CASE REPORT

Second Primary Lung Cancer after Breast Cancer. Challenges and Approaches

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Abstract

Breast cancer is one of the most common malignancies, with a 10-year survival rate for early non-metastatic stages of over 80%. However, recurrence or relapse may occur decades after completing therapy, and cancer survivors have also a risk of secondary neoplasia especially due to radiation therapy. This case highlights the challenges of an accurate diagnosis and appropriate treatment in patients with second primary cancer and uncommon metastasis.

Keywords: breast cancer, lung cancer, gastric secondary determinations, intestinal secondary determinations, hypersensitivity reaction, desensitization to Atezolizumab.

Rezumat

Cancerul de sân este unul dintre cele mai frecvente neoplazii, cu o supraviețuire la 10 ani de peste 80% în cazurile incipiente. Însă, la acești pacienți, există un risc crescut de recurență și de apariție a unui al doilea cancer ca urmare a radioterapiei efectuate pentru cancerul primar. Acest caz subliniază importanța diagnosticării corecte și a tratamentului adecvat în cazul pacienților care dezvoltă recidiva tumorală și o a doua neoplazie.

Cuvinte cheie: cancerul de sân, cancerul pulmonar, determinări secundare gastrice, determinări secundare intestinale, reacție de hipersensibilitate, desensibilizare la Atezolizumab.

BACKGROUND

Breast cancer is the most common neoplasm among women and the second leading cause of cancer death. Lung cancer is the leading cause of death cancer in the world.[1,2] The vast majority of lung tumors (85%) are classified as non-small cell lung cancers, and are diagnosed in advanced stage. This means that the survival remains poor despite the therapeutic advances[3].

Breast cancer has an increased vascularization and can easily spread to adjacent or distant organs. Most common sites of metastasis are lymph nodes, lung, liver and bones. Metastases to the gastrointestinal tract, although rare, should be considered in patients with specific symptoms, even if the breast cancer was treated many years ago.[4,5]

Moreover, patients with breast cancer treated with radiotherapy are at high risk for developing second primary pulmonary neoplasia. The presence of estrogen and progesterone receptors has also been shown to be a risk factor in the development of lung cancer[6].

Therefore, is essential to carefully investigate any new signs or symptoms experienced by cancer survivors, as a part of the follow-up care plan.

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We report the case of a 52-year-old patient with a history of breast cancer who was diagnosed 12 years later with breast cancer metastases and second primary lung cancer.

CASE PRESENTATION

A 52-year-old patient presented to the emergency room in July 2022 with severe abdominal pain, initially localized to the right iliac fossa, followed by generalized pain and fever, symptoms that began that morning. The patient had a history of breast cancer, diagnosed in 2009, and treated with neoadjuvant chemotherapy, followed by surgery (radical mastectomy with left axillary lymphadenectomy), and adjuvant chemotherapy and radiotherapy.

The patient was a former smoker (30 packs/year), worked in a toxic environment and was also known to have an uncomplicated gastric ulcer treated with antibiotics.

Investigations

A full assessment was performed, including laboratory tests and imaging investigations. Brain, thorax, abdomen and pelvis CT scans were performed, identifying intra- and extraneural metastasis, left upper lobe lung tumor with hilar and mediastinal adenopathies, and adrenal nodules. CT scans also described a loco-regional thickening of the ileal wall and lack of demarcation between the small intestine and the transverse colon. A surgical intervention was performed which revealed an extensive infiltrating abdominal tumor and multiple mesenteric adenopathies. Thus, an enterectomy was performed in July 2022, followed by an entero-entero anastomosis. The resection specimen and biopsy material from the mesenteric adenopathies were sent for histopathological and immunohistochemical evaluation. The results put the diagnosis of secondary intestinal metastases from breast cancer, triple-negative subtype, with a Ki 67 of 85%.

In August 2022 the patient performed a new thoracic CT scan, which revealed an increasing left lung tumor of 7.3 cm/5 cm/6 cm and lacunar images in the left atrium with extension to the left pulmonary veins, with thrombotic appearance. We recommended a cardiological evaluation, and the cardiac ultrasound did not reveal any other pathologies, but the patient remains on anticoagulant treatment.

Because the patient had at least one risk factor for lung cancer and the progression of the lung tumor on CT scan, we suspected a primary lung cancer and we decided to perform an ultrasound-guided transparietal lung biopsy and referred for histological and immunohistochemical evaluation. The diagnosis confirmed the presence of pulmonary adenocarcinoma, high grade, with negative ALK and EGFR and PD-L1 less than 1%.

Investigations were completed by upper digestive endoscopy which revealed an ulcerated tumor of the fornix. Biopsies were taken which confirmed the diagnosis of secondary lesions from triple-negative breast carcinoma.

Patient started palliative brain radiotherapy and systemic treatment with Paclitaxel, Carboplatin, Atezolizumab and Bevacizumab. At the second cycle of treatment, about 20 minutes after starting Atezolizumab infusion, the patient presented a hypersensitivity reaction, manifested by a sudden drop in oxygen saturation and generalized erythema and we decided to use a desensitization protocol. After 4 cycles of therapy the imaging evaluation showed a regression of the cerebral-metastatic disease, mild regression of the left hilum-pulmonary tumor, without parietal thickening in the gastrointestinal tract and stable adrenal nodules. The patient is currently on maintenance treatment with Atezolizumab with desensitization and Bevacizumab.

DISCUSSION

There is a wide range of risk factors in the development of lung cancer in patients with history of breast cancer, including the molecular profile of the tumor, the treatment administered, the patient's age, and the time from the first diagnosis.[7,8] There is strong evidence that support the relationship between radiotherapy in breast cancer and the occurrence of lung cancer, sarcoma, esophageal cancer, colorectal cancer, thyroid cancer, melanoma, or myeloid leukemia.[9] Since the incidence of developing lung cancer in this category of patients is significantly higher, they should be carefully monitored for early diagnosis.[10] Also, the proportion of patients with a history of radio treated breast cancer who developed lung cancer was higher in the smokers group compared to non-smokers.[11]

Solid tumors usually occur at least 10 years after radiotherapy in breast cancer, with a lower risk in the first 5 years after diagnosis.[12]

Our patient met a number of these risk factors, like smoking, which is not only a cause for lung cancer, but also for precancerous lesions and other cancer types[13].

So, it was essential to biopsy the lung tumor that had imaging features of a primary lesion.

Breast cancer has the ability to metastasize to almost any organ in the body, so a series of investigations are needed to identify both locoregional and distant metastases.[14] There is a predisposition to bone, lung or liver metastasis in ductal breast cancer, in contrast to lobular breast cancer, which frequently metastasis to the gastrointestinal tract.[15]

Given the patient's acute abdominal pain, the differential diagnosis was made between non-oncologic conditions such as vascular disease, digestive tract obstruction or perforation, ruptured spleen, gynecological complications, and others. Thus, imaging investigations were essential for a prompt and accurate diagnosis.

Metastases to the intestinal tract occur most frequently in the colon, followed by the small intestine and anus. Because the patient presented with sudden onset of acute abdominal pain, surgery was mandatory.[16] An upper digestive endoscopy was also required due the multiple secondary digestive lesions identified during surgery.[17] On the other hand, histopathological and immunohistochemical evaluation was essential to establish the diagnosis.

Because of these particularities, this case was challenging and required multidisciplinary team approach, including oncological, radiological, gastroenterological, radiotherapeutic, surgical and allergological evaluation. As the patient has two cancers, we had to choose the appropriate treatment in this case, to cover the first line treatment for lung cancer and the first line for breast triple-negativ metastatic cancer, so we chose to do Paclitaxel, Carboplatin, Atezolizumab and Bevacizumab. Thus, the oncological committee decided to perform palliative radiotherapy on the brain, followed by Paclitaxel, Carboplatin, Atezolizumab and Bevacizumab, as the disease was metastatic. The good performance status of the patient allowed for this therapeutic approach.

In general, allergic reactions can range from mild manifestations to life-threatening conditions, usually occurring between 10 minutes and 4 hours after treatment administration[18]. Therefore, the patch test was recommended 2 weeks after the allergic event. This test is generally performed between 2 and 4 weeks after the allergic reaction to avoid false negative results[19]. In our case, the positive intradermal skin test was at 0.6mg/ml Atezolizumab, manifested by an increase in the diameter of the initial papule by 4 mm and erythema. It was crucial to continue the treatment, and we decided to use a desensitization protocol with the help of our colleagues from the allergology department.

A desensitization protocol is a procedure that requires premedication and the administration of very gradual dose increments of the chemotherapy agent. Once the drug is completely removed from plasma**,** the tolerance state is lost, so a desensitization protocol is needed for each administration[20]. The patient received Atezolizumab with a 16-step desensitization protocol, with an initial concentration of 1:1000 and gradually increasing, and this protocol was repeated for each treatment course and was well tolerated.

CONCLUSION

In conclusion, we highlight that even in the early stages, well-treated breast cancer patients may experience long-term complications, such as loco-regional and distant recurrences, as well as a second primary cancer. Therefore, following curative treatment, it is essential to closely monitor the patient even for many years. We know from the studies that recurrence is more frequent in the first five years, but we have reports that show us that we have to be precaution with cured patients because they are at risk of second primaries. We have always to take in consideration the risk factors for a second primary.

We also recommend performing a biopsy of all suspected lesions for diagnostic accuracy. And if drug hypersensitivity reactions occur, to take into consideration desensitizing protocols.

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