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Original article

Sentinel lymph node biopsy in patients with operable breast cancer treated with neoadjuvant chemotherapy☆

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ABSTRACT

Aim: To evaluate the accuracy of sentinel lymph node biopsy (SLNB) in operable breast cancer patients treated with neoadjuvant chemotherapy (NAC).
Material and methods: Between January 2008 and 2011, 88 women, mean age 49.4 years, with infiltrating breast carcinoma, were studied prospectively. Patients were T1–3, N0–1, M0. Prior to surgery, the patients received chemotherapy (epirubicin/cyclophosphamide, docetaxel), and trastuzumab in Her2/neu-positive patients. Axillary status was established by physical examination, ultrasound-guided core needle biopsy of any suspicious lymph node. The day before surgery, 74–111 MBq of ^{99m}Tc-albumin nanocolloid was injected periareolarly. All patients underwent breast surgery, with SLNB, followed by complete axillary lymph node dissection (ALND). Sentinel lymph node (SLN) was examined by frozen sections, hematoxylin–eosin staining and immunohistochemical analysis or One Step Nucleic Acid Amplification (OSNA).
Results: Mean tumor size: 3.5 cm, histologic type: 69 invasive ductal, 16 invasive lobular and 3 others. Thirty-seven patients had clinical/ultrasound node-positive at presentation. Clinical response of primary tumor to NAC: complete in 38, partial in 45, and stable disease in 5 patients. A pathological complete response was achieved in 25. All patients were clinically node-negative after NAC.
SLN identification rate was 92.0%. Six of 7 patients in whom SLN was not found had clinical/ultrasound positive axilla before NAC. SLN accurately determined the axillary status in 96.5%. False negative rate was 8.3%. In 69.4% of patients, SLN was the only positive node. The mean number of SLN removed was 1.7 and nodes resected from the ALND were 13.2.
Conclusion: SLN biopsy after NAC can predict the axillary status with a high accuracy in patients with breast cancer, avoiding unnecessary ALND.

Biopsia del ganglio centinela en pacientes con cáncer de mama operable tratadas con quimioterapia neoadyuvante

Palabras clave:
Cáncer de mama
Ganglio centinela
Quimioterapia neoadyuvante
Terapia sistémica primaria

RESUMEN

Objetivo: Validar la biopsia selectiva del ganglio centinela (BGC) en pacientes con cáncer de mama tratadas con quimioterapia neoadyuvante.
Material y métodos: Estudio prospectivo de enero de 2008 a enero de 2011, 88 pacientes con una edad media de 49,4 años, con cáncer de mama infiltrante T1-3, N0-1, M0, tratadas con epirrubicina/ciclofosfamida, docetaxel y trastuzumab en Her2/neu positivas. El estatus axilar se estableció por exploración física, ecografía axilar y punción ecoguiada de ganglios sospechosos. El día antes de la cirugía se inyectaron periareolarmente 74-111 MBq de ^{99m}Tc-nanocoloide de albúmina. En todas se realizó cirugía mamaria, BGC y linfadenectomía axilar. El ganglio centinela (GC) se analizó por cortes de congelación, hematoxilina-eosina, inmunohistoquímica u OSNA.
Resultados: El tamaño medio del tumor fue de 3,5 cm. Según el tipo histológico, 69 se clasificaron como ductal infiltrante, 16 como lobulillar infiltrante y 3 como de otro tipo. Treinta y siete pacientes tenían axila clínica/ecográfica positiva al diagnóstico. La respuesta clínica del tumor primario fue: 38 completa,

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45 parcial, 5 no respuesta. En todas las pacientes la axila fue clínica/ecográfica negativa después del tratamiento. En 25 casos hubo respuesta patológica completa en el tumor primario.
El porcentaje de identificación del GC fue del 92,0%, 6 de las 7 pacientes sin migración eran axila clínica/ecográfica positiva al diagnóstico. En el 96,3% de los casos el GC determinó correctamente el estatus axilar. La tasa de falsos negativos fue del 8,3%. En el 69,4% de los casos el GC era el único afectado de la axila. El número medio de GC identificados fue 1,7 y el de ganglios axilares extirpados fue 13,2.
Conclusión: La BGC es una técnica factible en pacientes con cáncer de mama tratadas con quimioterapia neoadyuvante, pudiendo evitar linfadenectomías innecesarias.

Introduction

Breast cancer is the most frequent tumor in Western women, with the probability of developing the disease before the age of 75 years having been estimated at 8%. This incidence is increasing at an annual rhythm of 1–2% due to the progressive ageing of the population. However, a continued reduction has been observed in the mortality by this disease and 76% of Spanish women with breast cancer remain alive 5 years after diagnosis. This reduction in mortality is due to two fundamental pillars: early diagnosis and the advances in surgical and oncological treatment.[1]

There are two fundamental premises in breast cancer surgery: acceptation of conservative surgery as the standard treatment and the doubts related to the therapeutic efficacy of axillary lymphadenectomy. In addition, lymphadenectomy produces marked morbidity, with severe and definitive complications such as lymphedema. At present increasingly more breast cancers are diagnosed in early stages, questioning the role of the lymphadenectomy, since most of these patients do not have axillary involvement.[2]

Scintigraphic and intraoperative detection of the sentinel lymph node (SLN) is currently considered as a standard technique in the surgical treatment of breast cancer with the aim of avoiding unnecessary axillary lymph node dissection at the time of disease staging thereby decreasing the morbidity of this procedure and allowing a more extensive histopathological study. In the last years there has been a clear trend to an increase in the number of patients who may benefit from SLNB in breast cancer, including different indications from those initially considered.[3–6]

Neoadjuvant chemotherapy (NCT) (preoperative, induction, primary systemic therapy) has been the standard treatment in women with inoperable, locally advanced or inflammatory, breast cancer, with evidence supporting its use in early stages.[7,8] The indication of NCT is adequate in patients with tumors of 3 cm or even smaller when conservative surgery is not possible. Patients with operable breast cancer have tumors in stages I to III-A (T1–T3, N0–N1, M0) and may be treated with multiple therapeutic strategies.[7] The administration of NCT has the following possible advantages: it converts an initially non-surgical breast cancer into one that is operable, increases the number of conservative surgeries, evaluates the sensitivity of the tumor to chemotherapy *in vivo*, initiates systemic treatment early and is a model for clinical or translational investigation. The potential disadvantages include: delay in local treatment, the risk of progression during treatment and imprecise axillary staging.[8]

Neoadjuvant chemotherapy has classically been considered a contraindication for SLNB since the fibrotic changes produced in the primary tumor and in the axillary region (in both the lymph nodes and the lymph channels) and the presence of cellular material or metastatic emboli in the lymph channels of patients with tumors in more advanced stages could cause obstruction of lymph flow or deviation to other lymph node stations. Likewise, the response of the lymph nodes to chemotherapy may not be uniform, not being the sentinel lymph node (SLN) in these cases and reflecting axillary status. Nonetheless, numerous groups have reported their experience with SLNB after NCT, albeit with contradictory results.[9–12]

At present the convenience of performing SLNB prior to or after primary systemic treatment is under question, as are the advantages or disadvantages of when it should be performed. If the fundamental objectives of SLNB are correct staging and avoidance of unnecessary lymphadenectomies in patients without lymph node involvement, it seems logical that both objectives may be achieved if this diagnostic procedure is selectively carried out prior to or after NCT.[12–15]

The main objective of this study was to attempt to validate SLNB with periareolar injection of a radiotracer in patients with operable breast cancer previously treated with primary systemic chemotherapy.

Materials and methods

Study design

We performed a descriptive study of a series of prospective cases. The method followed for accreditation of the procedure is statistical validation of a consecutive registry of cases. The relationship between the histological results of the SLN and its correspondence with axillary lymph node status was analyzed as were the main clinical characteristics of the patients: age, menopausal status, size and localization of the tumor in the breast, axillary status at diagnosis, histological tumor type, clinical and pathological response of the tumor. We also compared the results obtained with our values in the SLNB validation phase in patients with breast cancer in early stages without primary systemic treatment.[16]

Patients

From January 2008 to January 2011 we prospectively studied 93 women consecutively selected from among patients referred to the Functional Oncologic Breast Cancer Unit of the University Hospital Virgen de las Nieves in Granada who fulfilled the following inclusion criteria: operable breast cancer histologically confirmed by thick needle biopsy puncture who had undergone preoperative primary systemic chemotherapy, breast cancer surgery and SLNB with immediate axillary lymphadenectomy. We excluded women with inflammatory breast carcinoma, previous breast surgery or axillary or breast radiotherapy, multifocal or multicentric tumors, systemic metastatic disease or second neoplasm, women who were pregnant or in lactation, under 18 years of age, with a history of allergy to human albumin or who withdrew consent at any time during the study. A total of 88 patients (Fig. 1) were finally included.

Axillary status was established by physical examination, axillary ultrasonography and ultrasound-guided puncture of the suspicious lymph nodes at both diagnosis and at the end of chemotherapy. Evaluation of the grade of clinical response to NCT was made from the changes produced in tumor size by physical examination and conventional imaging techniques, being classified as: complete response (cCR), partial response (cPR) or no response (cNR).