Lymphangiosis Carcinomatosa Peritumorales (L) – Marker of Lymphatic Nodule Metastasing, with a Fundamental Role in the Prognosis and Therapy of Mammary Cancer

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Introduction

Breast cancer is the most frequent female malign tumor and it must be considered as a systemic disease. By introducing the sentinel lymphnode technique (SLN), there is a chance that we can forego, in great part, the conventional axial dissection by using this minimally invasive method.

The main purpose of the lymph node technique was that of perceiving, integrally, or with a very small margin of error, patients with lymph node metastasis and to avoid postoperative morbidity of axial dissection for nodal negative women.

The first clinical data were so promising that this technique was quickly elevated to a therapeutical status, although some aspects were still unclarified, to be observed during other clinical studies. Based on this background and on our data, we attempt to evaluate the applicability and the correctness of this method as well as discovering other prognostic markers.

The target for conventional axial dissection is, first of all, the local control of the tumor and, secondly, the evaluation of the status of the tumor; that is why metastasis evaluation is very important. The nodal status is, for mammary carcinoma, the most important prognostic factor and serves as a parameter in order to predict the danger of local relapse as well as long term survival (Kühn et al, 1999). Besides this, the nodal status serves as decisive criteria in choosing an alternative system therapy.

Materials and Method

1. The studied lot

The studied group consisted of 500 patients, randomly selected. All the patients were diagnosed with breast carcinoma, cT1N0 clinical stage and had been selected for the sentinel lymphnode technique. The diagnosis was performed during August 2011 – December 2012; the patients were operated at the Rhein-Main Senological Oncology Centre in Germany.

2. Analysis Methodology

The available data in order to create the proposed analysis was grouped as such:
- data that describe the studied group from the demographical point of view (the age during diagnosis, age group structure);
- data that describe the studied group from the point of view of the medical parameters (type of breast cancer, size of tumor (T), lymphangiosis carcinomatosa peritumorales (L), existence/inexistence of metastatic lymph nodes (N), texistence/inexistence of metastatic sentinel lymph nodes (SN), tumor resection in healthy tissue (R), tumoral grading (G), Elston-Ellis values, estrogen (ER) and progesterone (PR) receptors, HER2/neu, the proliferation fraction ki67, tumor localisation);
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- data that express the connection between variables.

Breast lymphatic vessels extend to the entire gland, making possible the deep and superficial draining. There are separate lymphatic vessels for every lobe and milk duct. The lymphatic vessels communicate with the periareoral lymphatic plex and associate in this area with the vein plex. The direct deep lymphatic connections enter through the deep fascia in the subjacent muscles. The primary lymphatic eferences traverse the supero-exterior quadrant, along the great pectoral muscle towards the deep pectoral lymphatic nodules. Others communicate directly with the subscapular nodes. Thus, the lymph is drained towards the central axial group and, from here, towards the apical nodes of the axilla and then towards the supraclavicular nodes. The internal mammary perforants are accompanied by medial lymphatic channels that drain the parasternal nodes. The entire lymphatic network of the breast is tributary to these medial lymphatic nodes (BOSTWICK, 2000).

The lymphatic network of the breast is divided in cutaneous lymphatics that drain the lymph of the mammary skin and of the subcutanated adipose tissue and the lymphatics of the gland (ROUVIERE, 1970, CAPLAN, 1982).

The lymphatic vessels transport the humoral liquid between tissues and blood vessels. Before the lymphatic liquid drains into the blood vessels, it traverses the lymphatic nodes in which the imunocells act against the infectious agents, the metabolical rests and cancerous cells, which they try to neutralize. The tumors can give signs of expansion, which could stimulate the genesis of new lymphatic vessels to help them grow. The peritumoral lymphatic vessels (L) are classified by pathologists in four categories:
- L0 – Peritumoral lymphatic vessels, free of cancerous cells;
- L1 – Peritumoral lymphatic vessels invaded by cancerous cells;
- L2 – Peritumoral lymphatic vessels with macroscopical cancerous cells invasion and
- Lx – Peritumoral lymphatic vessels without the possibility to affirm the degree of cancerous cells invasion.

Results

We have analyzed the peritumoral carcinomatose lymphogenesis (L) with other important tumoral parameters (fig. 1).

It is interesting to observe that there is a low percentage of the L1 and N0 situation, while, in the meantime, we can observe a higher by three percentage of the L0 and N1 situation, explained probably by the metastasis theory of “seed and soil”.

63 cases (12.6 %) are in the simultaneous situation of L1 and N1. By comparing the shares for the studied characteristics there are some significant differences, especially regarding the size and grading of the tumor G1 and G3. G2 has a behaviour influenced by the prudent framing of this category (Table I).

![Fig. 1. The shares of the relationship types between peritumoral lymphagiosis (L) and lymphatic nodules (N).](image)

Table I. The medium profile of the comparative patients (L1/N1 shares) and total group

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>L1/N1 shares</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medium age, years</td>
<td>57.97</td>
<td>60.49</td>
</tr>
<tr>
<td>Tumor type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>invasive-ductal (%)</td>
<td>80.95</td>
<td>7776</td>
</tr>
<tr>
<td>invasive-lobular (%)</td>
<td>12.70</td>
<td>17.64</td>
</tr>
<tr>
<td>Tubular (%)</td>
<td>6.35</td>
<td>4.61</td>
</tr>
<tr>
<td>Tumor medium size (mm)</td>
<td>19.87</td>
<td>15.97</td>
</tr>
<tr>
<td>T1 (%)</td>
<td>60.32</td>
<td>76.60</td>
</tr>
<tr>
<td>T2 (%)</td>
<td>36.51</td>
<td>22.60</td>
</tr>
<tr>
<td>T3 (%)</td>
<td>3.17</td>
<td>0.80</td>
</tr>
<tr>
<td>Tumor grading</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumor grading G1 (%)</td>
<td>12.70</td>
<td>19.68</td>
</tr>
<tr>
<td>Tumor grading G2 (%)</td>
<td>60.32</td>
<td>60.04</td>
</tr>
<tr>
<td>Tumor grading G3 (%)</td>
<td>25.40</td>
<td>20.28</td>
</tr>
<tr>
<td>Elston – Ellis scale</td>
<td>6.00</td>
<td>6.09</td>
</tr>
<tr>
<td>Positive hormonal receptors (%)</td>
<td>69.84</td>
<td>72.56</td>
</tr>
<tr>
<td>Negative hormonal receptors (%)</td>
<td>9.52</td>
<td>9.52</td>
</tr>
<tr>
<td>Multiplication fraction</td>
<td>13.82</td>
<td>12.59</td>
</tr>
<tr>
<td>Right breast (%)</td>
<td>47.62</td>
<td>47.60</td>
</tr>
<tr>
<td>Left breast (%)</td>
<td>52.38</td>
<td>52.40</td>
</tr>
</tbody>
</table>

There are less significant conclusions in this special group of 63 patients compared to the ones revealed by the complete group of 500.

But a clear correlation can be seen for the L1/N1 subgroup of patients with the tumor size, the tumor’s hystological type, tumoral grading, age of the patient, positive hormonal status and the Ki76 proliferation fraction.

The metastasis risk grows in direct proportion with the tumor size.
The metastasis risk grows in direct proportion to the growth of the tumor grading.

The highest metastasis type appears to be for the invasive ductal type.

Tumor size is also very important, as the metastasis risk grows in direct proportion to its size, implying the formation of new lymphatic vessels.

Tumor grading also has an important role in the metastasis process. The higher the grading, the higher the risk for metastasis.
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In the case of negative hormonal receptors, the risk of metastasis is higher. The higher Ki67 multiplication fraction, the higher the risk of metastasis.

3. Survival data for sentinel patients

Survival data are significantly better, 96.8% being cases selected in the incipient stages of mammary cancer (T1 – T2).

4. Axial recidivism ratio

A total of 2 patients that have been treated with a SLN have been diagnosed with an axial recidivism. Both patients refused the axial dissection and have decided for a SLN so a ratio of 0.4%.

The ratio between patients with peritumoral lymphagiosis and lymphatic nodules in metastasis reveals, in the majority of the cases (76.80%) the L0/N0 type.

Discussions

By comparing the data of our research, we can say that peritumoral carcinomatose lymphogiosis in mammary cancer can have a very important role in the metastasic process of lymph nodes, including taking the role of marker in the metastasis process.

This theme has been very little treated in the specialized literature. Taking into consideration the free circulated cancer cells (a probable explanation of the L0/N1 phenomena) as well as the metastasis forming mechanisms, we consider that:

1. Cancer cells invasion in peritumoral lymphatic vessels, that is to say the L1 situation is tied in direct proportion with a high risk of the beginning of the metastasic process of lymph nodes, that is to say HIGH RISK of METASTASES (HRM)

2. The L0 situation has a LOW METASTATIC RISK (LRM) allowing that the size and biology of the tumor have favorable criteria.

3. Based on the above observations and the St. Gallen 2011 molecular classification of the mammary tumors:

We propose the following diagram for the LYMPHATIC NODULES METASTASING RISK:
Conclusions

1. An important role in establishing an oncological treatment is the biology of the tumor, followed by its size, nodal status, age, comorbidity and future quality of the patient’s life.

2. In the cT1-T2 CN0 clinical stage, taking into consideration the age, the option and the comorbidity of the patient, in some conditions, we can forego the sentinel node technique or the classical axillary dissection. Using the peritumoral carcinomatose lymphangiosis (L) as a marker, correlated with other factors, such as the biology and tumor size, we can evaluate the high (HRM) or low (LRM) risk of lymph node metastasis, this classification can be an option in selecting the following treatment, that is to say the inclusion or dismissal of chemotherapy, antihormonal therapy and/or radiotherapy.

3. The decision to forego the axillary dissection must be taken in agreement with the patient, who must be rigorously informed of the intra/postoperatory advantages and the disadvantages, as well as the risks of local relapse and metastasis.

4. By foregoing the axillary dissection, the above diagram can be a useful instrument in choosing a treatment, after the diagnosis.

5. The precise total of patients that do not profit from an axila lymphadenectomy must still be researched.

6. Peritumoral carcinomatose lymphangiosis seems to have an important role in the metastatic process of lymphnodes. Our study’s observations are a start in this very little researched field.

References