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Case Report

CASE REPORT

Breast cancer metastasis to the spleen: a case report and literature review

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Abstract

Splenic metastasis from cancers is extremely rare. They usually occur and are detected simultaneously with metastasis to other organs. We present a case of splenic metastasis from carcinoma of the breast occurring 5 years after initial treatment. The metastatic recurrence was an oligometastic form made from the association of a unique bone metastasis to a rib and the metastasis to the spleen. Treatment of the metastatic recurrence was a second line hormonotherapy as the primitive tumor was estrogen receptors positive and gave a 2 year's long control of the disease. A clinical progression occurred then, the patient complained from pain in the left hypochondrium and was objective on [18F]-FDG PET which leaded to splenectomy. This case is being reported because of the rarity of the lesion and its originality is the first reported case with use of an *in vivo* demonstration of estrogen receptors expression in the spleen metastasis using PET/CT with 16α-[18F]-Fluoroestradiol.

INTRODUCTION

Spleen metastases of epithelial tumors were previously regarded as rare [1]. However, in several studies, meticulous autopsy has shown that the spleen is affected by metastatic carcinoma in ~6–13% of the cases [2].

Spleen metastases tend to occur late during evolution of the disease. They are rarely symptomatic and therefore are rarely detected by clinicians. The most frequent primary tumors causing splenic metastases are melanoma, breast cancer, ovary, lung and colo-rectal carcinoma respectively by order of decreasing frequency [3].

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Angiogenesis is a vital process in tumor growth and development of new metastasis. One of the hypotheses that may explain that the spleen remains immune from metastasis compared to other organ is the fact that it produces an anti-angiogenic factor named angiostatin [4,5].

It is suggested also that immunological monitoring made by immuno-competent cells, which is abundant in the spleen, promotes resistance of the implantation of tumor cells [6].

By dint of medical imaging progress, reported case of solids tumors metastasis to the spleen has increased. We here reported a case of a breast cancer patient hormone receptor positive/epidermal growth factor receptor 2 (Her2) negative who present, 5 years later after initial management, a metastatic relapse in the spleen witch was overexpressing estrogenes receptors attested by 16α-[18F]-fluro-oestradiol ([18F]-FES) hybrid positron emission tomography/computerized tomography (PET/CT) scan. After 2 years of disease control under second line endocrine therapy, the patient underwent splenectomy when become painful at the left hypochondrium following disease progression.

CASE REPORT

The patient, a 65 year's old aged woman who was operated in 2008 by radical left mastectomy for luminal B invasive ductal carcinoma of the breast (estrogen receptor [ER]:100%/progesterone receptor [PR]:0%/human epidermal growth factor receptor 2 [HER2]–/proliferation index [Ki67] of 30%), staged pT3N1M0, followed by adjuvant sequential chemotherapy with four cycles of Adriamycine + Cyclophosphamide then four cycles of Docetaxel followed by external radiotherapy and was on adjuvant hormone therapy with aromatase inhibitor Letrozole.

Five years later, as part of an annual follow-up, ACE was increased at 25 IU/mL, CA 15-3 was normal at 4.6 IU/mL, a complementary CT scan of the thorax, abdomen and pelvis showed an heterogeneous splenic nodule measuring 2.5 cm of great axis, which was intensely hypermetabolic on the complementary [18F]-fluorodeoxyglucose ([18F]-FDG) PET/CT scan reaching a maximal standard uptake value (SUVmax.) of 10.1 and was associated with another right anterior costal hypermetabolic lesion (SUVmax. = 5.7). As part of a French prospective phase II multicentric trial (ESTROTEPRIDC, Clinical trials identifier: NCT0162 7704) she underwent a 16α-[18F]-fluro-oestradiol ([18F]-FES) PET/CT aiming at checking the estrogen receptors alpha *in vivo* that showed an increased uptake of the [18F]-FES ligand by both metastatic lesions, attesting the *in vivo* overexpression of estrogens receptors.

First-line metastatic hormone therapy was then initiated by Fulvestrant and the addition of bone-targeted agent Denosumab. A metabolic ([18F]-FDG PET/CT) and biological (ACE,CA15-3) evaluation was conducted every 3 months that showed a initial metabolic response after 6 months of endocrine therapy then a stability over 18 months. After 2 years of metastatic disease control, the patient becomes clinically symptomatic with left abdominal pain at the left hypochondrium level at palpation and a new biological progression with increase in serological markers ACE: 99 IU/mL and CA15-3: 34 IU/mL was found. 18F-FDG PET/CT confirmed a morpho-metabolic increase in splenic lesion (+30%) which was also confirmed by magnetic resonance imaging (MRI) of the spleen with the unique metastatic foci measuring 7 cm.

A splenectomy was decided by the multidisciplinary meeting regarding to the risk of spleen rupture and further subsequent peritoneal carcinomatosis after a primary splenic biopsy was performed which confirmed the mammary carcinoma origin of the lesion; histologic examination showed a poorly differentiated adenocarcinoma with immunohistochemistry expression of estrogen receptors at 100%; progesterone receptors at 0%, Her2 negative and Ki67 was 40%.

DISCUSSION

Breast metastasis to the spleen is a rare localization. However, the reported cases are increasing due to the improvement of imaging modality and a more attentive patient follow-up. Often asymptomatic, the discovery of these lesions occurs on

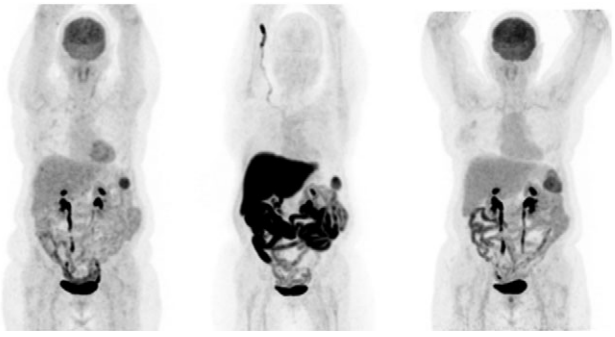

Figure 1: 3D maximum intensity projection (MIP) anterior view from left to right: [18F]-FDG PET on 6 February 2014, [18F]-FES PET on 14 February 2014 and [18F]-FDG PET on 25 April 2016 showing increased tracers uptake in the spleen metastasis

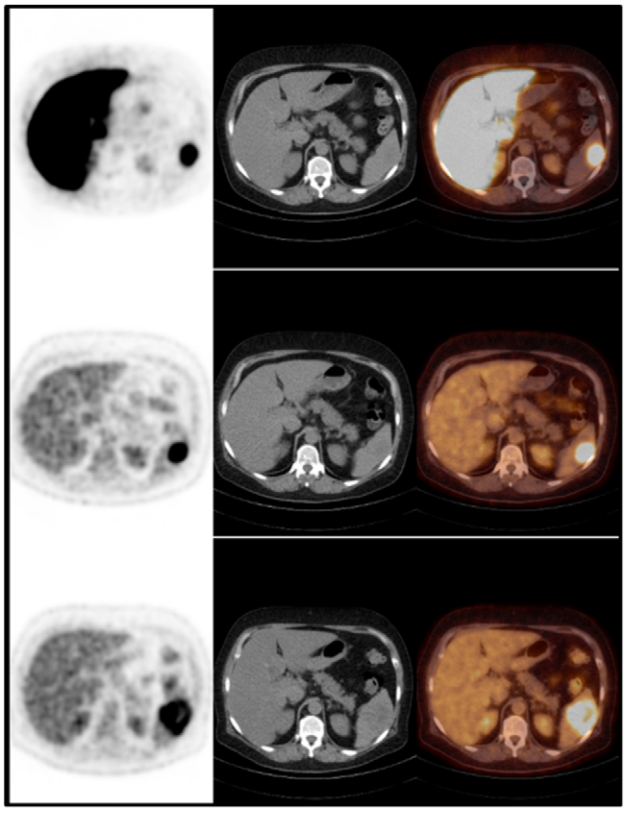

Figure 2: PET/CT axial views of the spleen metastasis from left to right and top to bottom: PET, CT and PET/CT fused images with [18F]-FES PET on 14 February then [18F]-FDG PET on 6 February 2014, and [18F]-FDG PET on 25 April 2016

imaging in the context of a multimetastatic disease [7]. The spleen metastases of mammary carcinoma are often visible on the CT scan, their high activity on the [18F]-FDG PET/CT supports their tumor origin [8]. For hormone-sensitive breast tumors, another tracer is recently currently available in France, the 16α-[18F]-fluro-oestradiol 16α 17β-estradiol (FES) which is able to detect secondary lesions with overexpression of functional estrogen receptors in the whole body. This potentiality give to the [18F]-FES PET/CT scan a very important value for tumors overexpressing hormones receptors, especially when biopsy tissue is unavailable or technically difficult. Therefore, [18F]-FES PET/CT scan represents a new non-invasive approach to determinate the hormonal status of breast metastasis with *in vivo* imaging [9].

Secondary to the vascular composition of the spleen, cytohistologic diagnosis has traditionally been made by splenectomy, as splenic biopsy and fine needle aspiration (FNA) were accompanied with a potential risk of hemorrhage. However, Caraway *et al.* [10] demonstrated in a series of 50 cases, that FNA can be safe and valuable diagnostic approach that can avoid an unnecessary splenectomy for the diagnosis of an isolated splenic lesion and benign conditions.

Splenectomy for splenic secondary lesions is indicated in cases of painful splenomegaly and in cases of isolated metastasis to the spleen. It also can be done to prevent complications such as thrombosis of the splenic vein or a splenic rupture [11]. Some authors have suggested a potential higher long-term survival when splenectomy is realized in such setting [12] (Figs 1 and 2).

CONFLICT OF INTEREST STATEMENT

None declared.

FUNDING

There was no funding for this report.

DISCLOSURE

The authors declare no conflict of interest.

ETHICAL APPROVAL

No ethical approval required.

CONSENT

This report has been writing with the approval of the patient. The patient gave an informed consent to use the data of her medical folder as well as the medical imaging folder, especially all the PET/CT scans, for teaching and/or medical and scientific publications purposes and this, according to the French rules for protection of individuals rights of patients undergoing examinations and participating to clinical trials.

The PET/CT using 18FES was realized as par to the ESTROTEPREDIC (Fluroestradiol PET Imaging in Predicting Response to hormone Therapy of Breast Cancer) registered at ClinicalTrials.gov under number NCT01627704.

GUARANTOR

Pr. Joseph Gligorov.

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