Sentinel node role in breast cancer surgery

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Abstract. - Radical surgery of breast cancer includes lymphadenectomy of axilla as well as the dissection of the neoplastic tissue. However recently many works have raised doubts on the opportunity of performing routinary axillary dissection, which elevates morbidity risk, in absence of axillary metastases.

However, unfortunately, information on axillary lymph node pathology, is not available with any other technique excluding complete dissection and istopathological examination.

Sentinel node technique is a new methodology that consents evaluation of lymph node status in the operating theatre. It allows the surgeon to judge on the opportunity of carrying out the lymphadenectomy or not.

Key Words:

Breast cancer, sentinel node

Introduction

The surgical treatment of breast cancer makes use of a multidisciplinary approach, above all thanks to the considerable progress of the adjuvant and neoadjuvant therapies. At the moment, anyway, the "gold standard" of the breast cancer therapy is still surgery, which provides the dissection of both the neoplastic and the lymphatic-cellular tissue of axilla.

However many studies have clearly shown that while axillary lymphadenectomy has an undoubtable and irreplaceable role in staging and prognosis it doesn't modify breast cancer mortality and the incidence of metastasis, but sensibly increases the morbidity.

These considerations originated a long series of researches with the purpose of defining a procedure allowing the surgeon to iden-

tify the axillary lymph nodes status already in the operating room. In this case, lymphadenectomy could be carried out only if effectively necessary. Sentinel node tecnique responds to these requirements and is beenig applied with increasing frequence.

This is a new, actually experimental, technique which consents an intra-operative staging of the breast cancer referred to the N parameter, allowing to establish if axillary metastases are present without recurring to large lymphadenectomy which, on the other side, becomes necessary if the technique results positive for a metastatic sentinel node.

Sentinel node tecniques offers a valid alternative to the number of superfluous lymphadenectomies, improving short and long term quality of life of patients with breast cancer and reducing the incidence of complications.

Materials and Methods

Sentinel node technique is based on the acquisition on lymphatic flow of Morton et al¹. Effectively lymph flows according to unidirectional pattern through forced lymphatic stations forced lymphatic stations. The sentinel node represents the first lymphatic drainage station of the axillary cable, and is therefore also the first structure to filter eventual carcinomatous cells; thus if this lymph node results infiltrated by neoplastic repetitions, also compromised will be the successive lymphatic stations whose excision will be useless.

The technique is based on the identification of the first lymph node of the axillary lymphatic chain and on its extemporary histologic analysis that allows the surgeon to decide whether carrying out lymphadenectomy or not in consequence of the presence or less of metastatic cells in this level. Sentinel node can be identified by two methods.

Preoperative lymph-scintigraphy

Injection of a radioactive tracer in the perineoplastic tissue two hours before surgery (colloids of marked albumin with ⁹⁹Tc). The substance is drained from sentinel node which will be identified by gamma camera, 45 minutes after injection, in the axillary cable as a warm area on the cutaneous surphace. In this precise location, after the tumour dissection, a small incision will be carried out to expose and remove the structure after ulterior confirmal of its radioactivity by direct positioning of the gamma camera on the lymph node.

Use of vital staining (patent blue V or methylene blue)

Injection, 15 minutes before surgery, of 1-2 cc of vital stain in the peri-neoplastic tissue, which is drained, through the efferent lymphatic ducts, to the sentinel node which therefore is visually identified like the first lymphatic station that assumes the blue colour.

Often both methods are associated to obtain superiore accuracy. And the surgeon may take advantage of the colouring tissue to have a confirmation of the sentinel node previously identified by the gamma camera. Sometimes more than one lymph node can be detected (even three).

Subjects

In our study we enrolled 15 patients from 45 to 78 years old with single breast cancer of 0.5 to 1.8 cm diameter. The tumour was localized in the upper external quadrant in 7 cases, upper internal quadrant in 3 cases, lower external quadrant in 2 cases, lower internal quadrant in 3 cases.

Patients were divided in three groups: in the first one the research of sentinel node was performed using the lymph-scintigraphy technique (group A: 5 cases), in the second group by the vital staining (group B: 5 cases), in the third group both the exams were associated (group C: 5 cases).

All patients were treated by:

- Lumpectomy with extemporary histologic examination.
- Sentinel node identification with dissection and extemporary histologic examination (18 sections).
- Axillary lymphadenectomy.

Sentinel node resulted positive at the extemporary histologic examination in 13 cases, confirmed later by definitive histologic examination. Only in two patients, one of the B group and one of the C group, the lymph node resulted negative at the extemporary histologic examination but positive at the definitive histologic examination (13.3% of false negative results). None of the 15 patients reported postoperative complications. A detailed analysis of the results is reported in Table I.

Table I. Demographi	c data of patients	undergone a	diagnostic procedures	i.
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Age	Lesion diameter	Quadrant	Technique	Sentinel node	False negative
45	5 mm	UEQ dx	Lymph scintigraphy	+	
52	7 mm	UIQ dx	-	+	
54	12 mm	LEQ dx	-	+	
47	15 mm	UEQ sn	-	+	
49	9 mm	UEQ dx	-	+	
65	13 mm	LIQ sn	Methylene blue	+	
65	14 mm	UEQ dx	_	+	
75	17 mm	UIQ sn	_	_	*
45	8 mm	LEQ dx	_	+	
78	12 mm	LIQ sn	_	+	
70	15 mm	UEQ sn	Combined	+	
68	18 mm	UIQ dx	_	+	
58	17 mm	UEQ dx	-	+	
50	18 mm	LIQ sn	-	-	*
74	9 mm	UEQ dx	_	+	

Discussion

Breast cancer surgery has lived alternate vicissitudes, from an initial extreme surgical aggressiveness in all cases (Halsted mastectomy), to the present, more conservative, guidelines.

Indipendently of this evolution, axillary lymphadenectomy remain till now an absolute and obliged surgical procedure in the radical therapy of breast cancer, and medical literature has always emphasized its therapeutic worth.

However, during the last years many studies have showed some interesting features:

- There is no unanimous agreement on the importance of the axillary dissection for global survival²⁻⁴ but lymphadenectomy is commonly deemed to have not a therapeutic role but only a prognostic and staging worth^{5,6}.
- Incidence of metastases is proportional to the increasing of the tumour dimension and is limited in early stages (situation more and more frequent thanks to the diffusion of the prevention campaigns)⁷⁻¹⁰.

These observations have lead to a revision of the necessity of routine axillary dissection which, moreover, is not exempt from complications as arm lymphedema¹¹, the onset of serum crop¹², postoperative functional limitations of the arm¹³, sensory-motorial brachial neuropathy¹⁴.

The axillary lymphatic chains status remains up to date the most important therapeutic index although in the last years other indexes as age, tumour grading, presence of neoplastic cells receptors, and ploidy, have aroused great interest however without demonstrating the same prognostic significance of the axillary lymph nodes status, that is the N parameter^{15,16}.

The sentinel node identification represents, from this point of view, a very promising technique which could offer a valid alternative to the routine axillary dissection and allow an accurate staging. In our study we have not noticed significant differences between the lymph-scintigraphy technique and the use of the vital staining in the identification of the sentinel node, but we are firmly convinced that best accuracy is obtainable only combining both techniques.

In our study, the incidence of false negative results has been about 13.3%, which is quite different from the other casistics where the average incidence is about $5\%^{17}$.

However it must be considered that this seemingly noticeable difference is related to the smaller number of patients we studied compared to the quoted casistics.

In conclusion, the sentinel node technique seems very promising and has gained notable popularity collecting wide agreement among professionals and patients especially for its scanty invasiveness. However, although we are not in conditions to draw definitive conclusions on the usefulness of this technique, we highlight that at present it cannot be proposed as alternative to the routine axillary lymphadenectomy in the breast cancer treatment but it should be considered an experimental procedure in need of further and more expanded researches for a definitive scientific validation.

References

- MORTON DL, WEN DR, WONG JH, ECONOMOU JS, CAGLE LA, STORM FK. Technical details of intraoperative lymphatic mapping of early stage melanoma. Arch Surg 1992; 127: 392-399.
- FISHER B, REDMOND C, FISHER ER, et al. Ten years results of randomized clinical trial comparing radical mastectomy with or without radiation. N Engl J Med 1985; 312: 674-681.
- CABANES PA, SALMON RJ, VILCOQ JR, et al. Value of axillary dissection in addiction to lumpectomy and radiotherapy in early breast cancer. Lancet 1992; 339: 1245-1248.
- 4) WHITE RE, VEZERIDIS MP, KONSTADOULAKIS M, COLE BF, WANEBO HJ, BLAND KI. Therapeutic options and results for the management of minimal invasive carcinoma of the breast: influence of axillary dissection for the treatment of T1a and T1b lesions. J Am Coll Surg 1996; 183: 575-582.
- FISHER B, BAUER M, WICKERHMAN DL, et al. Relation of number of positive axillary node to the prognosis of patients with primary breast cancer. An N.S.A.B.P. update. Cancer 1983; 52: 1551-1557.
- BONADONNA G, VALAGUSSA P. Adjuvant systemic therapy for resectable breast cancer. J Clin Oncol 1985; 3: 259-275.
- FISHER ER, SASS R, FISHER B. Pathology findings from the National Surgical Adjuvant Project for breast cancer (protocol n° 4). Cancer 1984; 53: 712-723.

- VERONESI U, RILKE F, LUINI A, et al. Distribuition of axillary lymph node metastases by level of invasion. An analysis of 539 cases. Cancer 1986; 59: 682-687.
- CIATTO S, ROSSELLI DEL TURCO M, BONARI R, et al. Non palpable lesions of the breast detected by mammography review of 1182 consecutive histologically confirmed cases. Eur J Surg 1994; 30: 40-44.
- FISHER B, BOYLE S, BURKE M, PRICE A. Intraoperative assessment of nodal status in the selection of patients with breast cancer for axillary clearance. Br J Surg 1993; 80: 457-458.
- PETREK JA, HEELAN MC. Incidence of breast carcinoma-related lymphedema. Cancer 1998; 83: 2776-2781.
- TADYCH K, DONEGAN WL. Postmastectomy seromas and wound drainage. Surg Gynecol Obstet 1987; 165: 483-487.

- JANSEN RMF, VAN GEEL AN, DE GROOT HGV, et al. Immediate versus delayed shoulder exercises after axillary lymph node dissection. Am J Surg 1990; 160: 481-484.
- 14) LIN PP, ALLISON DC, WAINSTOCK J, et al. Impact of axillary lymph node dissection on the terapy of breast cancer patients. J Clin Oncol 1993; 11: 1536-1544.
- GIULIANO AE, JONES RC, BRENNAN M, STATMAN R. Sentinel lymphadenectomy in breast cancer. J Clin Oncol 1997; 15: 2345-2350.
- 16) HELLMAN S. Natural history of small breast cancers. J Clin Oncol 1994; 12: 2229-2234.
- VERONESI U, PAGANELLI G, GALIMBERTI V, et al. Sentinel node biopsy to avoid axillary dissection in breast cancer with clinically negative lymph nodes. Lancet 1997; 349: 1864-1867.