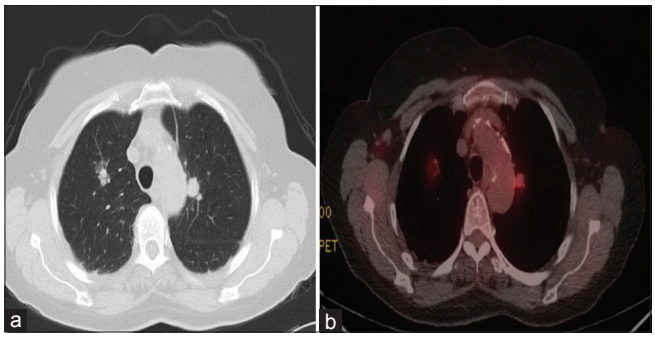

Figure 1: (a and b) Computed tomography of the thorax demonstrated a 1.5 cm spiculated left upper lobe mass and a 1.2 cm right upper lobe nodule. Positron-emitted tomography-computed tomography confirmed a 1.3 cm left upper lobe mass with a standardized uptake value of 4.2 and a mildly avid right upper lobe nodule

receptor positive, progesterone receptor negative, and Her-2 positive. Immunohistochemistry was CK-7 positive and CK-20, TTF-1, and napsin negative.

The breast carcinoma was managed with herceptin (trastuzumab), and she proceeded to a successful left upper lobectomy and mediastinal lymph node dissection. Final histopathology demonstrated a completely resected 20 mm squamous cell carcinoma and staged pT1aN2 (positive lymph node station 6). She had an uneventful postoperative recovery.

Interval CT imaging 3-months following surgery in preparation for resection of the second lung primary demonstrated a significant reduction in the size of the right upper lobe nodule. There was only a 12 mm focus of residual scarring with no discrete mass identified. These findings were confirmed on PET imaging which demonstrated only faint FDG-avidity and residual linear scarring at the site of the previous right upper lobe nodule [Figure 2a and b]. Retrospective analysis of the right upper lobe core biopsy confirmed an invasive adenocarcinoma that was CK-7, TTF-1, and napsin positive and CK-20 negative, verifying a lung primary. However, it was now also noted that there was focal weak membranous staining with Her-2 in more than 10% of tumor cells.

Discussion

This case demonstrated radiological regression of Her-2 positive lung adenocarcinoma in response to isolated herceptin therapy. The role of Her-2 is well established in breast cancer; however, its role in lung cancer pathogenesis and its potential as a therapeutic target remain under investigation.[3-5] Nonmutational abnormalities (protein overexpression and gene amplification) occur in 10–30% of lung adenocarcinoma, whereas the incidence of Her-2 (ERBB2) gain-of-function mutations in lung adenocarcinoma is approximately 3%.[1,3] Despite this, there is emerging data that suggest Her-2 targeted therapies may be beneficial in Her-2 gene mutations.[5] These mutations are associated with female gender and never-smoker status.[1]

In our case, there was an incidental but unique opportunity to evaluate this hypothesis. The patient had bilateral synchronous

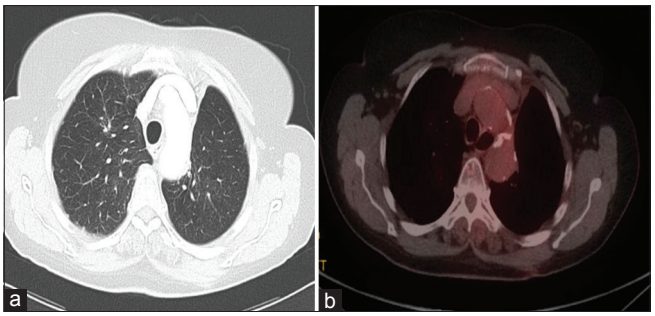

Figure 2: (a and b) Follow-up computed tomography of the thorax and positron emitted tomography-computed tomography post-left upper lobectomy demonstrated only a 12 mm focus of residual linear scarring and faint fluorodeoxyglucose avidity at the site of the previous right upper lobe nodule

lung primaries in conjunction with breast carcinoma and received herceptin treatment while undergoing surgical resection of a left-sided primary NSCLC. Interval imaging enabled evaluation of the effect of herceptin treatment on the right-sided Her-2 positive lung adenocarcinoma, and the result was radiological resolution of this cancer. To the best of our knowledge, this is the first reported case of isolated herceptin treatment for Her-2 positive lung adenocarcinoma. It highlighted the potential role of herceptin treatment in the management of Her-2 positive lung adenocarcinomas, particularly in those deemed inoperable, and consequently it is crucial to screen for these mutations.

Conclusion

This case demonstrates the potential role for herceptin treatment in Her-2 positive lung adenocarcinomas, a particularly important observation among patients deemed to be inoperable, and consequently highlights the importance of screening for these mutations.

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Conflicts of interest
There are no conflicts of interest.

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