



Resistant to treat diabetic foot with osteomyelitis and fingers amputation in type 1 diabetic patient with rheumatoid arthritis: a complicated primary care case report

Jūratė Pečeliūnienė¹, Rita Šulcaitė², Eglė Kabašinskaitė³, Rūta Vosyliūtė³

¹*Vilnius University Faculty of Medicine, Clinic of Internal Diseases, Family Medicine and Oncology*

²*Lithuanian University of Health Sciences, the Institute of Endocrinology, Kaunas, Lithuania*

³*Vilnius University, Faculty of Medicine*

Abstract

Background: Description of a primary care clinical case of a resistant to treat diabetic foot with rheumatoid arthritis and developed osteomyelitis leading to fingers amputations, who on admission to endocrinologist presents ulcerations on left foot, of three months of evolution. Until the patient's admission to the endocrinologist she has suffered repeated hospital admissions due to uncontrolled diabetes and feet ulcers, repeatedly changed orthopedic shoes, however, not completely fitting, which the patient finally refused to wear at all.

Aim, materials: The objective of this work is to demonstrate the importance of timely performing diagnosis of the lesion of diabetic foot, taking into account all risk factors that are present, and also the need to keep on diabetic foot management protocols, starting at the primary care institution level.

Methods, results: The information was evaluated with patient cooperation, after informed patient's consent signed, also by analyzing documents of medical history; literature search analysis of the newest guidelines and data, including American Diabetes Association, European Association for the Study of Diabetes, International Diabetes Federation and *International Working Group on the diabetic foot*, as well as the latest scientific diabetic foot articles, was performed.

Conclusion: In order to prevent diabetic foot lesions in complicated, uncontrolled, long lasting diabetes with chronic comorbidities, related to foot and joint pathologies, such as rheumatoid arthritis, certain protocols must be strictly followed by multidisciplinary team in close cooperation with primary care institution. An individual approach towards

patients' diabetic foot prevention and treatment plan should be applied in such cases to avoid diabetic foot ulcers' complications and lower extremities amputations.

Key words: Diabetes mellitus, resistant to treat ulcers, osteomyelitis, amputation, primary care.

Introduction

Diabetic foot wound, including diabetic foot ulcers (DFUs) and diabetic foot gangrene, is a relatively common complication of diabetes mellitus (DM) (1). Diabetic foot (DF) and its most serious complication – lower extremities amputation – are among the most life-threatening complications of DM, placing huge social and financial burden on healthcare and society (2, 3, 4, 5, 6). DFUs contribute to 80% of lower extremity amputations (7) and are known as a major contributor of non-traumatic lower extremity amputation (1). Although physicians currently rely on clinical signs along with non-specific biomarkers of infection, such as erythrocyte sedimentation rate and C-reactive protein, to diagnose and monitor DFUs, there is no specific and sensitive measure available to monitor or prognosticate the success of foot salvage therapy (7), especially if the case progresses in the resistant to treatment way. According

to the most recent meta-analysis by Wang et al., factors among local characteristics of the foot associated with major amputation in patients with diabetic foot are the ulcer reaching bone, gangrene, hind foot position, decreased ankle-brachial index, infection and peripheral arterial disease (8). Even though authors did not find a significant difference in the size of the ulcer, neuropathy, Charcot foot, osteomyelitis and intermittent claudication (8), osteomyelitis is kept one of the common complications of the foot related to amputation of lower extremities (9). According to International Diabetes Federation, >50% of all foot ulcers get infected, requiring hospitalization and 20% of lower extremity infections results in amputation (10). Successful steps to prevent and treat foot complications like lower extremities amputation depend upon a well-organized team – starting with primary care institution (2).

Understanding the challenges met by primary care doctor in DFUs management, the analysis was aimed to evaluate resistant to treatment diabetic foot with RA and osteomyelitis leading to finger amputation case report focusing on DFUs care and treatment by raising notice of multidisciplinary team work in order to timely prevent DFUs' complications.

Case report

51 year old female type 1 diabetes mellitus (T1DM) patient was referred from primary care (PC) doctor to the endocrinologist having complaints of the left leg pain accompanied by swelling, foot redness and ulcer between 3rd-4th fingers; patient also complained of unstable glycaemia. According to the patient, ulcer appeared 3 months ago after fingers rubbed into each other wearing shoes. It was noted, that the patient did not regularly visit diabetologist nurse, did not use orthopedic footwear (according to the patient, orthopedic shoes did not fit properly and were uncomfortable, also put pressure on bony feet structures). She only used saline fluids for ulcer treatment. Patient's medical history documented 33 years (yrs) of T1DM, treated with insulins: insulinum glarginum (Lantus) and insulinum lispro (Humalog) (under the scheme: long-acting insulin 18 U twice a day; short-acting insulin 12-12-12 U), and a long history of rheumatoid arthritis (RA) (26 yrs), treated with methylprednisolone sufficiently to poor enough with standard doses of 4 mg twice a day. Diabetic complications include: retinopathy (>26 yrs), polyangioneuropathy (22 yrs), nephropathy (7 yrs). Lastly the patient was hospitalized and treated with antibiotics (oxacillin and metronidazole) 4 months ago due to left leg pain and DF non-healing ulcer. Patient's glucose control was intermittent to poor (HbA1c% 7, 8 %– 8, 4%) with hypoglycemic states (~once a month). When admitted to endocrinology department, physical

examination revealed disturbed vibratory and tactile sensation, weak pulse of arteriae dorsalis pedis bilaterally, deformed left foot fingers (due to RA) and chronic trophic ulcer with pus between 3rd-4th fingers; blood test results: CRP 13,7 mg/l, erythrocyte sedimentation rate 35 mm/h, HbA1c% 7,9%. Ulcers' bacterial culture showed *Streptococcus aureus* sensitive to oxacillin. Left foot X-ray revealed foot fingers destruction; intravenous oxacillini 2g and oral metronidazole 500 mg per day were prescribed. However, decision to perform left foot fingers amputation from 2nd to 5th finger was made by doctors' console shortly after osteomyelitis was diagnosed while in hospital, later following successful outpatient rehabilitation. Despite that, 4 months after left foot fingers amputation, patient was hospitalized again to the endocrinology clinic due to recurrent ulcers of both feet (patient again complained on uncomfortable orthopedic shoes) for partial amputation of right foot 2nd finger. In the end, healing process required intensive antibiotics therapy (injections of cefadroxil 500 mg per day), also weekly, later - monthly visits to diabetologist nurse for wound clearing, necrotizing masses removal till patient recovered. The amputated fingers' wounds healed almost completely with one little superficial ulcer remaining in the left sole – both DF are shown in Figure 1 and Figure 2.

Discussion

Feet problems are common among people with DM. In particular early onset of complications and progression in more complex way is more frequent in T1DM patients requiring closer monitoring to avoid bothersome and disabling complication DFUs formation, which often leads to lower extremities amputations (11, 12). One of main DM complications associated with DFUs formation is neuropathy, which leads to sensory deprivation. It is essential to do visual feet inspection at each visit to primary care doctor, doctor specialist or DF office (11). The ADA 2019 “Standards of Medical Care

in Diabetes” includes ADAs' current clinical practice recommendations on Microvascular Complications and Foot Care, and stands for diabetic peripheral neuropathy diagnostics, which, by the way, up to 50% may be asymptomatic, to undergo evaluation for patients with T1DM for 5 or more years (13). Also, all patients with type 2 diabetes should be assessed annually for diabetic peripheral neuropathy using the medical history and simple clinical tests, knowing that symptoms may vary, and if not recognized, and if preventive foot care is not implemented, patients are at risk for injuries, especially if their feet are insensate (13). Other DM complication that leads to DF ulceration is peripheral arterial disease (PAD). PAD is diagnosed in 10% to 40% of patients with DM (14). Vascular obstruction disturbs normal blood circulation, foot ischemia promotes DFUs formation, recurrence and amputation rates (12, 14). In order to prevent DFUs and its' complications, it is crucial to identify and manage other risk factors for people who do not have DF ulcers yet. Severity of both, diabetic neuropathy and PAD, related to DM, depend on glucose control also pathogenetically – glucose is the main determinant factor in diabetic neuropathy and PAD evolution, with strong evidence indicating that hyperglycemia produces metabolic and physiological abnormalities, that trigger diabetic neuropathy (6, 15, 16, 17). According ADA 2019, near-normal glycemic control, implemented early in the course of diabetes, has been shown to effectively delay or prevent the development of diabetic peripheral neuropathy in patients with type 1 diabetes (13). In our case, patient's glycaemic control was intermittent to poor (established high HbA1c% rates), not stable including repeatable hypoglycemic states, what could have determined negative dynamics of DM complications. Additionally, insulin, that was used for treatment of T1DM (under the scheme insulinum glarginum (Lantus) 18 U twice a day and insulinum lispro (Humalog) 12-12-12 U), was not sufficient enough for DM management, therefore,

endocrinologist's interdisciplinary involvement supposed to be also more individual.

The most important risk factors for DFUs include the long duration of DM (>10 years), poor glucose control, cardiovascular, retinal and renal complications, anamnesis of DFUs or lower-extremity amputation (11, 12, 18). To add more, smoking and male patients with DM have a greater risk of DF ulcers, and bony deformities are related with higher risk of amputation (11, 13). Ultimately, primary care institution performs a key role in DF multidisciplinary team management, ensuring screening programs for DM complications. The lack of DF screening programs and its poor effectiveness, and uncertain use of multidisciplinary approach, starting with primary care institution, are believed to be related to DF development, and complications, including lower extremities amputations (19). Misuse of primary care doctors' institution and unexploited DF screening program are problems relevant to our patient's case – patient was visiting primary care doctor mainly for glucose control also referrals to endocrinologist, missing proper DF screening program in primary care institution. Also, orthopedic shoes problem was not solved and having comorbid RA disease, which in particular is associated with increased orthopedic care need for such patient, active multidisciplinary team approach was in a high requirement to prevent the incidence of DFU.

The selection of appropriate footwear and footwear behaviors at home should also be discussed with each diabetic patient, what is also the focus by ADA 2019. Patients' understanding of these issues and their physical ability to conduct proper foot surveillance and care should be always assessed (13), what was obviously lacking in our case, and it worked against the prevention of DFUs development. Knowing that education of patients with DM takes an important role in DFUs prevention and early treatment, continuous training and follow-up for our patient had to be implemented. Understanding that poor foot hygiene, inadequate

footwear increases risk of DFUs formation, also awareness on what are the first signs of tissue damage, may lead to better disease outcome patients' knowledge about pre-ulcerative signs leads to early treatment initiation (callus removal, large blisters drainage, treatment of ingrown nails, infection treatment) (12). Our clinical report shows how significant time of treatment initiation can be. Missing critical 3 months of adequate treatment lead to serious consequences. So what is kept as the most important for the primary DFU prevention to recognize all the red flags signaling about the risk of diabetic foot and at the same time the timely implementation of prophylaxis (19), were not performed in described case report.

When DFUs are diagnosed and secondary prevention of DFUs complications is the following goal, comprehensive taking and assemblage of the anamnesis a prior history of ulceration, amputation, Charcot foot, angioplasty or vascular surgery, cigarette smoking, retinopathy and renal disease and assessment of current symptoms of neuropathy (pain, burning, numbness) and vascular disease (leg fatigue, claudication), in order to have less complications of DFUs, are recommended (13). Also, ensuring adequate treatment in case of developed DFUs is kept as crucial part of management of DFUs (20). Success of DFUs treatment depends on the time the treatment was started, presence of the infection and depth of the injury. If an ulcer is deeper than subcutaneous tissue, intensive treatment is usually required. In case of infection it is recommended to debride the ulcer and start empiric oral antibiotic therapy targeted at *Staphylococcus aureus* and streptococci (10). According to the most recent ADA 2019 recommendations, most diabetic foot infections are polymicrobial, with aerobic gram-positive cocci (13). *Staphylococci* and *streptococci* are the most common causative organisms (13), what was the same in our case. Wounds without evidence of soft tissue or bone infection do not require antibiotic therapy (13). Empiric antibiotic therapy can be narrowly targeted at gram-positive cocci

in many patients with acute infections, but those at risk for infection with antibiotic-resistant organisms or with chronic, previously treated, or severe infections require broader-spectrum regimens and should be referred to specialized care centers (13, 21).

Another critical problem is the miscommunication among medical specialist and between patient and medical personnel in the development of difficult to treat DFU status that is also shown in our clinical case, while treating multimorbid DF patient with RA. When main treatment of DFUs was finished, it was essential again to focus on patient education in order to avoid the recurrence of ulcers, secondary prevention, which goes also as first priority to primary care doctor, diabetologist nurse, outpatient endocrinologist. Miscommunication with patient led to complications as repeating ulcers, following osteomyelitis that was showed in our case report.

Special, individual treatment and attention must be given for such complicated patients, based on certain comorbid conditions they have, such as RA and medications, used for the RA treatment, what can affect DFUs healing process. It is known that glucocorticosteroids lead to glucose level increase and immunosuppression that may complicate the healing process of DFUs (22, 23). Methylprednisolone, which was used in doses of 4 mg twice a day for RA management in our case, could not be discontinued for the patient because of complicated RA, even it is contraindicated for those with acute or chronic infectious conditions (such could be DFUs, etc.) (23). To add more, special precautions always should be taken if methylprednisolone is prescribed to a patient with DM (23). Regarding to all those with RA related challenges, rheumatologists' consultation, which is not a part of standard multidisciplinary DF team, was necessary in this case too, and on a repeatable basis.

Again, individual, proper orthopedic management is very relevant to difficult to treat DFUs and secondary DFU prevention, especially for such

patient as our patient, having several complaints on her shoes, next to her rheumatoid arthritis. In patients with DFUs, feet are often more damaged due to high pressure wearing inappropriate footwear and while walking, and it is self-clear that for patients, having RA as comorbidity, additional pressure is put on bony and damaged joints, if shoes do not fit orthopedically well for the patient. Early signs of soft tissue damage (redness, warmth, blister etc.) may show increased plantar pressure (11, 12). The most vulnerable foot areas are between toes and under metatarsal heads (2). Therefore, it is essential for primary care doctor to inform the patient about importance of appropriate model footwear that would distribute pressure all over the foot and refer to continuous and timely orthopedic management to orthoped-traumatologist (11). Our case demonstrates how difficult selection of proper orthopedic footwear might be to patients with complicated DF and additional health conditions like RA, that even very individual orthopedic footwear may rub and press the feet, leading to ulcers formation and patient's mistrust with orthopedic shoes. Properly, individually adapted orthopedic footwear is a key for healthy feet in diabetic patients if properly tailored to all foot deformities (13), including RA.

The frequency of controlling over the disease dynamics in complicated DM patients with DFUs and risk factors should be monitored tighter (12), especially having several comorbidities related to joint system diseases and other risks for diabetic feet. Even if there is no consensus on the frequency of patient monitoring, International Working Group on the diabetic foot suggested a screening frequency based on established DM complications (12). Similar recommendations are suggested by American Diabetes Association, European Association for the Study of Diabetes and International Diabetes Federation. Even though our clinical case patient was regularly monitored at the primary care level, only glycaemic control was regular, fitting diabetes care protocols, however missing essential part of more often

or at least regular feet inspection and treatment, mentioned in all protocols of previously mentioned world's diabetes associations. According to medical records and patient's story, feet monitoring was performed very rarely, and more out of patients' initiative, which might be the reason of following serious complications of feet, including poor patient's disease awareness and self-treatment at home.

To avoid major suffering caused by DF development and its complications, DFU management protocols must be followed by multidisciplinary team, starting with primary care institution (19). Education for patients, multidisciplinary caregivers and healthcare providers is an essential aspect of efficient treatment strategies. Therefore, efficient, well communicating interdisciplinary systems and structures such as, professional to professional and professional to a patient, are needed. We believe that our clinical case data, along with the literature and authoritative guidelines, suggest that primary care physicians' awareness and hence their

ability to identify the "foot at risk", along with proper foot care, may prevent diabetic foot ulceration and thus reduce the risk of amputation, also other DFU related consequences, especially in patients with comorbid chronic joint diseases such as RA. As this clinical case shows, DF with osteomyelitis and lower extremities amputations are very serious complications of DM, especially for those at risk with long lasting, complicated DM history, poor glycaemic control, comorbid with other chronic health conditions like RA, and those, who have not been taking DF care properly, starting regular management at the PC level. In this case patient not only had all previously mentioned risks factors, but also DFU management protocols were not kept sufficiently and all it caused DF complications with osteomyelitis and fingers amputation. DF trainings should be applied for PC doctors and DF patients, both, in order to improve DF management and prevent incidences of such complications.



Figure 1. Patient's left DF post - fingers amputation.



Figure 2. Patient's right DF post 2nd finger partial amputation.

Conflict of Interest

All authors declare no conflict of interest.

Informed consent

Individual consent was obtained from the patient for this study.

Literature

1. Kim SY.; Kim TH.; Choi JY.; Kwon YJ.; Choi DH.; Kim KC.; Kim MJ, Hwang HK.; Lee KB. Predictors for Amputation in Patients with Diabetic Foot Wound. *VascSpecialistInt*, 2018 Dec. vol. 34, pp. 109-116,
2. International Working Group on the Diabetic Foot (IWGDF). Prevention and management of foot problems in diabetes: a Summary Guidance for daily practice 2015, based on the IWGDF Guidance documents.
3. Shojaiefard A.; et al. Independent risk factors for amputation in diabetic foot. *Int J Diabetes Dev Tries* 2008 , 28(2): 32-37.
4. Alexiadou K., et al. Management of Diabetic Foot Ulcers. *Diabetes Ther* 2012. 3(1):4
5. World Health Organization. Global report on diabetes. WHO Library Cataloguing-in-Publication Data, France, 2016 ISBN 978 92 4 156525 7. pp 6-7.
6. Vera Bril, Ari Breiner et al. Neuropathy. 2018 Clinical Practice Guidelines. *Canadian Journal of Diabetes*. 2018; 42: 217-221.

7. MacDonald A.; Brodell JD.; Daiss JL.; Schwarz EM.; Oh I. Evidence of DifferentiaMicrobiomes in Healing Versus Non-Healing Diabetic Foot Ulcers Prior to and Following Foot Salvage Therapy. J Orthop Res. , 2019 Mar 25.
8. [Wang N](#), [Yang BH](#), [Wang G](#), [Gao Y](#), [Cao X](#), [Zhang XF](#), [Yan CC](#), [Lian XT](#), [Liu BH](#), [Ju S](#). A meta-analysis of the relationship between foot local characteristics and major lower extremity amputation in diabetic foot patients. 2019 Feb 19
9. Oliver TI et al. Diabetic Foot Ulcer. Treasure Island (FL): StatPearls Publishing, 2019 Jan 15.
10. International Diabetes Federation. Clinical Practice Recommendation on the Diabetic Foot: A guide for health care professionals. Brussels: International Diabetes Federation, 2017, ISBN 978-2-930229-86-7, p.: 9-11.
11. American Diabetes Association. Preventive Foot Care in Diabetes. Diabetes Care 2004 Jan; 27(suppl. 1): s63-s64.
12. Bus SA.; van Netten JJ.; Lavery LA.; Monteiro-Soares M.; Rasmussen A.; Jubiz Y.; Price PE.; International Working Group on the Diabetic Foot. Guidance on the prevention of foot ulcers in at-risk patients with diabetes. Diabetes Metab Res Rev, 2016 Jan; 32 (Suppl 1):16-24.
13. ADA 2019 11. Microvascular Complications and Foot Care: Standards of Medical Care in Diabetes 2019. Diabetes Care 2019;42(Suppl. 1):S124–S138 <https://doi.org/10.2337/dc19-S011>
14. Hart T., Milner R., Cifu A. Management of a Diabetic Foot. JAMA 2017; 318(14): 1387-1388.
15. Dobrovolskienė, Rimantė; Norkus, Antanas (aut.; sudaryt.); Pečeliūnienė, Jūratė; Petrikonis, Kęstutis; Stankutė, Ingrida; Šulcaitė, Rita; Urbanavičius, Vaidotas; Vaitkus, Antanas; Veličkienė, Džilda; Verkauskienė, Rasa; Žalinkevičius, Rimantas. Diabetinė neuropatija : [mokomoji knyga] Diabetic neuropathy: [educational book] Kaunas : Medicininės informacijos centras, 2017. 160 p. : pav, lent. ISBN 9786098070156.
16. **Quan, D.; Lin, HC.** Diabetic neuropathy. www.emedicine.medscape.com 2019. Available at: <https://emedicine.medscape.com/article/1170337-overview#a4>. Accessed: March 31, 2019.
17. Pop-Busui R, Boulton AJM, Feldman EL, Bril V, Freeman R, Malik RA, Sosenko JM, Ziegler D. Diabetic Neuropathy: A Position Statement by the American Diabetes Association. Diabetes Care 2017;40:136–154 | DOI: 10.2337/dc16-2042
18. Martínez Delgado MM. Clinical case: complicated diabetic foot ulcer. Rev Esp Sanid Penit. 2018 Sep-Dec; 20(3): 121-124.
19. Pečeliūnienė, J.; Norkus, A.; Žukauskaitė, I.; Kabašinskaitė, E.; Gataveckaitė, D. Šeimos gydytojų vieta tarpdisciplininėje diabetinės pėdos priežiūroje I dalis: diabetinės pėdos paplitimas, etiopatogenezė, pirminė prevencija = The Role of family doctors in interdisciplinary diabetic foot care. Part I: diabetic foot prevalence, etiopathogenesis, primary prevention //

Lietuvos endokrinologija. Kaunas: Medicininės informacijos centras. ISSN 1392-7213. 2018; 26(2-4): 84-94.

20. Niazi NS.; Drampalos E.; Morrissey N.; Jahangir N. et al. Adjuvant antibiotic loaded bio composite in the management of diabetic foot osteomyelitis - A multicentre study. *The Foot* , 2019 Jun, vol. 39:22-27.
21. Lipsky BA, Berendt AR, Cornia PB, et al.; Infectious Diseases Society of America. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. *Clin Infect Dis* 2012;54:e132 e173
22. Barnes PJ. Glucocorticosteroids: current and future directions. *Br J Pharmacol.* 2011;163: 29–43.
23. Methylprednisolone - Drug Summary. Available at: <https://www.pdr.net/drug-summary/Medrol-methylprednisolone-1014>. Accessed March 31, 2019.