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# Effect of Epidermal Growth Factor in a Patient with Diabetic Hand

## Diyabetik El Olgusunda Epidermal Büyüme Faktörünün Etkisi

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### Abstract

Diabetes mellitus, a multisystemic disease, is associated with microvascular and macrovascular complications in most patients due to its chronic course. Although diabetic hand infections are rarer than diabetic foot infections, its development is intricate. Herein, we report the case of a 38-year-old man with type 1 diabetes and restless leg syndrome who presented to our out-patient clinic with a necrotic wound on his right thumb. Despite attempts of needle aspiration, surgical procedures, and oral antibiotics, the wound worsened and underwent necrosis. Therefore, surgical debridement was performed by an orthopedist. Upon achieving healing and granulation tissue formation, epidermal growth factor was topically applied twice a day. The patient was discharged with a prescription for doxycycline and topical epidermal growth factor. Follow-up at 1 and 2 months after discharge revealed ongoing wound healing. In conclusion, the treatment and follow-up of diabetic hand infections should involve a comprehensive multidisciplinary approach. Furthermore, conservative treatments such as appropriate antibiotherapy, wound care and blood sugar regulation should be prioritized over amputation. Moreover, epidermal growth factor is a valuable therapeutic option, with its topical application being an advantage.

**Keywords:** Conservative treatment, diabetic hand infection, epidermal growth factor, prevention of amputation, wound healing

### Öz

Diabetes mellitus, multisistemik bir hastalık olup, kronik seyri nedeniyle mikro ve makrovasküler komplikasyonlara yol açmaktadır. Diyabetik el enfeksiyonları, diyabetik ayak enfeksiyonlarına göre daha az sıklıkta görülmekle birlikte, diyabetik el gelişimi de karmaşık bir süreçtir. Bu yazıda, 38 yaşında tip 1 diabetes mellitus ve huzursuz bacak sendromu olan bir erkek hastanın sağ el başparmağındaki nekrotik yara nedeni ile tarafımıza başvurusu sunulmaktadır. Olgumuzun, iğne ile drenaj, cerrahi müdahale ve oral antibiyotik tedavisine rağmen yarası kötüleşmiş ve nekroz gelişmiştir. Ortopedi uzmanları tarafından cerrahi debridman uygulanmıştır. İyileşme ve granülasyon dokusu oluşumu sağlandıktan sonra, hastaya günde iki kez topikal epidermal büyüme faktörü tedavisi başlanmış, doksisisiklin ile topikal epidermal büyüme faktörü kullanımı önerilerek taburcu edilmiştir. Taburculuk sonrası birinci ve ikinci ay kontrollerinde yaranın iyileşmeye devam ettiği gözlenmiştir. Bu nedenle, tedavi ve takip sürecinin kapsamlı ve multidisipliner bir yaklaşımla ele alınması gereklidir. Amputasyon düşünülmeden önce uygun antibiyotik tedavisi, yara bakımı ve kan şekeri düzenlemesini içeren konservatif tedavilere öncelik verilmelidir. Topikal uygulama avantajlarıyla epidermal büyüme faktörü, değerli bir tedavi seçeneği olarak öne çıkmaktadır.

**Anahtar Kelimeler:** Konservatif tedavi, diyabetik el enfeksiyonu, epidermal büyüme faktörü, amputasyonun önlenmesi, yara iyileşmesi

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## Introduction

Prevalence of diabetes mellitus (DM) was 366 million worldwide in 2011, and this figure is expected to increase to 552 million by 2030<sup>[1]</sup>. Several chronic complications develop due to DM. The development of both microvascular and macrovascular complications is associated with glycemic control. Multiple factors such as endothelial dysfunction, insulin resistance, increased glycation end products, polyol accumulation, and genetic factors are involved in the pathophysiology of DM. Skin and soft tissue infections are observed more frequently in diabetic patients than in healthy individuals. This may be attributed to poor glycemic control, diabetic microangiopathy, and impaired immune system response in diabetic patients<sup>[2]</sup>.

Diabetic foot wounds develop because of various factors such as neuropathy, vasculopathy, abnormal foot biomechanics, and impaired wound healing. Diabetic foot wounds are a leading cause of morbidity in patients with DM<sup>[3]</sup>. Chronic complications involving the hand may also be observed in such patients. For every hundred diabetic foot infections, there is one case of "diabetic hand" or "diabetic hand syndrome". Diabetic hand syndrome is a multifactorial and complex process, with risk factors similar to those of diabetic foot. If a diabetic hand develops as a result of structural changes in the hand, such as changes in the vascular structure, intrinsic muscles, joint capsule, skin, and subcutaneous tissue, there may be significant limitations in hand movements<sup>[4,5]</sup>.

Wound care, infection control, and debridement are the main treatment approaches for diabetic hand wounds. Finger or hand amputation should be considered as the last option after applying different treatment options, especially for thumb wounds. Herein, we have reported a case of a diabetic wound on the thumb that completely healed with epidermal growth factor (EGF) application after wound debridement.

## Case Report

A 38-year-old man with type 1 DM and restless leg syndrome presented to our out-patient clinic with a necrotic wound on his right thumb, which initially appeared as skin redness 15 days ago. Despite interventions such as needle aspiration, surgical procedures, and oral antibiotics (amoxicillin-clavulanic acid,

ciprofloxacin, and cefuroxime axetil), the wound worsened and underwent necrosis rapidly. Physical examination revealed a swollen red thumb with a draining wound. Treatment with piperacillin/tazobactam was initiated because of the history of multiple antibiotic use. Routine blood tests at the time of admission yielded unremarkable results (Table 1). A contrast-enhanced hand magnetic resonance imaging was performed to evaluate for osteomyelitis or abscess. However, no pathology was detected. Surgical debridement was performed by an orthopedists on day 10 of antimicrobial therapy (Figure 1A). Intraoperative tissue culture grew extended-spectrum beta-lactamases-negative *Citrobacter freundii*. After achieving healing and granulation tissue formation, topical EGF therapy (twice a day) was initiated. Parenteral antibiotics were discontinued after 21 days, and the patient was discharged. The patients was prescribed doxycycline and topical EGF, considering the absence of osteomyelitis/abscess. Doxycycline, which has good tissue penetration, was chosen because of the patient's history of multiple antibiotic treatments and lack of benefit from previous oral therapies. It was discontinued on the 20<sup>th</sup> day.

Follow-up at 1- and 2-months after discharge revealed ongoing wound healing (Figure 1B, C). At the 2-month follow-up, EGF therapy was discontinued. During both follow-up visits, the wound edges had merged. The HbA1c level was 11.5% in June 2023 and 13.2% in September 2023. Because the patient's blood glucose levels remained uncontrolled despite the high doses of insulin, he was referred to an endocrinologist. His insulin regimen and diet were revised, and lifestyle modifications were recommended.

## Discussion

DM, a multisystemic disease, results in microvascular and macrovascular complications in most patients due to the chronic course of the disease. Although diabetic hand infections are less common than diabetic foot infections, the development of diabetic hand is intricate. Infections may occur more frequently and may be more severe in diabetic patients than in healthy individuals. This may be attributed to hyperglycemia, phagocytic system disorders, decreased cellular immunity, and decreased vascularity that are the results of a chronic process in patients with DM.

**Table 1. Routine blood test results at the time of presentation**

Parameter	Value	Parameter	Value
Leukocytes	6.56 (10 <sup>3</sup> /μL)	AST	56 (U/L)
Neutrophils	72.6 (%)	ALT	18 (U/L)
Lymphocytes	1.11 (10 <sup>3</sup> /μL)	Creatinine	0.8 (mg/dL)
Hemoglobin	13.1 (g/dL)	C-reactive protein	15.94 (mg/L) (0-5)
Platelet	197 (10 <sup>3</sup> /μL)	INR	1.06

AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, INR: International normalized ratio



**Figure 1.** Wound image obtained A) immediately following surgical debridement, B) at the 1-month follow-up, and C) at the 2-month follow-up

Diabetic hand infections are as serious as diabetic foot infections. However, because they are rarer than diabetic foot infections, studies on them are limited<sup>[6]</sup>. The clinical presentation of diabetic hand infections ranges from cellulitis to ulcerated and gangrenous lesions. It usually occurs following a minor trauma to the hand, and are mostly observed in tropical regions. In the rural areas of Africa, most of the patients with diabetic hand infections were women because they are more frequently engaged in agriculture and exposed to agriculture-associated trauma than men. However, in urban areas, hand ulcers are more commonly encountered in men<sup>[7]</sup>, which is consistent with our case finding. Although *Staphylococcus aureus* is the most common causative organism of diabetic hand infections, polymicrobial agents have also been reported<sup>[7,8]</sup>. However, no previous study has reported *Citrobacter spp.* as the causative organism. Because diabetic hand infections are less common than diabetic foot infections, the number of studies on EGF use in hand infections are limited. Given its proven benefits in diabetic foot infections, it may be effective in hand infections. Although it is not a novel treatment approach, EGF can be beneficial in appropriate indications.

Amputations are more frequently performed for diabetic foot infections than for hand infections. This may be attributed to the fact that hands are frequently used to perform activities of daily living, which raises the question of how much these complications affect hand function and activities of daily living in diabetic patients.

The development of the diabetic hand is complex and multifactorial, which is similar to that of diabetic foot. The treatment and follow-up of patients with diabetic hand should be a multidisciplinary approach. Initially, primary and secondary preventive methods and optimal medical treatment should be sought. Conservative treatments such as wound care and blood sugar regulation should be prioritized before amputation because they affect daily functioning. If possible, patients and their relatives or care providers should be involved in the process, and adequate training should be provided for the prevention and treatment of diabetic hand and its complications<sup>[4,6]</sup>. It is crucial to prioritize conservative treatments such as appropriate antibiotherapy, wound care, and blood sugar regulation over amputation. EGF appears to be a valuable option, with its topical application being an advantage. In patients with abscess and osteomyelitis, debridement or amputation is required. In the study by Wang et al.<sup>[5]</sup>, healing was achieved without amputation in 76% of patients with diabetic hand infections. In osteomyelitis, treatment should last at least 42 days. However, 5 days of treatment is sufficient if no residual tissue remains postoperatively. Furthermore, without osteomyelitis or abscess, 14–21 days of treatment is sufficient. In our patient, the treatment duration was prolonged due to the use of multiple antibiotics and a delayed response. There are several studies on the use of EGF in diabetic foot. However, because diabetic hand is rare, there are no studies on EGF use in diabetic hand.

## Conclusion

In conclusion, our case report demonstrates that a multidisciplinary care framework for managing diabetic hand infections, which advocates for a judicious balance between conservative measures and surgical interventions, is crucial. By leveraging a collaborative and patient-centric approach, clinicians can navigate the complexities inherent to diabetic hand infections and facilitate favorable outcomes. This further highlights the pivotal role of comprehensive care in diabetic limb salvage initiatives.

## Ethics

**Informed Consent:** Informed consent was obtained.

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## Footnotes

## Authorship Contributions

Surgical and Medical Practices: D.K., G.V., M.C.S., M.I.T., Concept: M.C.S., M.I.T., Design: M.C.S., M.I.T., Data Collection or Processing:

D.K., G.V., Analysis or Interpretation: D.K., G.V., M.C.S., M.I.T., Literature Search: D.K., G.V., Writing: D.K., G.V.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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