

## HER-2 breast cancer treatment induced mediastinal sarcoid like reaction depicted on $^{18}\text{F}$ -FDGPET/CT

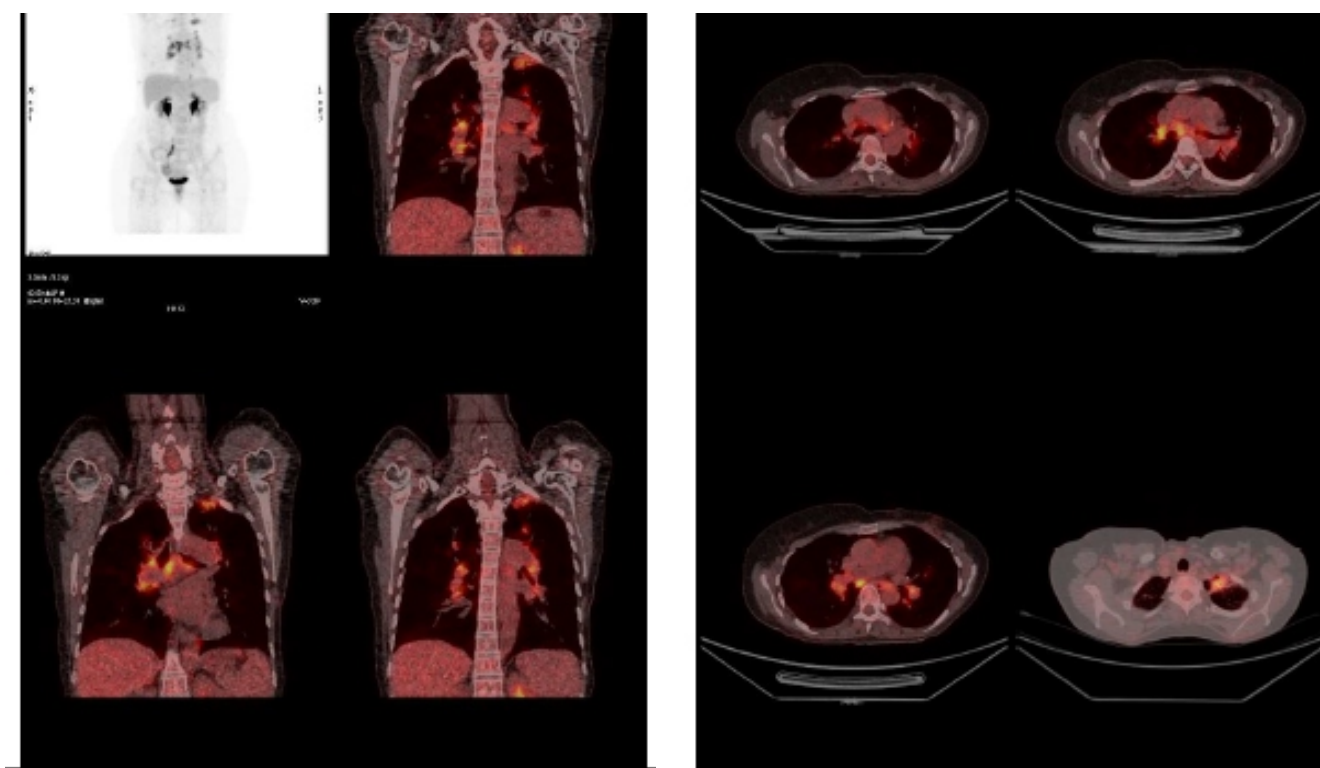
### Abstract

This is a case of a woman with breast cancer, who developed mediastinal sarcoid-like reaction, depicted on PET/CT, which was histologically confirmed, following treatment with trastuzumab and pertuzumab. The development of noncaseating granulomas in patients who do not fulfill the criteria for systemic sarcoidosis is known as sarcoid-like reaction, having been described in association with trastuzumab in a few case reports, but none with pertuzumab. Physicians should be aware of the potentially higher rate of sarcoid-like reaction in patients receiving HER-2 treatment. The symmetric pattern of mediastinal lymphadenopathy, although indicative, is not pathognomonic for sarcoid-like reaction, and biopsy is necessary to exclude disease progression.

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**Figure 1.**

A 45-year-old woman, who was diagnosed with locally advanced triple negative breast cancer in 02/2015, received neoadjuvant chemotherapy (4 cy EC, 4 cy docetaxel), followed by mastectomy (ypT1N2/3) and radiotherapy. In 09/2017 a solitary liver metastasis was depicted on CT, followed by a PET/CT scan, and then was confirmed histologically. Immunohistochemical pattern of the metastatic site was different from the primary tumor: ER-, Pr-, cerbb2:+3, fish+. The patient received 6 cycles of docetaxel- pertuzumab- trastuzumab and then she continued with maintenance (Pertuzumab and Trastuzumab). In 09/2020, she underwent PET/CT imaging for treatment monitoring, which showed complete resolution of the liver metastasis, but multiple new enlarged and FDG avid mediastinal lymph nodes in a symmetric pattern (low-paratracheal bilateral and hilar bilateral, max.d=1.3cm, SUVmax=8.4), (figure 1) which were considered most likely as a sarcoid-like reaction induced by treatment. An EBUS biopsy was conducted. The histopathology report revealed findings of granulomatous reaction pattern, which were attributed to HER2 treatment, given the fact that there were no other suspicious, clinical or laboratory, findings.

Trastuzumab, a humanized monoclonal antibody against the extracellular domain of the human epidermal growth factor receptor 2 (HER2), has been used since 1998 for the treatment of HER2 positive breast cancer. Although adverse effects are not common, some of the pulmonary complications associated with Trastuzumab are interstitial lung disease (1), organizing

pneumonia (2) and bronchospasm (3). There are a few cases worldwide that correlate the use of trastuzumab with sarcoidosis (4-7). The patient received trastuzumab with pertuzumab, so it is not certain which drug caused sarcoidosis, if not both. There are no cases in the literature, reporting sarcoid like reaction due to pertuzumab.

After a thorough discussion with the patient, we decided to continue treatment with subcutaneous trastuzumab. The stage of the sarcoidosis based on the PET CT findings was I, which means that the patient should remain on surveillance.

Oncologists, radiologists and nuclear medicine physicians should be aware of the potentially higher rate of sarcoid-like reaction in patients receiving HER-2 treatment. The symmetric pattern of mediastinal lymphadenopathy, although indicative, is not pathognomonic for sarcoid-like reaction, and biopsy is needed to exclude disease progression.

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