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A Rare Cause for Diabetic Foot: *Granulicatella elegans*

Diyabetik Ayakta Nadir Bir Etken: *Granulicatella elegans*

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SUMMARY

Granulicatella species are nutritionally variant streptococci and they can cause several infections like endocarditis. Our aim to present a case of diabetic foot osteomyelitis due to Granulicatella elegans, which is a rare cause of diabetic foot osteomyelitis. Vitek automatation system was used to describe it. Granulicatella species are rare causes of bone infections, and the majority of such cases have been reported in immunocompetent patients. They usually cause infective endocarditis, but osteomyelitis was present in this case without endocarditis.

Key Words: *Granulicatella elegans; Diabetes mellitus; Diabetic foot; Osteomyelitis*

ÖZET

Diyabetik Ayakta Nadir Bir Etken: *Granulicatella elegans*

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Granulicatella suşları başta endokardit olmak üzere çeşitli infeksiyonlara neden olabilen nütrisyonel varyant streptokoklardır. Olgumuzda nadir bir diyabetik ayak etkeni olarak Granulicatella elegans'ı tanımladık ve bunun için Vitek otomatizasyon sistemini kullandık. Granulicatella suşları sıklıkla infektif endokardite yol açar ancak bu osteomiyelit olgusunda endokardit yoktu.

Anahtar Kelimeler: *Granulicatella elegans; Diabetes mellitus; Diyabetik ayak; Osteomiyelit*

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INTRODUCTION

Granulicatella species are gram-positive bacteria which are normal members of the flora of the oral cavity, urogenital, and intestinal tracts[1,2]. They can cause a variety of infections such as infective endocarditis, dental abscess, osteomyelitis, septic arthritis, and neonatal sepsis[3]. This case represents a diabetic foot osteomyelitis due to *Granulicatella elegans*, which is a rare cause of diabetic foot osteomyelitis.

CASE REPORT

A 43-year-old man, with type 1 diabetes mellitus for 14 years, presented to our infectious disease outpatient clinic with pain, swelling, and purulent discharge from a diabetic foot. He was a factory worker and wore inappropriately heavy shoes for a diabetic patient. He was treated with antibiotics and hyperbaric oxygen therapy for diabetic foot infection on the plantar area 2 years ago. Also, he stated that his plantar callus formation had softened and moved away due to sea water exposure the previous summer. At that time, he stated that he had tried to manage the diabetic foot lesion by dressing with a pomade that included fucithalmic acid. However, the lesion did not totally clear and caused swelling of his left foot up to the knee. When seen at the infectious disease outpatient clinic, he was treated with oral ciprofloxacin and regular wound dressing. Initial laboratory values were as follows: WBC 15.900/mm^3, 68% segs, 2% bands, 27% lymps, %6.7 monos, Hb 10 g/dL, HCT 34%, platelets 290.000/mm^3, HbA1c 10.1% (reference 4-6%), C-reactive protein 12.6 mg/dL (reference 0-0.8 mg/dL), and eryrthrocyte sedimentation rate 103 mm/hour. The patient's HIV ELISA test was negative.

One week later, he was hospitalized when he presented with fever. On physical examination, he had a 2 x 1 cm wound with purulent discharge on his left plantar area (Figure 1). Cultures were drawn and the patient's therapy was broadened to ampicillin/sulbactam. The wound was dressed daily with physiologic solution. X rays revealed osteomyelitis of the 3rd metatarsal (Figure 2). Electromyelography revealed mixed severe chronic polyneuropathy with sensorial axsonal dominancy on the lower extremities. Pregabalin 75 mg b.i.d. was started. Cardiac oscultation and echocardiography were normal.

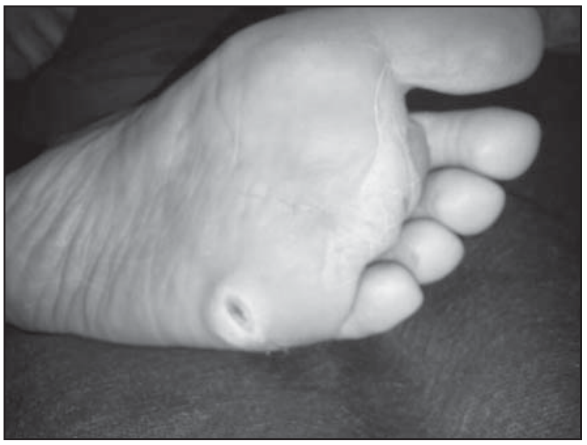

Figure 1. 2 x 1 cm wound on the left plantar area with a callus halo formation.

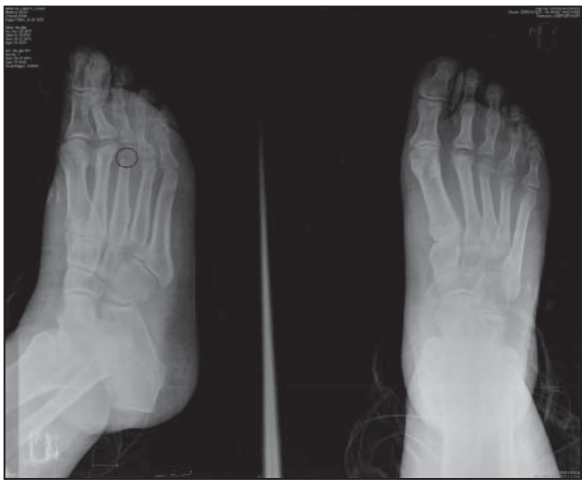

Figure 2. Osteomyelitis on 3rd metatarsal bone with plain radiogram (shown with a circle).

A specific etiologic diagnosis was made by culturing purulent material obtained by deep aspiration. Isolates of the deep aspiration of the wound grew well on blood agar; microscopy revealed gram-positive cocci arranged with chains.

The organism identified in this specimen by biochemical tests using Vitek automatation method was *G. elegans*. The antibiotic susceptibility profile of the pathogen was obtained. The microorganism was susceptible to all of the antibiotics such as ampicillin/sulbactam, amoxicillin/clavulonate, cephotaxime, cefazolin, cefuroxime, ciprofloxacin, gentamicin, trimethoprim sulfamethoxazole. We treated the patient with ampicillin/sulbactam. No growth was found in aerobic and anerobic blood cultures. A dental consult was obtained and tooth 47 with an apical periodontitis was extracted.

We regulated blood glucose levels with rearrengement of insulin doses and obtained strict glycemic control. The patient completed 2 weeks therapy with parenteral ampicillin/sulbactam and improved clinically. Leucocytosis, ESR and C-reactive protein levels were lower at the time of discharge. We planned to continue oral ampicillin/sulbactam for at least three months. At the time of the scheduled visit four weeks later, there was complete clinical and laboratory recovery of the patient.

DISCUSSION

Patients having known risk factors like diabetes are prone to osteomyelitis[4]. Disorders of local immunity associated with diabetes, neuropathy, vascular disease and pressure lesions all contribute to the pathogenesis of diabetic foot lesions[4]. Bone infection in a diabetic foot is usually a complication of a preexisting infected foot wound and its diagnosis can be suspected in two principal situations: no healing (or no depth decrease) in spite of appropriate care and off-loading[4]. The first diagnostic step is to obtain plain X-rays. *Staphylococcus aureus* is the most common pathogen followed by *Staphylococcus epidermidis*. Among *Enterobacteriaceae*, *Escherichia coli*, *Klebsiella pneumoniae* and *Proteus* spp. are the most common, followed by *Pseudomonas aeruginosa*. Surprisingly, bacteria usually considered contaminant [as coagulase negative staphylococci (CNS) and *Corynebacterium* spp.] have been documented to be pathogens in the osteomyelitis of diabetic foot.

Diabetic foot includes foot ulcers, and infections in diabetic patients involve the interaction of several factors such as abnormal foot biomechanics (such as inappropriate shoes), diabetic neuropathy, peripheral arterial disease (PAD) and poor wound healing[4]. Other risk factors are male sex, diabetes > 10 years duration, peripheral neuropathy, abnormal structure of foot (callus, thickened nails, etc), smoking, history of previous ulcer or amputation, and poor glycemic control[4].

Treatment of diabetic foot ulcers includes strict off-loading, topical treatment, optimal treatment of hyperglycemia, and antibiotic therapy on a case-by-case basis for osteomyelitis. Osteomyelitis usually requires some antibiotic treatment systemically. Acute hematogenous osteomyelitis can be treated with antibiotics alone. Chronic osteomyelitis, often accompanied by necrotic bone, usually requires surgical intervention. Without surgical resection of the infected bone, antibiotic treatment must be prolonged (≥ 4 to 6 weeks). The antibiotic regimen must target the causative pathogen[5]. Our patient working in heavy industry and wearing heavy steel shoes causing foot trauma was at a great disadvantage for a diabetic patient. He also had diabetic peripheral neuropathy of the lower extremities which contributed to structural changes in the foot. Autonomic neuropathy can cause skin drying and fissures by worsening the superficial blood flow in the foot. PAD and poor wound healing allow minor breaks in the skin to enlarge and to become infected. An infected ulcer is suggestive of the clinical diagnosis. Cultures should be obtained for optimal therapy. Cultures should be taken from the ulcer base or purulant drainage or by aspiration of the wound. Plain radiography must be obtained for the patient with diabetic foot.

Granulicatella species are catalase-negative, oxydase-negative, facultative anaerobic, gram-positive microorganisms and are called nutritionally variant streptococci (NVS) because they need pyridoxal or other nutritional agents to grow succesfully in standart agars. They show satellitism around other bacteria such as *S. aureus*[5,6]. NVS are classified on the basis of growth requirement characteristics, prolonged incubation period, satellite-promoting phenomenon, pleomorphic morphotypes, and variable Gram stain findings[1]. *Granulicatella* has 3 described species: *Granulicatella adiacens*, *G. elegans* and *Granulicatella balaenopterae*. The last one has not been isolated from human samples. *G. elegans* (originally known as *Abiotrophia elegans*) was first described in 1998 and called "elegans" because of its fastidious growth reqirement[6,7]. It poses variable morphology with the nutritional state; forms are coccoid in short chains with adequate nutritional supplements but if deficient, they are elongated and swollen[6]. In biochemical tests, *G. elegans* possesses arginin dihydrolase activity and other *Granulicatella* species do not[8]. *G. elegans* needs both pyridoxin and L-cystein to grow, but other species can grow with pyridoxine

without L-cystein[8]. Sato et al. have shown that strains of *G. elegans* account for aproximately 8% of all NVS isolates recovered from the oral flora[8].

Portal of entry of the organisms was thought to be an apical periodontitis on the number 47 tooth that was revealed in the oral examination done by the dentist. That tooth was pulled, but unfortunately, a culture of the infected material could not obtained.

Granulicatella species are rare clinical isolates and are usually recovered from blood cultures[7,9]. In a study, one hundred and one NVS isolates from 97 patients were obtained with the following distribution: *G. adiacens* (55 patients of 55 isolates), *Abiotrophia defectiva* (39 patients of 43 isolates) and *G. elegans* (3 patients of 3 isolates), which also shows that *G. elegans* infections are rare NVS infections[10]. *Granulicatella* and *Abiotrophia* species should be remembered when slow-growing alpha haemolytic streptococci are isolated from blood cultures or other sterile areas[9]. For poor growing isolates, > 48 hours it is suggested that a possible identification should be made by examining for satellitism around an *S. aureus* strain or growing in pyridoxal-suplemented blood agars[11].

In summary, a diabetic foot ostomyelitis due to NVS may be misdiagnosed as blood-culture-negative osteomyelitis. If a patient with osteomyelitis reveals gram-positive staining and blood cultures are negative, NVS should be considered and culture media should be supplemented with nutritional agents such as pyridoxal and L-cysteine. If bacteria are isolated, identification with automatation system should be instituted.

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