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Case Report

Atypical Carcinoid Breast Metastasis of Thymus: A Case Report

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Abstract

Thymic neuroendocrine neoplasms (Th-NENs) is a very rare disease. It accounts for about 5% of thymic tumors, which are mostly seen in men aged 40-59. At present, Th-NENs are usually divided into typical carcinoid (TC) and atypical carcinoid (AC) according to pathological features. AC is more common than TC in Th-NENs. A patient with atypical thymus carcinoid admitted to our hospital was admitted to the hospital because of "the right breast mass was found for 5 days". Complete preoperative examinations, the tumor was surgically removed on 2020.07.24. The pathological result was atypical carcinoid thymus. Etoposide combined with cisplatin chemotherapy was given for 4 cycles after surgery, and then the oral capecitabine combined with anlotinib was continued for maintenance treatment. In November 2021, due to tumor recurrence and metastasis, she was switched to treatment with teriprizumab combined with sofatinib. The prognosis of atypical thymic carcinoid is poor, and the effect of postoperative adjuvant chemotherapy and other treatments still lacks a large amount of clinical evidence to support. Currently, we are working hard to find treatment options that can effectively prolong patient survival.

Keywords: Thymus atypical carcinoid; Neuroendocrine neoplasms; Treatment; Case report.

Clinical information

The patient, a 46-year-old female, was admitted to the hospital for "discovering a right breast mass for 5 days". Physical examination revealed a right breast mass (2 X 1 cm), which was not palpable. On July 15, 2020, breast color ultrasonography was performed at the local hospital, which showed that there were hypoechoic nodules in the right breast, with slightly irregular shape and ARC BI-RADS 4A. Vacuum-assisted needle biopsy of right breast mass under local anesthesia was performed on July 17, 2020. Postoperative pathology showed invasive carcinoma of right breast. In our hospital, 2020.07.20 enhanced chest CT showed: mass high-density shadow in the upper quadrant of the right breast, with unclear boundary, small nodular high-density shadow in the local area, about 13 X 11 mm in size, mild to moderate enhancement in enhanced scan; in the anterior mediastinum, there was a mass of soft tissue density shadow with a clear boundary and a size of about 27 X 18 mm. Several enlarged lymph nodes were seen in the mediastinum, and the larger ones were about 9 mm in length. Impression: anterior

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mediastinal mass, considering the nature of the tumor, thymoma is likely. MRI of breast showed: 1. Postoperative changes in the upper quadrant of the right breast, no abnormal contrast enhancement was observed in the operative area, bi-RADS-MRI class 6, please refer to the clinic. 2. Obvious uneven enhanced nodule in the middle lateral quadrant of the right breast, category 5 BI-RADS-MRI, considering the possibility of tumor lesion (breast cancer), please combine with clinical and histological examination. 3. Moderately unevenly enhanced space occupying in the anterior superior mediastinum, the possibility of neoplastic lesions (thymoma) was considered.

The patient underwent right breast conserving modified radical mastectomy + axillary sentinel lymph node biopsy + axillary lymph node dissection + thoracoscopic thymoma resection under general anesthesia on 2020.07.24. (See the pathological test results below).According to the patient's pathological test results and relevant clinical examinations, the patient received 4 cycles of chemotherapy regimen (etoposide injection D1-3+ cisplatin injection D1-3) after surgery. The reexamination results showed that the chemotherapy was effective, and the patient continued oral capecitabine combined with anlotinib maintenance therapy. Postoperative pathology showed: (Right breast) Combined with immunohistochemically examination and the history of thymus mass, atypical carcinoid from thymus was considered. Tumor thrombus was found in the vein without obvious nerve invasion. (Thymus) atypical carcinoid, thymus lymph node metastasis 1/1. Right breast axillary lymph node metastasis (2/16). Immunohistochemistry of breast tumor: Cancer cells CK (+), Vim (weak +), ER (-), PR about 30% weak (+), CerbB2 (-), E-CAD (+), P120 (+), GATA3 (-), CK5/6 (-), P63 (-), Cgalponin (-), P53 (-), CD56 (+), CgA (-) , Syn (+), TTF1 (+), Ki-67 about 10% (+). Immunohistochemistry of thymic tumors: Cancer cells CK (+), CD56 (+), CgA foci (+), Syn (+), E-CAD (+), P120 (+), CD117 (+), GATA-3 (-), CK19 (-), P63 (-), CD5 (-), CD20 (-), CD1α (-), CD99 (-), TdT (-)), P40 (-), CK5/6 (-), GCDFP-15 (-), Ki-67 hot spots about 10% (+).

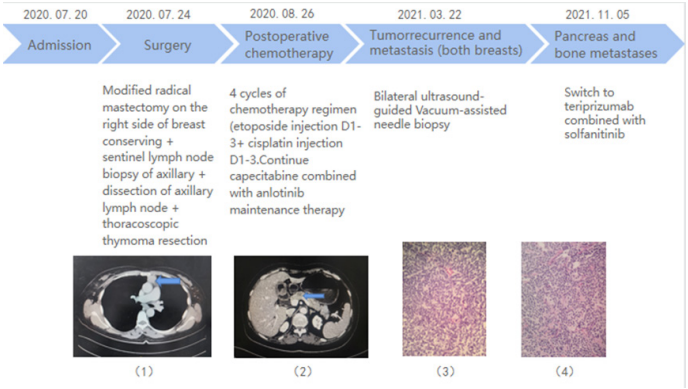

Figure 1: Is a preoperative enhanced CT of the chest, the arrow points to the thymus tumor; (2) is a contrast-enhanced CT of the abdomen, and the arrow points to the pancreatic metastases; (3) is the pathological picture of the thymus tumor after the first operation; (4) is the picture of the breast tumor after the first operation.

There were no obvious signs of recurrence or metastasis 4 months after surgery. Bilateral breast masses were found in reexamination on 2021.03.22, and bilateral ultrasound-guided Vacuum-assisted needle biopsy was performed under general anesthesia on 2021.03.22.Postoperative pathology showed that: (double breast) atypical carcinoid. Immunohistochemistry: Syn (+), CgA (+), CD56 (+), ER (-), PR about 60% (+), CERB-2 (-), P63 (-), CK5/6 (-), GCD117 (-), P53 (-), GATA3 (-), ki-67 hotspot about 5% (+). Capecitabine and apatinib regimen was continued after operation. When the patient returned to the hospital for review on November 5, 2021, abdominal MRI examination showed multiple nodules in the pancreas, which was considered as metastasis, multiple nodules in the vertebral body and pelvis, and bilateral partial ribs, which was considered as bone metastasis. The progression of the disease was indicated, and teriprizumab combined with solfanitinib was given on November 14, 2021.

All procedures in this study were in compliance with the ethical standards of the Human Research Ethics Committee (HREC) and Declaration of Helsinki (revised in 2013). Informed consent of patients has been obtained for reported cases and imaging pictures.

Discussion

Thymic atypical carcinoid is a rare tumor that occurs in the thymus, which is a primary thymic neuroendocrine neoplasm. (Thymic neuroendocrine neoplasms, Th-NENs). About 1/3 of T-NENs patients are asymptomatic. The symptoms of most patients are mainly cough, chest pain, and superior vena cava compression syndrome. Half of the patients have unrespectable locally advanced or distant metastases at the time of diagnosis. Th-NENs often metastasize to the lung, bone, liver, pleura, and pericardium, of which pleura and bone metastasis are the most common, followed by the liver [1]. AC mainly occurs in adults, with more males and obvious aggressiveness. The rate of lymph node metastasis is higher, and the prognosis of advanced cases is poor. Imaging examination combined with pathological examination and immunohistochemistry can make a clear diagnosis.AC is a classification of Th-NENs, and immunohistochemical markers include chromogranin A (CgA), synaptic protein (Syn), CD56, Ki-67, etc. Surgical resection is the preferred treatment method, but even if the tumor is completely removed by surgery, the recurrence of AC patients is still relatively rapid, and the patient's prognosis is poor. A retrospective study of the SEER database [2] showed that adjuvant radiotherapy and chemotherapy after Th-NENs can improve the overall survival (OS) of Masaoka-Koga III-IV patients. At present, there is still a lack of multi-center, prospective research evidence for the indications and survival benefits of postoperative adjuvant radiotherapy. The 2021 "Chinese Expert Consensus on Lung and Thymus Neuroendocrine Tumors" proposes: The research data of advanced Th-NENs is very limited, and it is recommended that the same treatment method should be applied to lung LCNEC.Suggestion [1] Patients with Th-NENs underwent EP (cisplatin + etoposide) or EC (carboplatin + etoposide) adjuvant chemotherapy±radiotherapy after surgery.The results of retrospective studies [3,4] show that: The ORR (objective response rate) of the EP or EC regimen for Th-NENs is 8%-23%, and the PFS (progression-free survival) is 7-8 months. [2]For patients with advanced disease progression ①Molecular targeted drugs: Everolimus; ②Anti-angiogenesis drug: Sofatinib; ③Somatostatin analogs (SSAs): SSA can be used for the first-line treatment of SSTR-positive Th-NENs with slow disease progression; ④Immune Checkpoint Inhibitors (ICI): ICI is rarely used to treat advanced Th-NENs. It is currently not recommended to use ICI to treat Th-NENs outside of clinical studies. At present, the first-line treatment recommended in this guideline is

EP, and there is no recognized second-line or above treatment. Fluorouracil or capecitabine combined with oxaliplatin or irinotecan can also be used as second-line treatment options [1].

The degree of malignancy of AC is significantly higher than that of other carcinoids. It is prone to recurrence and extra thoracic metastasis, and the prognosis is poor. The indicators of a good prognosis include fewer mitotic figures (less than 3/10 HPF), mild atypia, and lack of necrosis [5]. It should be pointed out that tumor size is not an effective indicator for predicting the long-term survival of carcinoids. The staging, grade, and completeness of surgical resection of the tumor are more related to the survival rate of patients [6,7].

The patient in this case is a 46-year-old female who was admitted to hospital because of breast malignant tumor. Preoperative physical examination of the patient found thymus mass, with no obvious symptoms at the early stage, and metastasis of right breast, thymus and right axillary lymph nodes. The patient underwent surgical removal of thymus gland, breast tumor and axillary lymph node tissue. CgA, Syn, CD56 and KI-67 were positive in immunohistochemistry of thymus and breast masses, which was consistent with the expression of TH-NENs marker. According to the most commonly used Masaoka-Koga staging system for thymic endocrine carcinomas [8], the patient's preoperative pathology and relevant clinical examination showed that the tumor invaded the pericardium with thymus lymph node, right breast and right axillary lymph node metastasis, and the patient was classified into stage IVb. After surgery, the patient received etoposide injection combined with cisplatin injection for 4 cycles of chemotherapy. Reexamination showed that chemotherapy was effective, and capecitabine combined with anlotinib was continued for oral treatment. The recurrence and metastasis of bilateral breast metastases were found 8 months after surgery, and PFS was 8 months, which was consistent with related researchs. Pancreatic and bone metastases were found on November 21, 2021. Teriprizumab combined with solvent nib was used for treatment. At the 2020 AACR annual meeting, the results of the phase I clinical study on the treatment of advanced solid tumors by sofatinib combined with treprizumab by Professor Lu Ming and others [9] last year confirmed that the scheme has a certain application prospect in advanced neuroendocrine cancer and a variety of advanced solid tumors. The phase II clinical trial of sofatinib combined with treprizumab in the treatment of advanced solid tumors is being carried out in China.The patient in this case has been treated with this regimen for 2 cycles, and the therapeutic effect needs to be followed up.

Conclusion

Atypical thymic carcinoid is a rare malignant tumor with no obvious symptoms in early stage and poor prognosis in advanced stage. It often metastasizes to lung, bone, liver, pleura, pericardium, etc. Breast metastases are more rare and less reported at home and abroad. At present, complete tumor resection as the main treatment means, postoperative adjuvant radiotherapy and chemotherapy have positive significance for long-term survival of patients, but a large number of high-level clinical trials are still needed. In this case, the patient received surgical treatment and postoperative adjuvant chemotherapy due to breast mass physical examination. The diagnosis and treatment plan and therapeutic effect are consistent with literature reports. Now, the patient continues to receive solfanitinib combined with terriprizumab, and follow-up is required for the significance of prolongation of survival.

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