

Occult breast cancer presenting with axillary nodal metastasis: a case report

Carcinoma mammario occulto ad esordio metastatico linfonodale ascellare: caso clinico

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Summary

We report a case of a 56-year-old woman with occult breast cancer (OBC) who presented with a hard metastatic mass in the left axilla, but no breast mass was palpable. Biopsy of the lymph node was performed and histological examination identified a metastatic ductal carcinoma poorly differentiated. Immunohistochemistry showed that the resected lymph node was positive for both estrogen and progesterone receptor. No pathological findings were obtained through mammography, ultrasonography and MRI of both breasts. Systemic examinations (CT, endoscopy) revealed no extramammary primary lesions. All these data suggested an OBC and a left modified radical mastectomy was performed. Pathological examination failed to find the primary cancer lesion on the removed specimen. The patient was treated with adjuvant chemotherapy and hormonal therapy and she presents no evidence of disease 4 years after surgery. Eur. J. Oncol., 14 (2), 109-113, 2009

Key words: breast cancer, occult cancer, axillary nodal metastasis

Riassunto

Si descrive il caso di un carcinoma mammario occulto riscontrato in una donna di 56 anni che presentava linfadenopatia metastatica in sede ascellare sinistra, senza reperto obiettivo di massa mammaria palpabile. La biopsia dei linfonodi evidenziava carcinoma duttale infiltrante metastatico scarsamente differenziato. L'immunoistochimica del linfonodo asportato era fortemente positiva per i recettori estroprogestinici. La valutazione clinicostrumentale (TAC, endoscopia, ecografia, mammografia, RM) non ha rilevato focolai primitivi sia mammari che extramammary. I dati ottenuti hanno orientato per un carcinoma mammario occulto per cui alla paziente veniva praticata mastectomia radicale modificata sinistra e l'esame istologico della mammella era negativo per neoplasia primitiva. La paziente, successivamente, è stata sottoposta a chemio-ormonoterapia ed a distanza di 4 anni dall'intervento chirurgico è libera da malattia. Eur. J. Oncol., 14 (2), 109-113, 2009

Parole chiave: carcinoma mammario, carcinoma occulto, metastasi linfonodale ascellare

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Abbreviations

CEA (carcinoembryonic antigen); CA15-3 (carbohydrate antigen 15-3); AFP (a-fetoprotein); TPA (Tissue Polypeptide Antigen); CA125 (cancer antigen 125); CA19-9 (carbohydrate antigen 19-9); OBC (occult breast cancer); MRI (Magnetic Resonance Imaging); CT (Computed Tomography); ER (estrogen receptor); PR (progesterone receptor); PET (Positron Emission Tomography).

Introduction

Occult primary breast cancer, i.e., isolated axillary adenocarcinoma without detectable tumor in the breast through either physical exam or mammography, represents up to 1% of operable breast cancer (1-3). Women who show adenocarcinoma in axillary lymph node as the unique clinical site of disease may represent a challenging diagnostic and therapeutic problem. Modified radical mastectomy is generally the accepted treatment for this condition although tumour is identified in only two-thirds of mastectomy specimens. This paper describes a case of OBC which was diagnosed by left axillary lymph node metastasis, together with a review of the literature.

Case-report

A 56-year-old woman was referred to our clinic in December 2004, complaining of a palpable painless mass located in her left axilla. She reported no complaints of night sweating, fatigue or weight loss. The patient was not using any medication and she had never taken oral contraceptives. Her family history did not reveal breast or ovaric malignancies.

At admission, upon physical examination a movable ovoid, solid mass (2x1 cm in size) was palpable in the left axilla.

No palpable mass in the both breasts, no nipple discharge and no sign of infection in the left arm were observed.

All vital signs, as well as blood and urine analysis and chest X-ray, were normal. Serum antibody tests to detect toxoplasma and Cytomegalovirus were negative. No signs of abnormality were found in the both breasts through mammography.

Ultrasonography revealed the presence of some lymph nodes (8 to 37 mm in diameter) that could not be definitively interpreted in the axillary process of the left breast.

A subsequent MRI of the right breast did not show any abnormalities, while a MRI of the left breast (figure 1) highlighted, in the axillary process, the presence of some formations (whose diameter ranged between 8 and 37 mm) which were referable to lymph nodes.

The mass was thought to be most probably due to breast cancer, but a metastatic lymph node from an extramammary primary lesion could not be excluded. Therefore, in order to identify the origin of the metastasis, the patient underwent a work-up including ultrasonography and CT of the neck, chest, abdomen and pelvis, gastrointestinal endoscopy and colonoscopy, and whole-body bone scintigraphy. Despite these investigations, no primary tumour was detected. Tumour marker analysis revealed that the TPA was mildly elevated (150 UI/l), while CA 15-3, CEA, AFP, CA 125 and CA19-9 levels were all within normal ranges.

Because the patient did not want to perform a fine needle aspiration cytology, an accessional biopsy of 15 lymph nodes was performed. Histological examinations showed a massive metastasis in a lymph node from an infiltrating poorly differentiated ductal carcinoma, while the other 14 lymph nodes were tumour-free.

However, immunostaining of the metastatic lymph node for both estrogen receptor (ER) and the progesterone receptor (PR) produced positive results (ER: 80%, PR: 80%). No mutation of c-erb-B2 in the PCR analysis of the lymph node was evident.

Based on these findings, we concluded that the axillary lymph node metastasis was caused by occult breast cancer (OBC). A modified radical mastectomy of the left breast was therefore performed in March 2005, after obtaining informed consent from the patient.

The removed specimen was serially sectioned in a 5 mm stepwise fashion and 45 sections were examined. Microscopy of the specimen failed to find the primary breast cancer.

Postoperatively, the patient was treated with adjuvant systemic chemotherapy and ormonotherapy. Chemotherapy consisted in 6 cycles of antracycline-

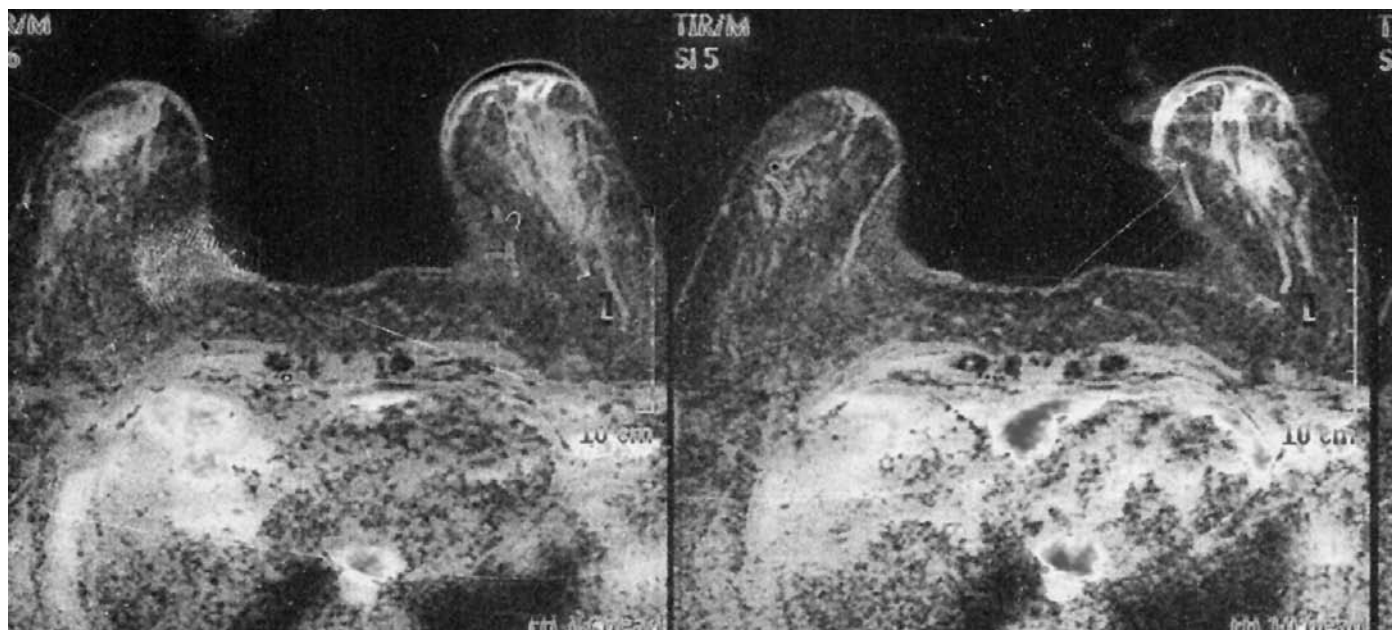


Fig. 1. MRI of left breast (before surgery) shows a hyperintensity, evident in STIR sequences, on skin planes and ductal course

based regimen (FEC ie. 5fluorouracile+epirubicin+cyclofosfamin).

Four years after surgery, the patient shows no clinical evidence of the disease.

Discussion

A carcinoma found in the axillary lymph nodes and caused by primary carcinoma of heterotopic glandular tissue is an extremely rare condition that must be differentiated from metastatic carcinoma.

Carcinomas arising in the heterotopic glandular tissue should accompany the pre-existing non neoplastic glandular component and the ectopic tissue may be present in more than one lymph node (4). In the case we present here, no heterotopic glandular tissues in the axillary lymph node were observed.

Occult breast carcinoma (OBC) presenting as axillary metastases is rare, accounting for less than 1% of all breast cancer patients.

The risk for OBC is higher in premenopausal patients (13.3%, versus 3.5% in postmenopausal women), which is in contrast with breast cancer, in which the risk is higher in postmenopausal women (5).

Aside from breast cancer, many other adenocarcinomas show the potential to spread to the axillary lymph nodes (2, 18, 19). The most common of them include lung, thyroid, stomach, colorectum and pancreas tumours (1, 6, 7).

It is therefore difficult to decide on how extensively an investigation should be performed in order to exclude other possible origins of metastasis. Although we performed CT scans and endoscopy in this case, a PET scan might be particularly useful in searching for the primary cancer in similar cases.

Immunohistochemical markers have been proved as useful for differentiating metastatic breast carcinoma from adenocarcinoma arising in other primary sites. Positive findings for ER/PR analysis are suggestive of breast cancer. Nevertheless, negative ER/PR does not exclude the diagnosis of breast cancer, and it is important to remember that other malignancies (e.g. colon, ovary, endometrium, kidney and melanoma) may demonstrate detectable ER/PR activity (8, 9).

Moreover, Han et al. (10) reported that mammoglobin expression in the lymph nodes was an important marker of metastatic breast carcinoma. Mammoglobin (17) is a protein which is produced by a gene that is more active in breast cancer cells. Patients without metastatic breast cancer have a steady, low baseline level of mammoglobin,

whereas patients with metastatic disease show much higher levels.

Tumour marker studies such as CEA and CA 15-3 may also contribute to a more reliable diagnosis. In the present case, CEA and CA 15-3 were negative, but analysis and stain of ER and PR were strongly positive.

Some cases were reported in which the primary breast tumour could not be identified even in radical mastectomy specimens as in our case. A primary breast cancer will be not found in the specimen in about one third of the cases in the western literature (1, 11, 12). Kyokane et al. (6) reported that the primary tumours of non-palpable breast cancer presenting as an axillary mass were smaller than 5 mm in 19 out of 62 cases and 9 out of 72 cases were represented by intraductal carcinoma with or without minimal invasion. Few cases have been reported on spontaneous regression of the tumour of breast carcinoma.

The treatment of OBC remains controversial. Traditionally, the therapy of choice was radical or modified radical mastectomy (12, 13, 14). However, recent studies have suggested that no statistically significant differences in the outcome between mastectomy and breast conservative treatment such as limited resection and/or radiation and/or chemotherapy were present (1, 11, 15). These findings suggest that breast-conserving therapy is an option for the treatment of OBC (16). In the present case, our patient chose a modified radical mastectomy, but the primary breast cancer was not detected.

The role of adjuvant chemotherapy or hormonal therapy is to provide the same treatment for these patients as for the other node-positive and palpable breast cancer patients.

The overall 10 year survival for patient with OBC is 50-71% (1, 10,14). Survival has not been shown to be dependent on whether the primary cancer in the mastectomy specimen is found. Both the nodal and ER status have been shown to be the major prognostic variable (1,12).

In the absence of good prospective randomized data, it is reasonable that these patients should receive appropriate systemic therapy depending on age, menopausal status and receptor status, similar to other patients with positive lymph node and palpable breast cancer.

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