Targeted axillary dissection: a new pathway to the precision

Jorge Sánchez-Lander*

It is absolutely impossible to write this science with the precision with I understand it in my heart. However, although the words are insufficient, the principles should be evident by themselves.

Miyamoto Musashi (1584-1645)

The presence of lymph node disease continues to be the most important prognosis factor in patients with breast cancer. In fact, a large proportion of patients with axillary disease receive neoadjuvant chemotherapy (NACT) and it is estimated that preoperative systemic therapy will be able to eradicate the lymph node disease in 40-75% of them. This is why it has recently emerged the need to design a rational approach in these cases. Taking into account that axillary dissection is still considered the standard conduct, in those patients with axillary pathologic complete response after the NACT, there will be no benefit in terms of prognosis and recorded increased morbidity.

At the beginning of April 2016 is published in Journal of Clinical Oncology the paper Improved Axillary Evaluation Following Neoadjuvant Therapy for Patients With Node-Positive Breast Cancer Using Selective Evaluation of Clipped Nodes: Implementation of Targeted Axillary Dissection¹. In this study, Abigail S. Caudle and cols, from the MD Anderson Cancer Center of the University of Texas, introduced a novel way to deal with the surgical management of positive axillary in patients subjected to Neo-Chem. 208 patients between 2011 and 2015, were prospectively included with axillary nodal disease proven by core needle biopsy in whom a clip were placed under ultrasound guidance on the positive biopsied node. The patients received NACT based on anthracyclines, complemented with taxanes in those with expression of the Her2-Neu in the lymph node sample. Five patients received neoadjuvant endocrine therapy. Upon completion of the NACT, between one to five days before surgery, was positioned a I-125 seed in the ganglion previously marked with clip. Similarly, Tc 99m and blue patent were administered in order to identify the sentinel nodes. All node dyed, radioactive, or increased in size were considered to be sentinel node (SN). Removal of the node with the clip and the seed of I-125 (TN) was confirmed by means of an ex -
**vivo** x-ray of the operatory piece. It was held an axillary dissection in 191 patients, biopsy of sentinel node in 134 patients and an axillary dissection directed or Targeted Axillary Dissection (TAD) in 96 patients. Histopathology management of all SN and MN was similar. The MN was reported separately and when this node also met the criteria for considering it a SN, was additionally immunostaining for cytokeratins. Those nodes with any malignant foci (presence of tumor cells isolated, micrometastasis and macrometastasis) were considered positive. For the statistical analysis is defined as false negative the absence of metastases in the node specified (SN or MN) with disease in the rest of the nodes in the axillary emptying.

Results emphasize the analysis of the MN, which registered a pathologic complete response at 37%. Of the 120 patients with lymph node disease, 115 had residual disease in MN, with a 4.2% proportion of false-negative (95% CI 1.4-9.5). When compared with the patients in whom biopsy was performed only to the SN plus axillary dissection, the false negative rate was 10.1%. The false negative rate was 10% with a single tracer and 10.3% with combined technique. Likewise the false negative rates for patients with 2 or more SN identified was 10.7% in comparison with 7.7% with less than two SN identified.

In the analysis combined of the SN and the MN, in six of the seven patients with SN falsely negative metastatic disease was identified in the MN, what reduced the rate of false negative to 1.4%. (95% CI, 0.03 - 7.3) compared to 10.1% in patients with biopsy of SN exclusively (P = 0.03).

The MN and/or SN were only positive nodes in 49% of cases, including the rest of the nodes in the axillary node dissection. This finding is the main argument against the exclusively use of the SN, since theoretically affected and previously marked node would be not removed in one of every five patients. Interesting to note that 23% of the MN were not included in this series within the SN by absence of staining or radioactivity, coinciding very closely with 20% of the Z1071 study. One of the factors considered by the authors as a possible cause for this discrepancy was the presence of 4 or more suspicious nodes at the initial ultrasound (Odds ratio, 3.5; 95% CI, 1.5 to 8.1). Of the 96 patients subjected to the TAD, in whom the SN and the MN were removed, 85 were subjected to axillary dissection. There was a single false negative case (2%) compared with 10.6% in the patients SN exclusively, difference that was not statistically significant (P = 0.13).

Identify precise patients with axillary residual disease after the NACT is now a real need. SENTINA² and ACOSOG Z1071³⁴ trials have been crucial in the definition of a new approach, which replace routine axillary dissection. Taking into account the statistical data available, the NACT is capable of removing the lymph node disease in a high proportion of patients, which would be at risk of being subjected to unnecessary axillary dissection, without any benefit and not exempt of morbidity. As is the case in early breast cancer, routine axillary dissection remains an indiscriminate measure in the majority of cases. However it must be recognized that at the moment, for many centres, is the only alternative. The sentinel node biopsy before or after the NACT has emerged in recent years as a valid and safe option, however the proportion of false negatives between 5 and 20% remains for many as a controversial topic. With this proposal of the TAD, which includes the removal of the SN and also the removal of the MN, it looks at a first glance, because of the low level of false negatives of 2%, an excellent and intelligent proposal.
On the other hand 37% of the patients presented pathologic total response in MN, which further reinforces the need to not only remove the SN, but also the MN, given the high likelihood of residual disease. By 2014 the NCCN recommended, as category 2A, pretreatment marking of positive nodes by core biopsy and subsequent removal of these nodes and also using the technique of identification of the SN with vital and technetium 99m.

This proposal of the MD Anderson Cancer Center team comes to expand the possibilities of identifying accurately and with low morbidity those patients with axillary complete pathologic response back to NACT and avoid exposing them to a dissection that will bring no benefit to the prognosis and could generate sequels with an important impact on the quality of life. Of course, something that worries greatly, especially in countries such as ours, with a greater proportion of patients with locally advanced breast cancer, is cost and the availability of devices for marking the node to allow starting the experience at our sites and improve the level of care for these patients.


References:


