TREATMENT OF EXTENSIVE NECROSIS OF THE FOREFOOT IN THE COURSE OF DIABETIC FOOT WITH THE USE OF BIOSURGICAL METHOD

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This thesis presents a case study of an effective treatment of an indolent diabetic foot ulcer with the use of larvae of Lucilia sericata.
The thesis draws the attention to the causes underlying the occurrence of diabetic foot and the influence of lower limb ischemia over the healing process of diabetic foot wounds and ulcers.
The author of the thesis evaluates how implementing effective treatment influences the regression of infections within wounds and ulcers.

Key words: diabetic foot, maggot therapy, Lucilia sericata

Early detection of diabetes and undertaking proper treatment in patients with high risk for the occurrence of changes within the foot decreases the number of above-knee amputations of lower limbs (1). The chief quality of diabetic foot is the highest risk for foot amputations, therefore infections within diabetic foot ought to be treated promptly and with determination.

Diabetic foot is defined as an infection, ulcer or destruction of deep tissues, accompanied by neurological disorders and peripheral vascular disease at different stages of progression, occurring within lower extremities in the course of diabetes (2). The most common causes of diabetic foot syndrome are neuropathies: motor neuropathy, sensory neuropathy and autonomic neuropathy. Motor neuropathy causes deformities of the foot as a result of muscular atrophy within the foot. Sensory neuropathy exposes the patient to uncontrolled injuries and wounds, due to aberration of pain and heat sensitivity. Autonomic neuropathy causes the occurrence of trophic changes within the foot, due to the decrease in foot perspiration, dryness of the skin and proneness to dermator-rexis (3).

In physical examination of the foot a doctor evaluates the look of the skin, they pay attention to any injuries, excoriations and ulcers. They evaluate the foot in terms of the occurrence of oedemas, trophic changes and calluses. They evaluate superficial and deep sensibility, blood flow, pulse and temperature as well as the occurrence of deformities. When examining an ulcer within the foot a doctor pays attention to its size and depth and also evaluates the structures surrounding the ulcer. They pay attention to the presence or lack of granulation tissue, exudate or inflammatory infiltration (4). Evaluation of the limb perfusion in patients with diabetic foot is of crucial importance to determining further therapeutic management. It is vital to pronounce or exclude the symptoms of critical ischaemia of lower limbs. Within ischaemic foot the skin is dry, it lacks in pilosity and its subdermic tissue is subject to atrophy. The foot is cold and the patient suffers from rest pains, especially at night. Digital palpation of the pulse in the
posterior tibial artery and dorsal metatarsal artery of the foot is the first diagnostic investigation performed to evaluate the perfusion of the foot. In order to confirm vascular changes ultrasound techniques such as laser Doppler flowmetry, colour Doppler imaging and spectral Doppler imaging are used (5).

The most common classification used to evaluate pathological changes within diabetic foot is Wagner grading system (tab. 1).

Insufficiently controlled inflammation of a wound in diabetic foot may result in its recurrence and even in amputation of the limb (7). One of the effective methods of wound clearing in the course of diabetic foot is maggot debridement therapy (MDT). Living larvae of fly remove necrosis, decrease the number of bacteria within the wound and activate healing processes. Due to their specific biological qualities, medicine makes use of larvae of Lucilia sericata as they exclusively feed on masses of necrotic tissue and living tissue within their reach remains undisturbed (8). Positive effects of applying maggots on chronic indolent wounds have been known for centuries (9).

Maggot debridement therapy (MDT) was first introduced in the United States of America in 1931 and was routinely used there until mid-1940s in over 300. With the advent of antibiotics, maggot therapy was almost forgotten until the early 1990s, when it was re-introduced first in the United States and then in Israel, Great Britain, Germany, Sweden, Thailand, Switzerland and Ukraine. Sterile maggots of the common green bottle fly, Lucilia sericata, are used for MDT. This therapy is a form of artificially induced and controlled myiasis. Maggot debridement therapy is most useful in chronic, purulent wounds. In a wound, maggots feed by the secretion of proteolytic enzymes that liquefy the necrotic tissue, remove bacteria from the wound through triggering an increased production of exudate and actively destroy the bacteria which die in their digestive systems. Maggot excretion contains substances proving potent antibacterial activity and they also change pH of the wound from acidic to alkaline, which accelerates wound healing. Chronic wounds do not respond to typical treatment. They are characterised by prolonged inflammation, inhibition of cell proliferation, incomplete extracellular matrix (ECM) remodelling and a failure to epithelialize. Lack of balance in the environment of chronic wounds explains why they may persist for many years. In order for a healing process to commence and successfully progress through different stages from proliferation to epithelialization, infection needs to be eliminated. The pathogen which is most frequently isolated from acute and chronic wounds is Staphylococcus aureus (10). The majority of wounds host both anaerobic and aerobic bacteria, thus antimicrobial treatment of non-healing wounds should encompass broad-spectrum activity antibiotics. There is no single method of wound clearing effective for all patients. Depending on the wound milieu, the successive application of different methods of wound treatment in a given patient may prove beneficial (11). The recent resurgence and re-introduction of maggot debridement therapy is due to the steep rise in the emergence of antibiotic-resistant strains of bacteria, which can be removed by means of mechanical debridement of an infected wound (14).

The interest in MDT on the part of clinicians also stems from the fact that effective clearing of an infected, indolent wound enhances its healing process (15). The only limitation of this method is the access to proper, good-quality biological material (13). Maggot debridement

<table>
<thead>
<tr>
<th>Stage of progression of pathological changes within diabetic foot</th>
<th>Depth of ulceration within diabetic foot</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>high-risk foot with morphological changes; free from ulceration</td>
</tr>
<tr>
<td>1</td>
<td>superficial ulceration</td>
</tr>
<tr>
<td>2</td>
<td>ulceration accompanied by dermatitis and panniculitis</td>
</tr>
<tr>
<td>3</td>
<td>advanced ulceration penetrating to bone, foot phlegmon</td>
</tr>
<tr>
<td>4</td>
<td>topical dry necrosis (conservatively treated) or moist gangrene</td>
</tr>
<tr>
<td>5</td>
<td>extensive necrosis qualifying for amputation</td>
</tr>
</tbody>
</table>
therapy can be successfully administered to both ambulatory and hospitalized patients. It is a simple, efficient, well-tolerated and cost-effective tool for treatment of indolent wounds which fail to respond to conventional methods of treatment and surgical interventions (12).

CASE REPORT

A 77-year-old patient with long-standing type 2 diabetes was admitted to the surgical department in October 2007, due to dry necrosis of the right foot toes in the course of diabetic foot, accompanied by oedema and inflammatory erythema of the dorsum of the foot, high body temperature (up to 39°C) and hyperglycaemia of over 400 mg%. After the admission to the department the patient was intravenously administered an antibiotic: Amoxicillin in combination with cavulonic acid 2.2 g every 12 hours and Metronidazole 500 mg every 8 hours. He was also hypodermically administered short-acting insulin – 12 insulin units every 12 hours. The patient’s foot was applied dressing material containing Povidone-Iodine solution. The progression of pathological changes within the patient’s foot was classified according to Wagner grading system and was evaluated as stage 4. The patient’s blood morphology, C-reactive protein, procalcitonin, bleeding time, coagulation time, creatinine, ionogram and concentration of urea in blood serum were determined.

Then, ultrasound of the patient’s lower limb arteries was carried out. It was ultrasonography presentation B employing colour Doppler imaging and spectral Doppler imaging techniques. In aortic bifurcation the presence of atheromatous plagues was stated; they were parietally situated and had no impact on hemodynamics of the blood flow. In common iliac arteries and external iliac arteries, short-segment atheromatous plagues were revealed; they narrowed the vascular lumen to the mediocre extent with no impact on hemodynamics of the blood flow. In the right superficial femoral artery, before the entrance to adductor canal, an atheromatous plaque, significant in terms of hemodynamics, protruding into the lumen and causing the narrowing of 70% was recognized. Past the narrowing, the blood flow had a turbulent character. In the right popliteal artery, the increase in hemodynamical disturbances was observed and in the end-part of the right posterior tibial artery the disturbance took on the character of pathological monophasic Doppler waveform, with a significant decrease in the blood flow velocity. In the right anterior tibial artery a slight disturbance of the blood flow, in the form of diphasic Doppler waveform, was noticed. In the left lower limb arteries numerous short-segment calcified atheromatous plagues were revealed and in all the examined sections, up to popliteal artery, they did not cause significant hemodynamical disturbances (triphasic Doppler waveform). In the final sections of tibial arteries, a slightly disturbed blood flow in was observed (diphasic Doppler waveform).

The X-ray of the patient’s right foot was also performed and it revealed osteolitic changes in the second and third metatarsal bone. Having considered the patient’s general condition, the condition of the foot and additional examinations performed in the surgical department, the patient was qualified to metatarsal amputation by the method of Jäger. By this method the shafts of metatarsal bones were amputated and covered with skin flap sutured to the dorsum of the foot. In the course of postoperative treatment, a growing inflammatory erythema and oedema of the foot were observed. Initially, the symptoms only concerned the dorsum the foot and then they also concerned the crus. Within the wound, necrosis of tissue was observed. The postoperative wound was surgically cleansed, the stitches were removed and the margins of the wound were broadened. Sceptic purulent exudate was evacuated from the wound and necrotic tissue was cut out. Then, the tissue sample from the wound was taken for microbiological examination to provide a quantitative and qualitative evaluation of aerobic and anaerobic bacteria and to perform an antibiogram. Twice a day the wound was bathed with a 0.9% NaCl solution and dressing material of Povidone-Iodine solution was applied.

On the receipt of antibiogram results, Amoxicillin in combination with cavulonic acid was replaced with Aminoglycoside 500 mg. It was administered intravenously every 12 hours and the level of creatinine and concentration of urea in patient’s blood serum was controlled twice a week. Despite the administered treatment there was no satisfactory topical improvement. The wound got covered with a layer of colliquative necrosis accompa-
nied by purulent exudate (fig. 1). The area of necrotic tissue around the wound increased. The inflammatory erythema and oedema of the foot was still present. Therefore, an attempt to cleanse the wound with the use of ozone therapy was made. In order to apply this therapy, the patient was discharged from the surgical department and admitted to the dermatological department. There, ozone produced by an ozone therapy apparatus was applied on the wound once a day for 20 minutes, by means of a plastic chute. After two weeks of such treatment, purulent exudate from the wound decreased and the surface of the wound got partially covered with dry necrosis. As there were no positive results of the treatment and the condition of the foot was deteriorating, the patient was suggested that above-ankle amputation of the limb should be necessary. The patient did not consent to the suggested level of amputation. In this case, the decision to employ a biological method of wound clearing was taken. The method chosen was maggot debridement therapy (MDT) – the method using larvae of Lucilia sericata. The patient was informed about the suggested method of treatment and gave his informed written consent to it. Then, a written consent to employ this biological method of wound clearing was issued by the Bioethics Committee in Opole (reference number: 156/08). The treatment was carried out in the outpatient surgical department of the hospital.

Disinfected larvae of Lucilia sericata were imported from Biomonde Laboratory in Germany in containers specifically designed for the carriage of bacteria cultures and dully protected against accidental opening. Each container was provided with an antibacterial filter and it was properly labelled in terms of the quantity and the species of larvae it contained as well as the date of preparation of the biological material. These containers were put into larger containers where they were surrounded by plastic bags filled with ice and protected so as to maintain the temperature of about 4°C. On the day of receipt of the biological material, the patient reported to the outpatient surgical department. The wound on the patient’s foot was bathed with 0.9% NaCl solution and the margins of the wound were covered with a thick layer of vaseline in order to protect the skin from mechanical injury and maceration.

The surface area of the wound was calculated with by means of a computer programme called “IRIS Laboratorium”. According to the producer’s suggestions, 10 larvae ought to be applied on every 1 cm² of the wound. After opening the container with disinfected larvae kept in 0.9% NaCl solution, the content was poured onto a disinfected gauze pad which was then applied directly on the wound. The two-layer dressing was performed. The outer layer comprised a 1 m² gauze which the patient changed twice a day (16). The biological dressing was applied for the period of 72 hours.

After the 72 hours the dressing was removed and larvae were rinsed off with 0.9% NaCl solution. There was a decrease in the amount of purulent exudate and in the intensity of the accompanying offensive odour. Regression of inflammatory erythema and oedema of the foot were also stated. In the wound base the stumps of metatarsal bones and islets of granulation tissue became noticeable (fig. 2). Biological dressing was re-applied, following the above mentioned formula, and it was removed again after the period of 72 hours. The result obtained was a complete clearing of the wound from necrotic tissue. The patient was admitted to the surgical department with the aim of re-amputation of the foot. After the necessary preparations, exarticulation at

![Fig. 1. Colliquative necrosis and purulent exudate to the extensive infected metatarsal amputation wound (November 2007)](image-url)
Lisfranc’s joint was performed. By this method of amputation, metatarsal bones were removed through tarsometatarsal arthrotomies and plantar skin flap was formed in order to cover the stump (17). The amputation was completed by performing a linear incision of the fascial compartment within the metatarsus (18). The wound was left to heal by granulation (fig. 3). After discharging the patient from the surgical department, further treatment was carried out in the outpatient department. The wound was applied hydrocolloid and hydro-gel dressings changed by the patient on alternate days. After five months of treatment the wound healed. The treatment of the patient was completed in June 2008. Thanks to the application of this method of treatment, the patient did not lose the lower limb (fig. 4).

CONCLUSIONS

1. Maggot debridement therapy is an effective method of clearing of chronic indolent wounds within the foot in the course of diabetes.

2. Effective clearing of wounds from necrotic tissue significantly influences the decrease in the number of lower limb amputations, which, in turn, has impact on the locomotor aptitude of patients.

3. Removal of necrotic and infected tissue from wounds decreases patients’ demand for insulin, thus enabling efficient further treatment of the primary disease - diabetes.

REFERENCES


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COMMENTARY

Treatment of ulcerations of the diabetic foot is a difficult task, requiring not only adequate expertise and skills, but also enormous engagement of a surgeon. Healing of the ulceration can be achieved in majority of patients with diabetic foot with early and correct management. It must be emphasized that the risk of recurrence or new ulceration is as high as 70% within five years.

However, it must be strongly pointed out, that the basic management of diabetic foot is to improve its blood supply by revascularization, elimination of infection through surgical removal of necrotic and infected tissues and antibiotic therapy as well as decompression of the ulcerated site. No other treatment method can replace the basic treatment and should not delay it. Therefore, the above presented treatment method should only be considered as supplementary to the basic treatment. Also, it can be considered in the event of non-healing ischemic ulcerations and when revascularization is impossible.

A typical feature of atherosclerosis of lower limb arteries in diabetes mellitus is its peripheral and disseminated nature. In vast majority of cases, atherosclerotic lesions are located below the inguinal ligament and are multi-level lesions. Obstruction of deep femoral artery, popliteal artery and shank arteries is significantly more common than in non-diabetic subjects. However, lesions in the foot arteries are significantly less developed than in shank arteries. Therefore, patients with ischemic diabetic foot most commonly require reconstruction of femoral-popliteal segment or peripheral by-passes to shank or even foot arteries. However, it must be emphasized, that some patients present with significant lesions of the aortic-iliac segment, sometimes despite pulse being present in the groin. This supports the requirement for visualization of arteries
starting from abdominal aorta in the preoperative vascular imaging, irrespective of the level that the pulse is examined. Poor inflow may be the cause of femoral-popliteal reconstruction failure.

Recent advances in vascular surgery made endovascular revascularization of ischemic limbs possible. These procedures involve percutaneous restoration of patency or widening of arteries (PTA – percutaneous angioplasty) using balloons and/or vascular stents.

Surgery remains essentially the treatment of choice in the management of lesions of the common iliac artery. However, it can be combined with endovascular procedures when there are other atherosclerotic lesions in the arteries. Such procedures are called hybrid operations.

Endovascular treatment of the superficial femoral artery stenosis and obstruction remains one of the most challenging tasks of the modern vascular surgery. Despite the fact that it is now four decades after the first angioplasty of the superficial femoral artery, there is still no ideal endovascular management for this segment of arterial system.

Utility of PTA in the treatment of lesions in the superficial femoral artery is often limited by possible complications, including elastic recoil and by common occurrence of arterial dissection, causing total blockade of blood flow. Stent implantation can improve the treatment results, however may cause long-term complications, because an implanted stent may stimulate hyperplasia of intima and media, resulting in complete obstruction of the artery.

Subintimal angioplasty is another technique useful in the treatment of patients with long obstruction of the superficial femoral artery. This method involves creation of space underneath the vessel intima, with a special catheter, proximal to the lesion, to by-pass the obstructed arterial segment and reach the patent segment of the artery, immediately after the lesion. Then the whole length of the dissection is dilated with a balloon and the procedure is completed by placement of a vascular stent. The procedure results in a formation of a new lumen inside the wall of previously obstructed blood vessel (extraluminal neolumen). In theory, this new lumen between intima and muscular layer is free from atherosclerotic plaques and is likely to remain patent for longer periods of time.

Distal lesions, i.e. located below the popliteal artery, are a special therapeutic problem for patients with atherosclerosis and coexisting diabetes mellitus. In the pre-endovascular treatment era, surgical treatment was associated with high failure rate.

Endovascular therapy, both endovascular angioplasty and subintimal revascularization, leads to significant decrease of limb amputation in this group of patients. These method became treatment of choice for these patients.

Development of endovascular surgery became a “milestone” in the treatment of diabetic foot. Endovascular procedures can be easily repeated, they are well tolerated by patients and concurrently they are rarely associated with serious complications.

In conclusion, it must be emphasized that treatment of diabetic foot requires multimodal approach. Occurrence of necrotic lesions in this group of patients requires aggressive treatment that may lead to a significant reduction of the number of amputations and recurrences of ulceration, comparable to that achieved in non-diabetic subjects. Therapeutic success requires a combination of various revascularization methods, surgical wound management and use of adequate anti-diabetes treatment.