

Lymphoedema in the aspect of breast cancer treatment – pathogenesis, principles of treatment, and prophylaxis

Obrzęk limfatyczny w aspekcie leczenia raka piersi – patogeneza, zasady leczenia i profilaktyka

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Słowa kluczowe: wtórny obrzęk limfatyczny, fizjoterapeutyczne metody leczenia, profilaktyka, edukacja.

Abstract

Secondary lymphoedema is a complication after oncological treatment. Rehabilitation management is aimed at reducing lymph stasis and improving mobility. Long-lasting lymphoedema can cause changes in the bones and joints. Increasing oedema significantly restricts the mobility of joints, and after some time leads to degenerative changes. Progressive changes in the appearance and function of the limb also cause emotional and mental changes. The problem of lymph stasis in patients after mastectomy is very serious and requires an appropriate early implementation of physiotherapy. Applied physiotherapeutic methods can be used in an independent or associated way. Currently, treatment of lymphoedema is based on symptom treating, so the knowledge of the lymphoedema pathogenesis can significantly contribute to the patients' awareness of the need to apply antiedematous prophylaxis.

Streszczenie

Wtórny obrzęk limfatyczny jest powikłaniem po leczeniu onkologicznym. Postępowanie usprawniające ma na celu redukcję zastojów chłonnych oraz poprawę sprawności ruchowej. Długo utrzymujący się obrzęk limfatyczny może spowodować zmiany w obrębie kości i stawów. Narastający obrzęk istotnie ogranicza ruchomość w stawach, a po dłuższym czasie prowadzi do zmian zwyrodnieniowych. Postępujące przemiany w wyglądzie i funkcji kończyny powodują również zmiany emocjonalne i psychiczne. Problem zastojów chłonnych u chorych po mastektomii jest bardzo poważny i wymaga odpowiednio wczesnego wdrożenia zabiegów fizjoterapeutycznych. Metody fizjoterapeutyczne mogą być stosowane w sposób samodzielny lub skojarzony. Obecnie leczenie obrzęków limfatycznych opiera się na postępowaniu objawowym, dlatego wiedza o patogenezie obrzęku limfatycznego może się istotnie przyczynić do uświadomienia pacjentom konieczności stosowania profilaktyki przeciwobrzękowej.

Introduction

Lymphoedema can be defined as an excessive accumulation of interstitial fluid, rich in protein, in the intercellular space. Primary and secondary lymphoedema are distinguished. Primary lymphoedema develops because of congenital defects of the lymphatic system, and secondary lymphoedema is formed as a result of an acquired damage (Table 1) [1].

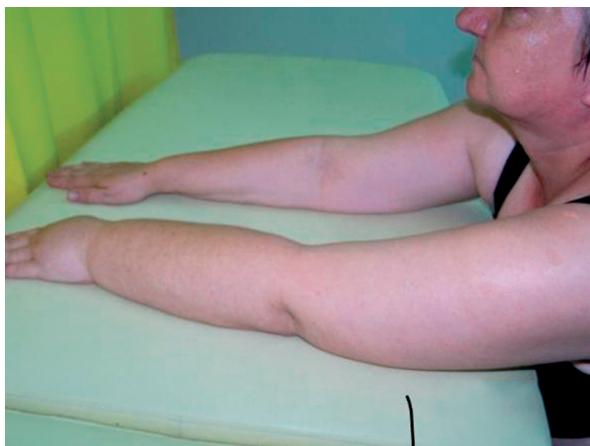
In the group of ontological patients, lymphoedema can develop as a result of primary malignancy attacking lymph nodes, invasion of lymphatic vessels, or due to antineoplastic therapy. Damage to the lymphatic system reduces transport of high-molecule

proteins from the tissue space into the bloodstream. This has an influence on an increase in colloid osmotic pressure and water retention in inter-tissue spaces, simultaneously leading to the reduction of hydrostatic pressure and the loss of tension by lymphatic vessels [2–4]. This failure of the system is revealed in the form of lymphoedema (Figure 1).

Tissue fluid, called the lymph, flows in the lymphatic vessels. It is similar to blood plasma, however, in different parts of the lymphatic system it has a different composition and appearance, which owes to the bodies through which it flows. The lymph 'flows from blood to blood', that is from the intercellular space in

Table 1. Classification of lymphoedema

Types of lymphoedema	
Primary	Secondary
Congenital	Postinflammatory
	Postoperative
Early	Tumour
	Traumatic
	Post-radiation
Late	Mixed lymphatic-venous
	Parasitic

**Figure 1.** Lymphoedema of the upper extremity on the left side (author's picture)

which it is formed as a filtrate of blood plasma into the blood veins. Creation of lymph is dependent on the function of capillary vessels. The lymphatic system is responsible for the fluid balance in the body. Ninety percent of the volume of the creating filtrate comes back into the blood system from the intercellular space through blood venous vessels, and remaining 10% through lymphatic vessels. In this way, the lymphatic system facilitates the circulation of the blood plasma proteins. Under pathological conditions the concentration of proteins exceeds the transport capabilities of lymphatic vessels leading to the stagnation of proteins in the tissue. As a result of these actions, activating fibroblasts, keratinocytes, and fat cells leads to the deposition of collagen in the skin and subcutaneous tissue, and consequently to hypertrophy and fibrosis of the skin. Abnormal flow of lymph favours the development of an inflammation process and leads to the reduction of immunity [4, 5].

According to Földi [6], there are three types of lymphatic system failure: high-volume, i.e. dynamic, failure; low volume failure, i.e. mechanical disorder; 'safety valve' failure.

Disorder of the dynamic type occurs when the lymphatic load is higher than the transport capacity of an efficient (anatomically and physiologically) lymphatic system. Lymph accumulates in the tissue creating an extracellular oedema.

The second type of disorder – mechanical – occurs when the transport capacity of the lymphatic system is lower than the level of a normal lymphatic load [1–3, 5]. In this case, high-protein extracellular stasis leads to severe tissue damage [3, 6, 7].

'Safety valve' failure occurs when the transport capacity of the lymphatic system decreases with an increase in liquid lymphatic load containing protein substances [6].

In the process of treating breast cancer, dysfunction of the lymphatic system is a very serious complication. Lymphoedema begins insidiously and without symptoms. Most often it develops in the proximal or distal part of the upper limb, sometimes it occurs only in the vicinity of the armpit or shoulder blade. The lymph stasis created slowly in the intercellular spaces causes the extension of tissues, which creates a feeling of pain and 'fullness'. In this period of development, lymphoedema is soft and of pasty nature. Over time, when the failure of the lymphatic system deepens, the upper limb on the operated side becomes harder and the skin drier. The persistent inflammation state causes the stimulation of fibroblasts changing the lymph rich in protein into a fibre structure. Over time, keratosis of epidermis, condyloma, and warts appear on the surface of the skin. The upper limb with oedema becomes harder and heavier and is significantly enlarged. Impaired lymphatic drainage from the chest and upper limb may increase the risk of streptococcal infections. The infection may lead to the closure of the lymphatic vessels and the development of elephantiasis of the upper limb on the operated side [8–11]. The increasing oedema reduces the mobility of joints and decreases muscle strength, making it difficult to perform everyday activities. Secondary lymphoedema as a complication after breast cancer treatment has a chronic progressive character. Recurrent inflammation of the skin and subcutaneous tissue also applies to small lymph vessels resulting in deepening lymph flow disturbance and worsening of the clinical condition of the patient. A common complication of chronic lymphoedema is emotional disorders. Sometimes they result from the deterioration of the appearance and functioning of the limb, the need to perform nursing treatment exercises every day, or unsatisfactory effects of physiotherapy [12, 13].

Aim

The main aim of this work is to discuss the pathomechanism of lymphoedema creation in women after mastectomy due to breast cancer and to present physiotherapeutic techniques to reduce lymph stasis.

The causes of lymphedema

In clinical practice, in the process of breast cancer treatment, as the causes of lymphoedema are recognised, the factors are divided into two main groups:

Direct:

- the intersection of lymphatic vessels and the removal of axillary lymph nodes,
- post-operative area scarring changes,
- inflammation of the post-operative wound due to infection [3, 6, 14].

Indirect:

- reduction or complete loss of tissue elasticity following radiation therapy, called post-radiation fibrosis of soft structures,
- recurrence of cancer,
- cross-sectional narrowing of the axillary or subclavian vein due to scarring or reflex spasm,
- secondary infection of the upper limb on the operated side,
- supraclavicular vein oppression, so-called ‘shoulder strap syndrome’,
- obesity,
- limited activity and physical fitness [6–8].

Secondary lymphoedema occurs in every fourth woman after surgery, and after a complementary treatment even in every third, at different times after finishing the treatment [9, 10]. However, the presence of the so-called latent phase suggests that the actual number of people affected by lymphoedema is higher. It is worth emphasising that it can reveal itself at any time after a performed mastectomy and is dependent on:

- The way of treatment: the applied method of treatment, the course of the postoperative period, scar healing, and the introduction of radiotherapy.
- Factors related to individual features: predisposition to hypertrophic scarring causing adhesions and contractures, sensitivity to radiotherapy and chemotherapy.
- The effects of non-compliance anti-oedematous prophylactic management, lack of motor improvement in the early postoperative period, discontinuation by the patient physiotherapy in the post-hospital period.
- The compensating possibilities of the lymphatic system and the formation of ‘collateral circulation’ [12, 13].

Lymphoedema treatment

Treatment of lymphoedema is difficult and constantly in the phase of research. Surgery involving the production of venous-lymphatic and lymphatic-lymphatic anastomoses and removal of damaged vessels and lymph nodes requires expensive equipment and a skilled team of microsurgeons. Applying liposuction consisting of fatty tissue aspiration is often

ineffective and carries a high risk of complications [15, 16]. Furthermore, the lack of positive effects of treatment with pharmacological means results in the group of people with a higher risk of lymphoedema prophylactic management is implemented most often. It is generally known that the earlier the therapy is introduced, the greater the benefit for the patient. Lymphoedema requires a systematic and comprehensive treatment with the use of available options.

Motor rehabilitation

A motor rehabilitation plays an important but sometimes under-appreciated role in improving the quality of life [17, 18]. Physiotherapy is a branch of medicine that in recent years has been developing very dynamically. In the treatment of lymphoedema it plays a very important role [10]. The main aim of physiotherapy is to reduce undesirable consequences of oncological treatment. This can be achieved by reducing the lymph stasis and improving the functional condition of the patient. As a primary method of lymphoedema treatment, the International Lymphology Society recognised Complex Decongestive Therapy, which consists of four elements: manual lymphatic drainage, multi-layer bandaging, a set of exercises supporting the outflow of lymph, and skin care. Apart from the classical form of lymphoedema reduction (KTU), an increasingly used method is Kinesiology Taping (KT). In Poland, it also known as dynamic taping. The basis of this system is a specially designed tape, which with its parameters is similar to the human skin. Implemented applications, depending on the dysfunction, cause the normalisation of muscle and fascial tension, pain reduction, and reduction of lymphoedema. Dynamic taping can be a method used separately or it can be a highly effective complement to complex decongestion therapy [12, 19, 20]. A highly valued form of anti-stasis therapy is also a pneumatic massage. It is performed with the use of a device equipped with cuffs that, via lines in a cyclic manner and in a specific sequence, are filled with air. Periodic pressure on the limb on the side of oedema facilitates the lymph flow to the collecting lymphatic vessels, and during a break, during the phase of relieved pressure, their filling up [21]. These three presented methods can complement one another. The study carried out by Tsai *et al.* [22] is such an example. The authors evaluated Complex Decongestive Therapy in a group of women with lymphoedema after mastectomy in one scheme of the treatment using: manual lymphatic massage, a set of decongestive exercise, and multi-layer bandaging, which was performed interchangeably with lymphatic kinesiology taping applications. Although they did not observe any statistically significant differences in efficacy of either of the methods, because they both improved the lymph flow, a higher tolerance of ‘tapes’ by patients was for the benefit of

KT. A similar positive assessment of kinesiomyology taping was given by Schwenzer *et al.* [23], and patients of Dortmund clinical hospital described the 'elastic tapes' as a pleasant element of the therapy and as more comfortable to wear.

A very important component of a comprehensive anti-oedema therapy is education. It is essential that the patient knows the causes of the secondary lymphoedema and is aware of irreversible changes in the lymphatic system, as well as the fact that physiotherapy management will be necessary for the rest of his/her life. Education should include prophylaxis and anti-oedema self-therapy. These measures should apply to both patients at risk of lymphoedema, as well as those who have already experienced clinical symptoms of lymphatic system failure.

Summary

The article presents the mechanisms affecting the dysfunction of the lymphatic system in the group of patients oncologically ill. The consequence of anticancer treatment is the secondary lymphedema, which if not treated, favours the development of a very dangerous for health and life lymphatic angiosarcoma. It also presents the leading methods of physiotherapy, which in the process of conservative treatment of lymphedema, can be employed in an individual or associated way. Suggested treatments support the outflow of lymph from the upper limb and the adjacent part of the trunk on the operated side. Currently, treatment for lymphatic stasis comes down to symptomatic treatment, so anti-oedema prevention and patient's education are important issues. A very important point in terms of reducing side effects after breast cancer treatment is diagnosis of lymphedema. The assessment based on clinical methods is insufficient. It seems that in the era of evidence-based medicine an objective tool to assess the failure of the lymphatic system is necessary. Early recognition of the degree of a lymphatic vessels dysfunction will allow the implementation of an appropriate preventive management. A delay in the rehabilitation process leads to fibrosis and degeneration of the system. Treatment of chronic lymphatic oedema is very difficult, time consuming and not always satisfactory to the patient.

Conclusions

Physiotherapy is an integral part in the treatment of breast cancer. The problem of Lymphedema is very serious and requires further consideration and research. It is necessary to introduce an early diagnosis of lymphedema in order to assess the degree of secondary lymphedema risk.

Conflict of interest

The author declares no conflict of interest.

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- nego kończyny górnej u kobiet po mastektomii. *Kwart Ortop* 2010; 1: 95-112.
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Erratum

In the paper “Extracellular DNA as an essential component and therapeutic target of microbial biofilm” by Urszula Wnorowska, Marzena Wątek, Bonita Durnaś, Katarzyna Głuszek, Ewelina Piktel, Katarzyna Niemirowicz, Robert Bucki (Studia Medyczne 2015; 31 (2): 132–138) the Figure 2 should be follow:

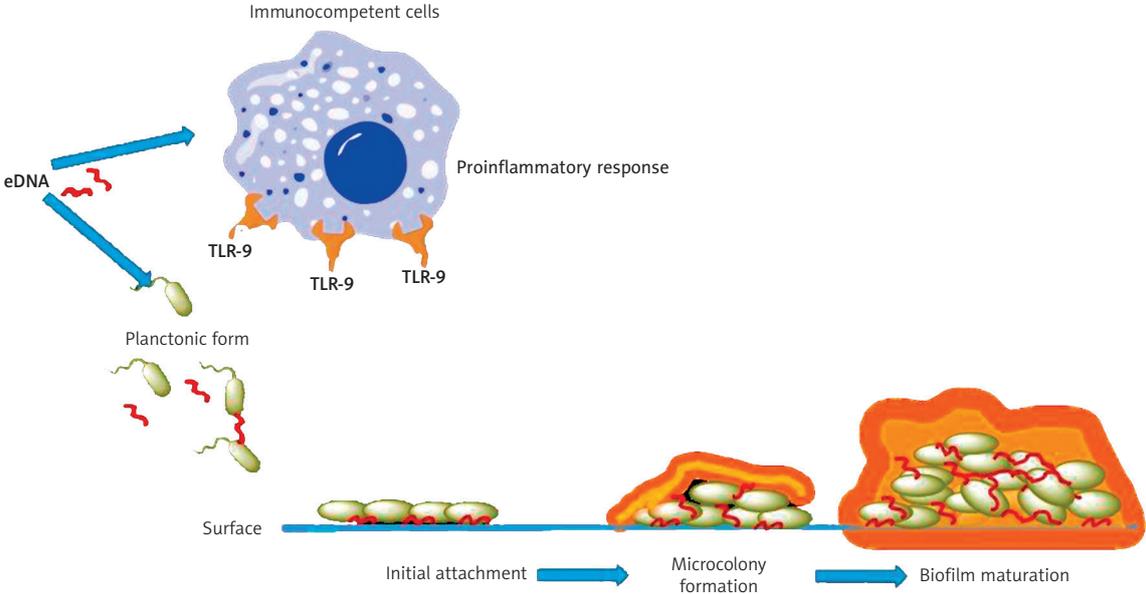


Figure 2. Major functions of extracellular DNA (eDNA) consist of activation or pro-inflammatory responses that involve the activation of TLR9 pathways and the initiation of bacterial biofilm formation