

Breast cancer and gastrointestinal metastasis.

A case report and review of the literature



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INTRODUCTION: *Invasive lobular cancer (ILC) is the second most common type of a heterogeneous group of different histological types of invasive breast carcinoma. Breast cancer can metastasize anywhere, the most common sites are bones, liver, lungs and brain. Gastrointestinal tract (GI) metastases observed in autopsy studies account for about 6% to 18% of the overall metastases from breast cancer.*

OBJECTIVE: *We describe a 54-year old woman with recurrent ILC in the contralateral breast. She underwent right mastectomy 16 years before. After symptomatic presentation a duodenal invasion was found and subjected to diagnostic scrutiny (FDG PET/CT, diagnostic CT, MR, EGDS). In particular, we analyse if FDG PET/CT is enough accurate in the restaging of the patient. A review of our database and of the literature of similar cases were made.*

RESULTS: *In this patient CT and RM were suspicious for a slow developing process of the duodenum but FDG PET/CT did not show pathological uptake in the affected duodenal tract. A highly intense focus was described in a cervical lymph node, that there isn't metastatic lesion, whereas the recurrent breast lesion had only slight increased glycolytic activity.*

CONCLUSION: *Metastatic lobular carcinoma of the breast is a rare entity with a heterogeneous range of clinical presentations. Detection of eventual gastrointestinal metastases are complicated to assess. ILC has various scale of glycolytic activity both in the primary lesion as well in the metastatic foci. When the level of suspicion is high and there is no uptake of FDG, further investigations are necessary.*

KEY WORD: Abdominal metastasis, FGD PET-TC, Lobular Breast Cancer

Introduction

The primary areas of metastasis from breast carcinoma are the bones, lungs, pleura, liver, and brain. Gastrointestinal (GI) tract metastasis from breast carcinoma is relatively rare, and abdominal metastasis from breast carcinoma is very rare.

We presented a rare clinical case of lobular breast cancer metastasis.

Case Report

Our patient is a 54 year-old woman with positive anamnesis for breast cancer in 2000 (ILC T2 N22/25 Mx ER PgR ki 67) who underwent right mastectomy, omolateral axillary clearance with subsequent prosthetic reconstruction and adjuvant CHT, OT (Epirubicina and Tamoxifene) and RT. She conducted a regular follow up until 2011, when radiological controls identified a 9 mm lesion at the superior lateral quadrant of the left breast; as a consequence, she underwent an enlarged tumorectomy with sentinel node sampling (I.E. mammary neoplasia T1N0 Er-, Pgr-, HER2-), followed by 6 chemotherapy cycles (CMF protocol) and 25 radiotherapy sessions.

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The subsequent follow up was annually performed with total body contrast-enhanced CT.

In March 2016 a new eco-mammographic control showed the presence of thickening areas with irregular profiles in the left breast parenchyma, especially in the upper lateral quadrant; the ultrasound control specifically appreciated an hypoechogenic sharpened expansive neoformation in the lateral portion of the left breast (max diameter 27 mm).

PET/CT FDG showed slightly increased metabolic glycolytic activity (SUV max 2.3) in the same, suspected area of the left breast, faintly dense on CT viewer. This particular metabolic behavior is often noted with some histotypes of breast carcinoma, usually ILC with lower grade. Metabolic imaging also depicted faint FDG uptake in many omolateral subcentimetric axillary nodes, with morphologic inflammatory features in the ones of greater size at correlative CT imaging (from hybrid PET/CT scan). Furthermore, it pointed out a hypermetabolic area (SUV max 11.3) in the right lateral cervical lymph node chain.

The core biopsy of this breast lesion documented: invasive lobular carcinoma, classic type, G2 HER 1+, Ki-67:17%, ER 40%, PgR neg.

In April 2016 the patient was admitted to hospital for recurrent vomit episodes. The CT images documented: "Important gastrectasia with levels, with a stop in the pyloric area: here it is noted a concentric thickening of the organ's walls, while the downstream duodenum has a regular diameter. No other relevant abnormalities of abdominal organs are shown, except for a little hepatic angioma and a 2 cm pancreatic cyst (localized in the uncinate process)". Abdomen MR: "Pronounced gastrectasia, absence of suspected focal areas at the hepatic parenchyma. Minimal ectasia of the intrahepatic biliary ducts, regular diameter of the bile duct. Pancreas with conserved thickness, multilocular cystic formation of 25 mm at the uncinate process, with benign macroscopic features. Dismorphic pancreatic head, with a 'saddle' feature in relation to the presence of a tissue portion that embraces for 180° the fore portion of duodenum. The Wirsung duct appears regular; dominance of the Santorini duct. The second portion of the duodenum, at the papilla minor level, is regular: beneath this portion, at the inferior flexure, duodenal walls appear concentrically thickened and occlude the lumen. These findings, together with the CT description and the late contrast enhancement, suggest a slow developing process interesting the duodenum, with high fibrotic features". The following EGDS documented an ab-estrinseco constrictive compression at the superior duodenal flexure, extended for about two centimetres and not completely approachable with the probe. After contrastography, a thickening at the superior flexure and the first part of descending duodenum was evident.

Having completed all the preoperative procedures, the patient undergone surgery: "during laparotomy, the pres-

ence of "sleeve" constrictive neoformation of the inferior duodenal flexure was confirmed (I.E. ILC metastasis) and a transverse retroduodenal dolico-colon was found. The surgeon performed a gastro-entero-anastomosis "en Y de Roux" with resection of transverse colon".

At present, the patient is fine and she has started chemotherapy for the mammary relapse.

Discussion

Breast cancer is the most widespread type of cancer in women and, according to the Istat data, it was the main cause of death in Italy in 2012.

ILC represents the second most prevalent histological type of breast cancer after invasive ductal cancer (IDC) and its incidence has been constantly growing in the last few years. This trend is largely related to the use of MR as a radiological diagnostic method of second level, although the incidence of IDC remains stable over the years.

The lobular histotype includes atypical epithelial lesions, originated from the ductal-lobular unit and characterized by a proliferation of small not thick cells with minute and uniform nuclei, with or without pagetoid involvement of terminal ducts.

Breast cancer can metastasize anywhere, the most common sites are bones, liver, lungs and brain. ILC has been seen to localize in uncommon sites, like the peritoneum, retroperitoneum, hollow viscera (including the gastrointestinal and genitourinary tracts), and leptomeninges¹³⁻¹⁶. Gastrointestinal metastases (GI) can occur years later from the primary diagnosis. According to the literature, the rate of GI metastases of ILC is low (6 to 18%), they often reveal themselves with aspecific symptoms after at least 6-8 months from the first cancer diagnosis.

A 2005 Mayo Clinic study reports the occurrence of GI metastasis in 41 of 12.000 patients with a primary diagnosis of breast cancer, with a medium rising gap of 7 years. Of these 12.000 patients, 41, 25 (61%) had a ILC. (Among those women, 25 in 41 (61%) had a ILC). The patients with a primary diagnosis of ILC were 12% of the whole population analyzed: this demonstrated that the ILC GI metastasizes were considerably more frequent than the invasive ductal cancer ones⁵.

The prevailing gastrointestinal localization of this histotype could be related to the biological and histological features of the neoplasia itself; effectively, it has been noted that, contrary to the other breast cancer histotypes, ILC is characterized by the inactivation of E-cadherin, a cellular cohesion; furthermore, many studies demonstrate that ILC with GI metastases do not express HER2/neu (human epitelial growth factor)^{1,2}.

The clinical features of these GI metastasis are very heterogeneous, and the symptoms can make the diagnosis very difficult; their long time of rising often do not let

attribute them immediately to the previous mammary cancer, so that the histological diagnosis is in most cases essential and crucial. Metastasis can present as nodules, erosions and ulcerations; many cases of plastic inflammation with wide infiltration of mucosa and submucosa have been described ¹⁰.

The histological evaluation of these lesions could not be so easy; ER and PgR markers, that are often negative in colorectal and gastric cancer, can be very helpful for the achievement of a right diagnosis.

We performed a revision of the database at our institution and looked for these key words: ILC, metastases, receptor, grading, imaging. We discovered that among a population of 10000 patients diagnosed with breast cancers and followed from 2000, 40 women with ILC metastatized (mean age 60.32, range 34-79 years) principally in bones (75%), liver (40%), peritoneum (12.5%), brain (10%), thorax wall (7.5%), GI tract (5%), adrenal and kidney (2.5%). All the metastatic patients performed a whole body diagnostic CT scan, 14 women an FDG PET/CT while 17 patients underwent MR. PET/CT and CT were both positive in 6 patients, PET/CT had 4 false negative results (FN), while contrast-enhanced CT had 3 FN results and one FP result (vertebral collapse due to osteoporosis). Overall CT saw more lesions in the liver, brain, lung and GI tract, conversely PET/CT was more active in revealing pathologic nodes and bone lesions.

Results

In this patient CT and RM were suspicious for a slow developing process of the duodenum but FDG PET/CT did not show pathological uptake in the affected duodenal tract. A highly intense focus was described in a cervical lymph node, that there isn't metastatic lesion, whereas the recurrent breast lesion had only slight increased glycolytic activity.

Conclusion

In conclusion 18F-FDG uptake depends on several factors, mainly the histologic and biologic characteristics of the breast tumor: IDC showed higher uptake than ILC in several studies ^{1,2,17}. High grade (G3) invasive tumors exhibit higher 18F-FDG uptake than lower-grade tumors ^{1,2}. There is evidence that SUVmax is higher in tumors that are negative for hormone receptors, like in Triple-negative breast cancer ^{2,3}. Some studies showed a correlation between the tumor proliferation index (Ki-67 expression) and the intensity of 18F-FDG uptake ¹.

ILC is more difficult than IDC to detect on imaging, including mammography, ultrasound, and MR imaging ^{7,8}. FDG PET/CT demonstrates lower SUV and less accuracy both in primary as well as in metastatic ILC compared

to IDC ⁹⁻¹². Moreover, the patterns of metastatic spread differ between ILC and IDC ¹³⁻¹⁶.

PET/CT interpretation must be assessed with the knowledge of all the factors described above, principally the histologic subtype, stressing on the fact that ILC may have lower 18F-FDG uptake, so all the unusual finding on the hybrid CT imaging with faint or even normal FDG uptake should be considered and reported (osteosclerotic bone lesions, visceral enlargement, peritoneal nodules) ⁵.

This case report pointed out that ILC can cause GI metastases and that PET-CT, if negative, cannot be considered a reliable method to define the stage of the disease.

Riassunto

Il carcinoma lobulare invasivo è il secondo tumore più frequente tra i tumori della mammella dopo il duttale invasivo con percentuali che si aggirano attorno al 5-15% di tutti i tumori della mammella. Per definizione il cancro mammario può metastatizzare in qualsiasi distretto corporeo e tra le localizzazioni più frequenti abbiamo: ossa, fegato, polmoni e cervello. Le metastasi a livello del tratto gastrointestinale sono più rare e studi autoptici ne stimano un'insorgenza tra il 6% e il 18% di tutte le metastasi da cancro mammario.

Il nostro lavoro vuole porre l'accento su un particolare caso clinico di una giovane donna di 54 aa con un carcinoma lobulare invasivo della mammella sinistra, comparso 14 anni dopo un precedente tumore lobulare invasivo alla mammella destra. In concomitanza alla recente scoperto del nuovo tumore mammario la paziente è stata sottoposta a stadiazione mediante FDG TC PET, TC total body di stadiazione, RM ed EGDS. In particolare abbiamo analizzato il risultato della PET/TC nella valutazione del carcinoma lobulare invasivo ed eseguire una revisione del nostro database e della letteratura riguardante casi simili.

In questa paziente TC e RM erano sospette per un lento processo evolutivo a carico del duodeno, mentre la PET/TC non mostrava un uptake patologico a carico del tratto duodenale. Veniva descritto solamente un focus di captazione a carico dei linfonodi cervicali, i quali non erano però metastatici, solo l'area con il cancro della mammella presentava attività glicolitica.

In conclusione possiamo sostenere che la captazione del 18F FDG dipenda da molti fattori, l'istologia del tumore in primis, ma anche le caratteristiche biologiche del cancro; i grading tre, i triple negative e i tumori con un ki 67 più alto, presentano un indice di captazione maggiore.

Di conseguenza anche le metastasi da tumore lobulare della mammella non presentano captazione, la possibilità quindi che si presenti con metastasi gastrointestinali ne complica maggiormente il quadro. Dalla nostra analisi,

possiamo affermare come l'utilizzo della FDG TC/PET nei tumori lobulari della mammella debba essere eseguita con maggiore attenzione, e un risultato negativo non debba essere considerato assoluto per assenza di malattia.

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