Postmastectomy neuropathic pain: Results of microsurgical lymph nodes transplantation

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Abstract

Postmastectomy chronic pain may be divided into widespread and regional pain. Almost half patients with regional pain, which is more likely related to neuropathic phenomena, do not benefit any pain relief from medication. Our purpose was to report results on pain relief obtained by axillary lymph nodes autotransplantation.

Methods: Six patients presented with chronic regional neuropathic pains and upper limb lymphedema after breast cancer surgery and radiation therapy. Despite medication, pain was intolerable and daily activity dramatically reduced. Lymph nodes were harvested in the femoral region, transferred to the axillary region and transplanted by microsurgical procedures.

Results: Lymphedema resolved in 5 out of 6 patients. Pain was relieved in all, permitting return to work and daily activity; analgesic medication was discontinued.

Conclusion: This procedure proved efficient and may be advocated in case of neuropathic pain when discussing lymphedema management.

Keywords: Breast cancer; Lymphedema; Chronic pain; Lymph node; Neuroma; Autotransplantation

Chronic pain following breast cancer surgery is now a common and well-recognized problem with prevalence rates as high as 42.9% (175/408) and 46% (59/85) in retrospective studies,1,2 such rates being also observed in prospective study (48.4%, 46/95).3 Chronic pain is defined by the International Association for the Study of Pain as that persisting beyond the normal healing time of 3 months (IASP, 1986). Little is known about its long-term outcome, but chronic pain can resolve with time. MacDonald and Coll1 reported a cumulative prevalence of 43% at 3 years (mean) postoperatively and of 17% at 9 years (mean). The exact cause of chronic pain is unclear and various aetiological theories have been postulated, the main 1 being neuropathic origin. Chronic pain following breast cancer surgery has been divided into widespread and regional pain.4 Widespread pain, which is diffuse, persistent pain mainly due to other factors than neuropathic, may induce significantly more severity of pain, pain impact and lower physical health status than regional pain. However, in case of widespread pain, medication is rated as at least somewhat effective for relieving this pain. On the contrary, only 56% of patients with regional pain will benefit any pain relief from medication.4 Regional pain which is chronic pain related to neuropathic phenomena,1 so remains a therapeutic challenging problem.

Other major problem following breast cancer treatment is lymphedema. Whatever the treatment proposed, the possibility of curing lymphedema remains questionable. Over the last 13 years, our team has treated limb lymphedema by transplanting lymph nodes.5 Results obtained with this procedure proved satisfactory demonstrating disappearance or a noteworthy improvement in postmastectomy lymphedema, especially in the early stages of the disease.6

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In some other patients, chronic pain was associated with postmastectomy lymphedema. The purpose of this study was to report the results obtained with this procedure in such a case.

Patients and methods

From October 2000 to December 2005, 6 patients suffering upper limb lymphedema presented with a chronic regional neuropathic pain localized in the axilla and characterized by its intensity and by spontaneous exacerbations or exacerbations evoked by mechanical stimuli. Breast cancer surgery consisted in 3 lumpectomies and 3 mastectomies. All patients underwent a full level-3 axillary lymphadenectomy, followed by postoperative radiation therapy with lymphatic irradiation (sternal, supraclavicular, and axillary regions). Pain appeared immediately after surgery except in 1 patient, pain occurring at the end of radiation therapy. Neurona-like exacerbating characteristics took place early thereafter. Pain had a great impact on daily life, and all patients had stopped working and/or reduced their at home activity. Patients characteristics are figured in Table 1. All patients had an upper limb lymphedema: stage I, \( n = 4 \) and stage II, \( n = 2 \). Lymphedema was right sided in 3 patients and left sided in 3. Absence of lymph node (LN) and of lymphatic drainage was assessed by isotopic lymphangiography. Patients with lumpectomy had also a slight breast edema. All patients were seen by their oncologist and considered in breast cancer remission. Intervals between breast cancer and lymph node transplantation ranged from 12 to 216 months (mean = 85) (Table 2). One patient (patient 3) had already been reoperated on, but unsuccessfully. Three patients had associated intercostobrachial nerve neuropathy. Plexopathy in the T3–T4 territory and 1-finger algodystrophia (following hand burn-injury) were also present in, respectively, patient 3 and patient 4. All patients were asked to rate their pain on 0–10 numerical rating scales. Medications used for their pain were categorized as opioid analgesics, nonopioid (e.g., acetaminophen, nonsteroidal anti-inflammatory drugs) and tricyclic antidepressants. Emotional functioning such as depression was mentioned.

Surgical approach of the axillary region of the previous breast cancer surgical area was performed through the previous scar without resecting it. Fibrotic tissues were dissected and adhesions released until the anterior border of the latissimus dorsi, and then more deeply in search of the thoracodorsal and axillary vessels, and of the “scapular” pedicle which was dissected and isolated. In this area, thoracodorsal nerve branches were commonly found entrapped in the fibrosis at the level of “clipped” vascular vessels (Fig. 1): some of these branches presented as hypertrophic nervous formations (Fig. 2), the presence of clips indicating that they were sectioned during breast surgery. The circumflex posterior branches were further individualized and prepared for microanastomoses.

Lymph nodes were then harvested in the inguinal region. The dissection began by visualizing the superficialis circumflex iliac vein. In that region are located LN irrigated by the circumflex iliac vessels and mainly receiving the lymph from the abdominal wall,\(^5\)\(^6\) so as harvesting them does not impair the lymphatic drainage of the inferior limb. These nodes were dissected, freed, and elevated external to internal at the

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**Table 1**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (year)</th>
<th>Side</th>
<th>Breast treatment</th>
<th>Breast edema</th>
<th>Lymphedema</th>
<th>IC pain</th>
<th>Other pain</th>
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<tbody>
<tr>
<td>1</td>
<td>54</td>
<td>L</td>
<td>Lu + Ly + RT + CT</td>
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<td>I</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>52</td>
<td>R</td>
<td>Lu + Ly + RT + H</td>
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<td>I</td>
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<td>0</td>
</tr>
<tr>
<td>3</td>
<td>53</td>
<td>R</td>
<td>Ma + Ly + RT</td>
<td>0</td>
<td>I</td>
<td>+ T7–T8 territory algodystrophia</td>
<td>Finger algodystrophia</td>
</tr>
<tr>
<td>4</td>
<td>66</td>
<td>L</td>
<td>Lu + Ly + RT</td>
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<td>II</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>69</td>
<td>R</td>
<td>Ma + Ly + RT</td>
<td>0</td>
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<td>+</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>69</td>
<td>L</td>
<td>Ma + Ly + RT + CT</td>
<td>0</td>
<td>II</td>
<td>+</td>
<td>0</td>
</tr>
</tbody>
</table>

L = left; R = right; Lu = lumpectomy; Ma = mastectomy; IC = intercostal; RT = radiation therapy; CT = chemotherapy; H = hormonotherapy; I = lymphedema stage I; II = lymphedema stage II; and Ly = lymphadenectomy.

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**Table 2**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Interval between breast and pain surgery (month)</th>
<th>Pain scale (1)</th>
<th>Medical treatment (1)</th>
<th>Follow-up (month)</th>
<th>Pain scale (2)</th>
<th>Medical treatment (2)</th>
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<td>24</td>
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<td>7</td>
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<td>14</td>
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<td>4</td>
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<td>10</td>
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<td>3</td>
<td>NOA</td>
</tr>
<tr>
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<td>12</td>
<td>5</td>
<td>NOA</td>
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</tr>
<tr>
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<td>5</td>
<td>NOA</td>
<td>19</td>
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<td>0</td>
</tr>
</tbody>
</table>

TAD = tricyclic antidepressant; NOA = nonopioid analgesics; and OA = opioid analgesics.

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Fig. 1. Nerve branches entrapped in fibrosis at the level of “clipped” vascular vessel.
level of the muscular aponevrosis. The nodes were then harvested with an abundant amount of surrounding fat tissue which could be extended medially and contralaterally (Fig. 3) when necessary. LN was then transplanted in the axillary receiving site. Artery and vein were anastomosed with the vessels previously prepared, using microsurgical techniques (Fig. 4). Both axillary and inguinal approaches were closed on suction drainage. No elastic compression dressing was applied following surgery to avoid compression of the transplanted LN and microsurgical anastomoses. Antisludge treatment was administrated during the postoperative period. Manual drainage (physiotherapy) was performed on the first postoperative day and daily during the first 3 months, and then discontinued.

Results of the procedure were evaluated according to patients 0–10 numerical rating scale evaluations, changes in pain medications, and daily activity resumption. Effects on other associated neuropathic disorders and on lymphedema were also analyzed.

Results

Postoperative course was uneventful and no complication was observed, neither at the axillary nor at the inguinal sites. Neuropathic pain disappeared immediately after surgery, and results remained unchanged after follow-up intervals ranging from 13 to 38 months (mean = 21) (Table 2). All patients recovered a normal daily activity and the 3 patients having interrupted their work were able to work again. Pain medication was stopped in all, except the patient suffering finger algodystrophy who kept on taking anti-inflammatory steroids. Inter-costal neuralgia did not totally disappeared but was changed to dysesthesia rather than pain and did not require particular treatment any longer. Breast edema resolved in 2 out of 3 complaining patients, and upper limb lymphedema in 5 out of 6.

Comment

Postmastectomy neuropathic pain consisting in “neuroma” pain located in the axilla appeared related to neuromatous
development and fibrotic entrapment of latissimus dorsi nerve branches in the proximity of the vascular pedicles, and was relieved following "neurolysis" obtained by local fibrosis resection and replacement "coverage" of the released tissues by a free LN–fatty flap transplantation.

Neuropathic pain is defined as pain "initiated or caused by a primary lesion or dysfunction in the nervous system." Neuropathic pain arises from damage to nociceptive axons. In "post-mastectomy pain syndrome", pain is typically localized to the axilla, medial upper arm, and/or the anterior chest wall on the affected side. Jung et al. distinguishes 4 different types of chronic neuropathy pain following breast cancer:

- phantom breast pain;
- intercostobrachial neuralgia (intercostobrachial nerve);
- neuroma pain (intercostobrachial nerve and scar tissue);
- other nerves injury (motor nerves).

This chronic neuropathy pain is generally attributed to sensitive nerves and more particularly intercostobrachial nerve injury (somatic and preganglionic sympathetic innervation), but motor nerves may also be concerned as the serratus anterior muscle nerve behind the axillary nodes, and the latissimus dorsi nerve in close proximity to the subscapular (artery and vein) vessels.

In "post-mastectomy pain syndrome", sensory findings and symptoms reflect the maintenance of central sensitization by input from damaged primary afferent nociceptors that remain in continuity with their central targets. However, the mechanism of neuroma pain is different and attributed to abnormal neuronal activity originating in neuromas or entrapped axons within scar tissue. Neurona can be a source of ectopic discharges that contribute to pain. These can be either spontaneous or evoked by mechanical stimuli.

Microneuromas can form in scar tissue and have been reported following breast cancer surgery, and can cause chronic neuropathic pain. Patients who have axillary dissection and radiotherapy appear more likely to have scar pain. Development of a neuroma at the level of transected intercostal nerve at the time of breast surgery has been reported by Wong. Other nerves have been incriminated as sources of neuropathic pain, mainly the thoracodorsal nerve which is routinely spared but may be injured by traction during mastectomy or by scarring. This appears to be corresponding to what we observed in our patients, nerves branches being entrapped in the soft tissues scar fibrosis (Figs. 1 and 2), most often at the level of "hemostasis" vessels clipping.

Conflict of interest statement

None declared.

References


