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Benefit of sentinel node biopsy in patients with breast ductal carcinoma in situ

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A B S T R A C T

Introduction: Patients with a diagnosis of breast ductal carcinoma in situ (DCIS) have a low risk of developing axillary metastases. The use of sentinel node biopsy in this group of patients is controversial. The objective of this study is to determine if the sentinel node biopsy benefits a subgroup of patients with DCIS.
Patients and method: Between April 2002 and December 2007, patients with a diagnosis of DCIS and who underwent a sentinel node biopsy were included in the study. In our centre the sentinel node biopsy was performed in patients with DCIS who required a mastectomy, high grade and >2 cm DCIS, and palpable DCIS.
Results: Forty-seven patients were included in the study. In all cases the sentinel node was identified. Twenty-five (53.1%) patients underwent a mastectomy due to extensive DCIS; 14 of these (56%) with immediate reconstruction with implants. Twenty-five (53.1%) patients had high grade DCIS. In 7 (14.8%) patients the tumour was palpable. Fourteen patients (29.7%) were upgraded to invasive breast cancer in the definitive histology. In 2 (4.2%) patients who underwent a mastectomy a positive sentinel node was found.
Conclusions: Performing sentinel node biopsy in this group of DCIS patients has lead us to identify 4% of patients with positive sentinel nodes. Furthermore, 29.7% of the patients have avoided a second invasive diagnostic procedure for definitive histology. For these reasons we consider it appropiate to perform sentinel node biopsy in this subgroup of patients with DCIS of the breas

Beneficio de la biopsia del ganglio linfático centinela en pacientes con carcinoma in situ de mama

Palabras clave:
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R E S U M E N

Introducción: Las pacientes con carcinoma ductal in situ (CDIS) de la mama tienen un riesgo de metástasis ganglionares bajo. Las indicaciones de la utilización del ganglio centinela en el CDIS son controvertidas. El objetivo de este estudio es determinar si la biopsia del ganglio centinela beneficia a un grupo determinado de pacientes con CDIS.

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Pacientes y método: Se ha incluido a las pacientes diagnosticadas de CDIS y con biopsia del ganglio centinela entre abril de 2002 y diciembre de 2007. En nuestro servicio, el protocolo para realizar ganglio centinela en CDIS ha sido: CDIS extenso que requiera mastectomía, de alto grado y tamaño >2 cm, y los CDIS que se acompañan de tumor palpable.
Resultados: Se incluyó a 47 pacientes. Se identificó el ganglio centinela en todos los casos. En 25 (53%) pacientes se realizó una mastectomía por CDIS extenso, y en 14 (56%) de estas pacientes se realizó reconstrucción inmediata. En 25 (53%) pacientes el CDIS fue de grado histológico alto (III). En 7 pacientes la lesión fue palpable. En el diagnóstico histopatológico final se observó que en 14 (29%) pacientes apareció carcinoma invasivo en el diagnóstico definitivo. En 2 (4%) pacientes con mastectomía se encontró un ganglio centinela positivo.
Conclusiones: Las indicaciones seguidas en el protocolo permiten identificar un 4% de ganglios centinelas positivos. Además, en el 29% de las pacientes cuya anatomía patológica definitiva muestra invasión se evita una segunda intervención quirúrgica. Por todo ello, creemos recomendable la realización de la biopsia del ganglio centinela en estos casos determinados de CDIS.

Introduction

With the use of screening programmes, the detection of breast ductal carcinoma in situ (DCIS) has led to an increase of 20% in all cancers diagnosed by mammography.[1] Axillary dissection is not considered a part of the DCIS treatment, due to the low rate of positive nodes (<5%).[2] While sentinel node biopsy for studying the extending of invasive breast carcinoma has replaced axillary dissection, the indications for sentinel node biopsy in DCIS continue to be the subject of debate. Although breast DCIS is a local disease, metastasis of the axillary nodes may occur if there is a non-diagnosed or non-detected invasive tumour in the excised section.

Expert panels do not recommend the use of sentinel node biopsy for all patients diagnosed for DCIS,[3-5] but it is true that a subgroup of these patients would certainly benefit from sentinel node biopsy.

The purpose of this study is to identify whether a group of patients with DCIS exists that could benefit from a sentinel node biopsy.

Patients and method

The prospective study was made up of patients diagnosed for DCIS and sentinel node biopsy during the period starting April 2002 and ending December 2007 who were operated on the Breast Pathology Unit of Hospital Universitario Vall d'Hebron. The preoperative diagnosis for DCIS was in all cases made following a thick-needle biopsy. The sentinel node biopsy was performed on patients with a preoperative diagnosis of high-grade DCIS >2 cm, in patients who preferred or needed a mastectomy and in patients with DCIS and palpable tumour. The patients signed an informed consent form for performing the sentinel node biopsy.

The lymphatic map was prepared using a subareaolar injection of 4 mCi of nanocolloid tecnecium-99 (Nanocoll, Amersham, UK) the day before surgery. A preoperative lymphogammagraphy was performed on all patients and the lymphatic drainage pattern was described. Using a detection probe (Europrobe, Nucliber SA, Spain), the axillary and other lymphatic chain drainage areas were identified. Each lymphatic sentinel node was removed and sent to the pathological anatomy service. An intraoperative study was conducted on the sentinel nodes by freezing. While the result of the intraoperative study was being obtained, the breast surgery procedure was carried out by means of a tumorectomy or mastectomy, as scheduled. When the sentinel node was found to be positive during the operation, the axillary lymphadenectomy was completed.

Sentinel nodes giving negative for metastasis by freezing were subjected to series sections of approximately 1 mm in thickness, including the whole node, and stained with haematoxylin-eosin. Nodes without metastasis following the analysis were stained for immunohistochemistry. The positive nodes were classified based on the TNM[6] classification.

The statistical analysis of the data was performed by a descriptive data analysis.

Results

Forty-seven patients were included in the study. The average (interval) age was 54 (31–80) years. The patient characteristics are described in Table. In all patients, the diagnosis for DCIS was made by thick-needle biopsy. In the final pathological anatomy, 14 (29%) patients had microinvasive or invasive ductal carcinoma.

The surgical technique used was mastectomy in 25 (53%) patients, in 14 (56%) of whom an immediate reconstruction was performed, with expanders being placed in all of them. In the remaining 22 (46%) patients, conservative surgery was performed. In 2 of these patients, no negative margins were obtained, for which reason they were later subjected to a mastectomy.

Patient Characteristics

Characteristics	No. (%)
Radiological injury	
Microcalcifications	41 (87)
Nodule	2 (4)
Distorsion	4 (9)
Clinical	
Palpable injury	7 (15)
Non-palpable	40 (85)
Histology, DCIS	
Pure	41 (87)
Papillary	4 (9)
Cribiform	2 (4)

The size of the DCIS in the final pathological anatomy was 24 (8–70) mm. In 25 (53%) patients, the histological grade of the tumour was grade III.

In all cases, the sentinel node was identified. Two patients had a sentinel node in the internal mammary artery and of these, 1 patient only showed drainage to the internal mammary artery which was removed during surgery, and showed negative. The other patient had axillary drainage and drainage to the internal mammary artery and only the axillary sentinel node was removed, which was also negative. The average number of sentinel nodes removed was 2.3 (1–5). Two (4%) patients had metastasis of the sentinel node, both with a mastectomy. In 1 patient, no invasion was found on reviewing the mastectomy part, and there was ductal carcinoma in situ with a micro papillary pattern and size of 7 cm. In the other patient, infiltrating ductal carcinoma was detected, of 16 mm and another positive node on completing the axillary dissection. All the sentinel node metastases were detected with haematoxylin-eosin and were macrometastases.

After an average follow-up period of 24 (3–71) months, no local recurrence or metastasis were detected in this group of patients.

Discussion

During the last decade, sentinel node biopsy has replaced axillary dissection in breast-cancer patients for the purpose of studying the extension of the disease. Like other new techniques, there are certain indications for sentinel node biopsy that still give rise to debate. Among these, is sentinel node biopsy in neo-adjuvant chemotherapy, in the recurrence of breast cancer and in DCIS.

The controversy about its use in DCIS arises from a series of characteristics of DCIS that differ from invasive breast carcinoma. Firstly, the problem of determining whether it is necessary to perform the sentinel node biopsy technique in patients with DCIS is that with the initial diagnosis, it is not known which patients will have an invasive focus in the final diagnosis. We know that in patients with suspicious injuries, the best diagnosis prior to surgery is thick-needle biopsy. Studies have shown that in up to 20% of patients diagnosed for DCIS using the thick-needle technique, an invasive tumour is detected in the tumorectomy or mastectomy.[7] In our study we found that 29% of patients diagnosed for DCIS with the thick-needle biopsy technique had invasive carcinoma in the final histopathological study following surgery. This result is slightly higher than in other series,[8,9] therefore, there would be 29% of patients requiring a second operation to determine the state of the axillary nodes.

Secondly, patients with DCIS have a good survival rate, approximately 98%, and studies have shown that in 1.5%–2% of patients there are positive axillary nodes shown by haematoxylin-eosin[10] and, therefore, there is agreement that, since the risk of axillary metastasis is very low, there is no indication for an axillary dissection in patients diagnosed with DCIS.[3]

However, these figures have changed since the sentinel node biopsy technique was introduced. The complication arises because, when performing the sentinel node biopsy on patients with DCIS, the proportion of metastasis in the nodes starts to increase when the diagnosis is made using immunohistochemical techniques. In the sentinel node biopsy series published that were performed on patients with DCIS, metastases were found in the sentinel node in 3%–12%.[10-13] In our study, 2 (4%) patients had a positive sentinel node, which was detected by haematoxylin-eosin. The relevance of the node metastases diagnosed by inmunohistochemistry in patients with DCIS is undergoing investigation, since despite these increases in the tumoural classification of the patients, survival of patients with DCIS is around 100%, which does not agree with a percentage of affected nodes of up to 12%.

The question lies in determining which group of patients with DCIS would benefit from sentinel node biopsy in such a heterogeneous disease as DCIS. There are different studies that try to determine this subgroup of patients with DCIS who will have invasive carcinoma in the final pathology and that this is the group in which knowing the state of the axillary nodes is interesting. These publications include patients with DCIS who will need a mastectomy, patients with high-grade DCIS or patients with palpable DCIS with differing percentages of affected nodes.[14-17] In our study, we decided to include this subgroup of patients, which the researchers appear to agree that is the subgroup with the greatest possibility of invasive carcinoma in the final pathology. We verified that not only was a second operation avoided in 29% of patients with invasive carcinoma in the final pathology, but we could also identify this hidden group of patients with invasive carcinoma with metastasis in the sentinel node. These patients with hidden invasive carcinoma make up the subgroup with the greatest risk of metastasis and a lower survival rate.

In a recent meta-analysis by Ansari et al[17] on sentinel node biopsy in DCIS, it was observed that in most studies, a palpable mass, a mass by mammography, a high-grade injury and a large size of the tumour were related to a significant risk of invasive carcinoma in the resection part.

As in the case of invasive breast carcinoma, studies have been conducted on genetic profiles of breast DCIS and the genetic changes associated with the histological appearance of the disease have been determined. However, there are still no studies for determining the genetic changes that could predict the risk of invasive carcinoma. The ratio between

DCIS and invasive carcinoma has yet to be determined. Future studies are based on finding the molecular markers that will accurately predict the nature of the progression of DCIS to invasive carcinoma.[18]

Sentinel node biopsy is not exempt from morbidity, for which reason we agree with most groups that sentinel node biopsy should not be performed on all patients diagnosed with DCIS. Until we are able to determine which subgroup of patients with DCIS has the highest risk of developing invasive carcinoma, we think that the indications in our sentinel node biopsy study comply with the objectives. Naturally, there will always be patients with DCIS who, although not having palpable or high-grade DCIS, will have an invasive focus in the tumorectomy section; however, these patients can always be subjected to a sentinel node biopsy in a second operation.[19]

We believe that in this selected group of patients with DCIS, sentinel node biopsy reduces the need for a second operation and the morbidity, and, therefore, improves the treatment of breast cancer patients.

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