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Clinical and neurophysiological evaluation of persistent sensory disturbances in breast cancer women after mastectomy with or without radiotherapy

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ABSTRACT

Purpose: Breast cancer surgery or radiotherapy (RT) are potential causes of persistent pain syndrome. It remains to be clarified whether numbness or pain reported by patients after mastectomy and RT are conditioned by changes in nerve transmission. The aim of this study was to examine the potential relationship between subjective sensory complications and neurophysiological examinations in breast cancer survivors with post-mastectomy pain syndrome.
Methods: Sixty breast cancer survivors (30 patients only after mastectomy – group A; and 30 after mastectomy with RT – group B) complaining of pain and sensory disturbances in the brachial plexus area and 20 healthy women (group C) were studied with regard to sensory perception and pain intensity using the Visual Analogue Scale and electroneurography (ENG).
Results: There was a statistically significant decrease in the amplitudes in SCV recordings following stimulation of the ulnar ($p = 0.04$) and lateral cutaneous antebrachii nerves ($p = 0.02$) in group B in comparison to group C. Additionally, a significant decrease in the amplitude and conduction velocity parameters was detected in the sensory fibers of the median and medial cutaneous antebrachii nerves in group A ($p = 0.00$ and $p = 0.02$, respectively) in comparison to group C.
Conclusions: The results of this pilot study suggest persistent post-mastectomy pain syndrome sometimes appears as a result of nerve injury in course of breast cancer surgery and RT. Therefore studies in nerve conduction may be added to the comprehensive patient assessment used in planning breast cancer patients' rehabilitation after oncological treatment has finished.

1. Introduction

Persistent post-mastectomy pain in patients is a major problem. Pain, tightness in the surgical area and paraesthesia are often reported after breast cancer treatment (Alves Nogueira Fabro et al., 2012; Miguel et al., 2001; Vilholm et al., 2008). Neuropathic pain is a common symptom of post-mastectomy pain syndrome (PMPS) or post-radiation fibrosis syndrome (Vilholm et al., 2008). An abnormal sensation at the axilla and the medial aspect of the arm has been reported in 20–65% of women presenting with PMPS (Mejdahl et al., 2013; Wallace et al., 1996). These patients still complain of muscle pain, which consequently causes physical disability and decreases quality of life (Miguel et al., 2001). The criteria for diagnosis of PMPS include a history of post-operative pain in the anterior chest wall, upper extremity, axilla, and/or shoulder (Blunt and Schmiedel, 2004). Symptoms include an electric shock-like pain with forms of continuous aching and burning associated with chronic dysesthesia (Pradat and Delanian, 2013). Their mechanisms are complex and involve processes in the central and peripheral nervous systems (Baron et al., 2010). Disturbances in the transmission of nerve impulses in patients after

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mastectomy and post-operative treatment are reported, but its etiology remains unclear (Johansson et al., 2000; Pradat and Delanian, 2013). Risk factors for the development of persistent post-surgical pain have been proposed, including adjuvant therapy, age, psychosocial status, preoperative breast pain, and type of surgery (Andersen and Kehlet, 2011; Mejdahl et al., 2013). One identified risk factor is adjuvant radiotherapy (RT), which has been associated with pain (Delanian et al., 2012; Mejdahl et al., 2013). However, radiation may cause significant injury to the peripheral nervous system (Pradat and Delanian, 2013). Peripheral nervous system dysfunction after RT can result from ischemia due to stenosis of the vasa vasorum or from external fibrosis of soft tissues (Pradat and Delanian, 2013; Delanian et al., 2012). Some authors propose that the exact terminology of radioactive nerve injury should be "radioactive neuropathy" (Pradat et al., 2012). Other studies have suggested a number of other potential risk factors for PMPS, including more extensive surgery (total vs partial mastectomy), axillary lymph node dissection or reconstruction (Andersen and Kehlet, 2011; Gartner et al., 2009; Miguel et al., 2001). Adjuvant treatment, such as chemotherapy, and hormone therapy has also been associated with persistent pain too (Alves Nogueira Fabro et al., 2012; Gartner et al., 2009; Mejdahl et al., 2013; Miguel et al., 2001). Additionally, demographic (age), psychosocial, and physical factors have more consistently correlated with PMPS (Wallace et al., 1996; Gartner et al., 2009; Mejdahl et al., 2013). However, particular changes in the parameters of sensory conduction study recordings after mastectomy were not presented in detail, except for the general findings of Harper et al. (1989). It remains clarifying whether numbness or pain reported by patients after mastectomy and RT are conditioned by changes in nerve transmission. Neurophysiological data may contribute to the proper differentiation between brachial plexopathies of radiation or tumoral origin (Pradat et Delanian, 2013; Delanian et al., 2012).

2. Aim

In this preliminary study, we analyzed the incidence of persistent sensory disturbances after breast cancer treatment (RT and mastectomy) with neurophysiological methods. The attempt was undertaken to reinvestigate changes in nerve impulse transmission within motor and sensory fibers of the upper extremities on the symptomatic side of patients after mastectomy.

3. Materials and methods

Women after breast cancer treatment with complains of PMPS were recruited in the Department of Rehabilitation of Greater Poland Cancer Center in Poznan (Poland) using posters. This pilot study was performed in accordance with the principles of the Declaration of Helsinki, and the protocols were approved by the Bioethical Committee of the University of Medical Sciences in Poznan, Poland.

3.1. Study criteria

Post-mastectomy women were initially selected using their participation in surgery (modified Patey radical mastectomy) or surgery with external beam RT and declared sensory disturbances in the upper extremity and anterior chest wall, axilla, and/or shoulder as the inclusion criteria. Participants had to undergo unilateral breast surgery from which specimens for histological testing were obtained and, in general, represented a good health status (ECOG performance status 0–1). They did not report cardiac, endocrine, rheumatic neuromuscular or musculoskeletal disorders, or neurologic impairments and other tumor.

Women were excluded from the study if they had the following criteria: distant metastases and/or disease progression requiring the introduction of chemotherapy; lymphedema; rotator cufftears, frozen shoulder or, acromioclavicular arthritis; history of direct trauma to the shoulder; secondary shoulder pain, resulting from referred pain from cardiac and pulmonary disorders; primary fibromyalgia; presence of underlying neurologic, inflammatory or rheumatic diseases or extrinsic diseases such as cervical spondylosis with referring pain to the shoulder.

Participants were divided into groups:

A – women after mastectomy and without RT or chemotherapy,
B – women after surgery with post-operative RT (without chemotherapy).

Women in group B received external beam RT, which was started between 4 and 7 weeks after surgery. In all cases, the standard fractionation scheme was used with 5 days of treatment per week for 5 weeks. The affected volume after surgery (chest wall) and regional lymph nodes (supraclavicular lymphnodes) were treated up to a total dose of 50 Gy with a daily fraction of 2 Gy (Hjelstuen et al., 2012). Treatment planning in each case was based on computed tomography and the conformal 3 dimensional external beam RT was applied to reduce radiation dose to the heart and both lungs according to the dose constrains, which were fulfilled in each case. In general, we did not use the dose constraints for the axial plexus.

The results recorded in patients were compared with a group of healthy women (group C – control group). The control group was formed and was matched in age and gender with group A and B and who had not experienced shoulder or leg pain previously or had not undergone cancer treatments and signed an informed consent for participation in the study. In addition, while selecting the control group, the other exclusion criteria which were applied to the patient group were used and were recruited from the general population and selected as controls (using poster).

3.2. Subjective examination

Examinations included assessment of sensory perception (0 – hypoesthesia, 1 – normal perception, 2 – hyperesthesia) in areas of axilla and lower brachial plexus innervation. The testing procedure was described and demonstrated to the patients. The patients were instructed to close their eyes and concentrate on the sensations evoked by stimuli administered by a physician. Test results were blinded for participants during the test procedure. Tests were first performed on the contralateral forearm and chestwall, next in the postmastectomy area and lower brachial plexus on the same side. The control group was assessed in both sides of the chest. In order to assess general pain hypersensitivity a visual analog scale (VAS) was used, with 0 representing "no pain" and 10 representing "pain as severe as I can imagine". Patients were asked to describe their pain as transient or chronic as well its duration from onset (Buckup, 2004).

3.3. Neurophysiological examinations

Neurophysiological studies were performed in the Department of Pathophysiology of Locomotor Organs at Karol Marcinkowski University of Medical Science in Poznan. All participants were examined with the Keypoint System (Medtronic A/S, Skovlunde, Denmark). Electroneurographic tests included the assessment of nerve impulse transmission in motor (MCV) and sensory (SCV) nerve fibers of the upper extremities on the symptomatic side.

Motor nerve conduction studies (MCV) included: median