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# Recurrent diabetic foot ulcer: An educational image and expert opinion

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#### Abstract

The occurrence of diabetic foot ulcers is commonly attributed to factors including infection, diabetic neuropathy that are commonly associated poor control of blood sugar. History of foot ulcer is generally considered an important risk factor. The case of a diabetic and hypertensive male patient who had a history of previous foot ulcer, and developed a recurrence at the same site is described with emphasis on the current evidence-based therapeutic recommendations. A 55-year diabetic hypertensive male who had a history of foot ulcer which healed completely after aggressive treatment before more than one year. The first ulcer was associated with clear evidence of infection with cellulitis and pus formation, but there was no evidence of gangrene. The first ulcer was treated successfully with antibiotic therapy followed by monthly intramuscular injection of benzathine penicillin. Topical treatment included topical antibiotic (fusidic acid) and topical dexpanthenol. Pentoxifylline was used instead valsartan to control hypertension and to improve peripheral vascular impairment. The patient also received alpha-lipoic acid supplementation. Few weeks before the occurrence of the second ulcer, the patient visited the practitioner of the organization who was working with, and for unclear reason, the doctor switched pentoxifylline with Coveram (Perindopril 10 mg + Amlodipine 10 mg). The ulcer was not associated with evidence of serious infection, and cellulitis like the first ulcer. However, the patient received oral antibiotics and topical therapies. To avoid injudicious frequent changes of antihypertensive medication, oral pentoxifylline was added in a dose of 400 mg daily. The second ulcer healed within one week. The medical treatment of the diabetic foot ulcer follows the principles of wound healing which include treatment of soft tissue infection, in addition to controlling factors more specifically related to diabetes such as neuropathy and peripheral vascular impairment. The current expert opinion suggests the use of monthly intramuscular benzathine penicillin, alpha-lipoic acid supplementation, and pentoxifylline in the long-term preventive therapies.

Keywords: Recurrent diabetic foot ulcer, expert opinion

#### Introduction

The occurrence of diabetic foot ulcers is commonly attributed to factors including infection, diabetic neuropathy that are commonly associated poor control of blood sugar. History of foot ulcer is generally considered an important risk factor [1].

#### **Patients and methods**

The case of a diabetic and hypertensive male patient who had a history of previous foot ulcer, and developed a recurrence at the same site is described with emphasis on the current evidence-based therapeutic recommendations.

#### Results

A 55-year diabetic hypertensive male who had a history of foot ulcer which healed completely after aggressive treatment before more than one year. The patient was receiving oral anti-diabetics (Glibenclamide and metformin), and oral valsartan for the control of blood pressure. However, the glycemic control was not considered good because of frequent elevations of blood sugar because of non-adherence to the dietary regimen. The patient also had clinical evidence of diabetic neuropathy and also of impaired

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peripheral circulation.

The first ulcer was associated with clear evidence of infection with cellulitis and pus formation, but it was not convenient to perform bacterial study because of covid-19 disease lockdown during that time. There was no evidence of gangrene.

Aggressive treatment was based on the evidence provided by Prabhakar and colleagues (1981) and Unachukwu and colleagues (2005), and included intramuscular ceftazidime plus oral metronidazole and clindamycin [2, 3].

With improvement in the cellulitis after one week of therapy, the patient continued the antibiotic therapy with monthly intramuscular injection of 1.2 million units benzathine penicillin with the aim of preventing recurrence of cellulitis based on the evidence provided by Lin et al (2017) [4].

Topical treatment included topical antibiotic (fusidic acid) and topical dexpanthenol based on the evidence and recommendation presented by Proksch et al (2017), Baron and colleagues (2020), and Robson and Edstrom (1977) [5,6,7].

Pentoxifylline was used instead valsartan to control hypertension and to improve peripheral vascular impairment based on the evidence and recommendations presented by several authors. Pentoxifylline was used in a dose of 400 mg 2 times daily, and can be increased to three times daily if necessary [8-13].

The patient also received alpha-lipoic acid supplementation (600 mg daily) based on the evidence presented by Al Mosawi (2022) [14].

Few weeks before the occurrence of the second ulcer (Figure-1), the patient visited the practitioner of the organization who was working with, and for unclear reason, the doctor switched pentoxifylline with Coveram (Perindopril 10 mg + Amlodipine 10 mg). The ulcer was not associated with evidence of serious infection, and cellulitis like the first ulcer. However, the patient received oral antibiotics and topical therapies. To avoid injudicious frequent changes of antihypertensive medication, oral pentoxifylline was added in a dose of 400 mg daily. The second ulcer healed within one week.

### Discussion

This patient received highly effective evidence-based treatment with the necessary preventive measures of recurrence including monthly intramuscular injection of million units benzathine penicillin which was successful in preventing the recurrence of severe infection and cellulitis. However, the loss of the beneficial effect of pentoxifylline on peripheral vascular disease contributed to ulcer recurrence.



Fig 1: The second ulcer was not associated with evidence of serious infection and cellulitis like the first ulcer

Prabhakar and colleagues (1981) reported a bacteriological study of 61 patients with diabetic foot ulcers with or without evidence of gangrene. Ulcers without evidence of gangrene in 12 patients had single infections with Staph pyogenes, and beta haemolytic streptococcus.

The antibiotic treatments recommended according to antimicrobial susceptibility included co-trimoxazole, cephaloridine, and penicillin. Clindamycin and metronidazole were recommended when anaerobic bacteria are suspected [2].

Unachukwu and colleagues (2005) reported a bacteriological study of 60 patients with diabetic foot ulcers with or without evidence of gangrene observed during the period from January 2001 to April 2002. Aerobic bacteria were found in 95.4% of the cases while anaerobic bacteria were found 4.6% of the cases. Staphylococcus aureus was cultured from 32 (56.1%) of infected patients and accounted for 24.4% of all cases.

The aerobic bacteria were markedly sensitive to ciprofloxacin (78.4%), pefloxacine (71.2%), ceftazidime (73.6%) and cefuroxime (69.6%). Anaerobic bacteria were sensitive to metronidazole and clindamycin.

Unachukwu and colleagues recommended that empiric antibiotic treatment include a combination of clindamycin or metronidazole and either a second or third generation cephalosporin (Ceftazidime or cefuroxime) or a fluoroquinolone [3].

Lin et al (2017) reported the largest cohort which

showed that monthly intramuscular injection of 2.4 million units benzathine penicillin can markedly decrease the incidence of recurrent cellulitis [4].

Diabetic ulcer healing is can be facilitated by treatment and protection from infection and free radicals, reduction of inflammation, and enhancement of cell proliferation and migration. An important goal of diabetic ulcer healing is tissue regeneration which re-establishes skin functionality. Dexpanthenol is a mild antiseptic that has skin barrier restoring effect and beneficial effects on various factors affecting wound healing and as has been increasingly considered as a facilitator of wound healing [5, 6].

Pentoxifylline has been used in the treatment of diabetic patients with peripheral vascular disease as early as the 1970s [8].It is a xanthine derivative with vasodilatory properties and rheological properties on blood and has been used in hypertensive condition [12, 13].

There is convincing research evidence suggesting that lipoic acid has a benerficial effects in diabetes, and is particularly useful in the prevention and treatment of diabetic neuropathy. The beneficial effects of lipoic acid in diabetes and diabetic neuropathy are attributed to increasing insulin sensitivity, reduction of hyperglycemia-induced oxidative stress, and lipid peroxidation. Lipoic acid can possibly help in preventing diabetes in susceptible individuals, and the current expert opinion suggests that lipoic acid can be used in patients with patients with impaired glucose tolerance [14].

Another agent that can possibly has a role in the treatment and prevention of diabetic ulcer is L-arginine [15].

# **Conflict of interest**

None.

# Conclusion

The medical treatment of the diabetic foot ulcer follows the principles of wound healing which include treatment of soft tissue infection, in addition to controlling factors more specifically related to diabetes such as neuropathy and peripheral vascular impairment. The current expert opinion suggests the use of monthly intramuscular benzathine penicillin, alpha-lipoic acid supplementation, and pentoxifylline in the long-term preventive therapies.

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