

A Very Rare Diabetic Foot Co-infection Due to *Escherichia hermannii* and *Enterobacter aerogenes* in an Elderly Patient

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ABSTRACT

Escherichia hermannii is a microorganism very rarely isolated from clinical specimens, since its first identification in 1982. So far, there are around 17 human cases reported in medical sources. This small number of isolated case, eventually leads to a lack of information about the pathology and pathogenesis of infections caused by this microorganism.

In the present article, we report a diabetic foot co-infection due to *Escherichia hermannii* and *Enterobacter aerogenes*. The treatment of the patient was started with a combination of empiric piperacillin/tazobactam and teicoplanin therapy. Later, based on the microbiology test results, this medication was converted to meropenem. When the patient's septic condition improved, coronary artery bypass and transtibial amputation operations were performed. The patient recovered completely and was discharged without further issues. To the best of our knowledge, this is the first *E. hermannii* infection report from Cyprus and the Middle East.

Keywords: Cyprus, Diabetic foot co-infection, Rare microorganism

CASE REPORT

A 62-year-old male patient was admitted to the Cardiology Department with severe chest pain which has been persistent for a week. He also had severe uncontrolled diabetic foot infection for two months and fatigue lasting for one week.

His previous diagnosis were Coronary and Peripheral Artery Diseases (CAD and PAD) and uncontrolled type II diabetes mellitus (since 16 years). He had severe leg pain, even after walking for about only 10 meters. He underwent a femoropopliteal balloon angioplasty on the same site six months ago, but despite this surgery, his leg pain had become chronic.

Physical examinations revealed generalised weakness, an approx. 4 cm diameter-infected wound on the left plantar site of the fourth toe. The wound was covered with purulent discharge and was malodorous. The indexing of the patient's wound was "11" according to "PEDIS Scoring System" [1]. The patient's "critical limb ischemia" was positive, the extension of skin lesion was larger than 3 cm², the depth score of the wound was "three", the abscess formation and the loss of sensation were positive.

Additionally, the femoral pulse was positive, while the popliteal and distal pulses were negative. The patient was diagnosed with CAD and PAD on cardiological examination.

Routine hematological and biochemical tests were performed and a deep wound aspiration culture sample was collected. Laboratory test results were as follows: WBC: 9.70x10³/UL; RBC: 3.21x10⁶/UL; HGB: 9.0 g/dL; HCT: 30.6% UL; NEU: 73.34%; HbA1c (%): 6.6; CRP (Sensitive): 10.91 mg/dL. Blood glucose level was uncontrolled and above 200 mg/dL.

Wound biopsy and bacteriologic culture was performed. Samples were collected and inoculated onto routine bacteriological blood agar and MacConkey agar. The next day, two different types of colonies were isolated and identified as *Enterobacter aerogenes* (White colonies) and *Escherichia hermannii* (yellow colonies) by BD PhoenixTM 100 Automated Microbiology System (Becton Dickson, USA). Antibiotic susceptibility tests were conducted on both microorganisms by the same test system.

The patient was taken to the intensive-care unit because of the appearance of a septic condition (acute respiratory distress syndrome and fever). Empiric anti-infective therapy consisting of teicoplanin IV

(12 mg/kg twice-a-day for a loading dose than once-a-day for maintenance dose) and piperacillin/tazobactam (4.5 g every eight hours) was started. Additional supportive treatment was also provided. The septic condition of the patient improved. With this appropriate medical treatment, blood glucose level returned to normal levels and stabilised, effective tissue oxygenation was achieved. Two days later antibiotic susceptibility test results were obtained as in [Table/Fig-1].

Antibiotic	<i>Escherichia hermannii</i>	<i>Enterobacter aerogenes</i>
Amikacin	S*	S
Amoxicillin/Clavulanate	R**	R
Aztreonam	S	S
Ampicillin	R	R
Ceftazidime	S	S
Cefepime	R	S
Ceftriaxone	R	S
Ciprofloxacin	R	R
Colistin	S	NT***
Cotrimoxazole	S	S
Ertapenem	R	R
Gentamycin	R	R
Meropenem	S	S
Netilmycin	R	R
Piperacillin/Tazobactam	R	R

[Table/Fig-1]: Antibiotic sensitivity test results of *Escherichia hermannii* and *Enterobacter aerogenes* isolated from the clinical specimen.

*Sensitive; **Resistant; ***Not tested

Anti-infective therapy was modified to meropenem 500 mg Q12H instead of piperacillin/tazobactam, after the results of the susceptibility test were analysed. On day three, clinical stability was achieved.

Transtibial amputation was performed and one month later, a CABG operation was conducted. The patient was discharged on the 80th day with total recovery.

DISCUSSION

E. hermannii was first described as a new species of *Escherichia* genus in 1982 by Brenner DJ et al., [2]. Hata H et al., suggested that this microorganism was a member of a new genus, *Atlantibacter*,

rather than a member of the *Escherichia* genus [3]. However, this suggestion was not widely accepted by other authors, and *E. hermannii* still belongs to the *Escherichia* genus.

In very few clinical specimens, this microorganism has been isolated as a sole or co-existing causative agent [4], like bacteremia [5], conjunctivitis [6], wound infection, sepsis [7], even in neonates [8].

Ioannou P in his study, compiled the major reported *E. hermannii* cases in the world [9]. According to this review, the most common infections with *E. hermannii* were bacteremia, urinary tract infections, and central nervous system infections while the least common infections were conjunctivitis, and skin and soft tissue infections (the latter was 5.9%). According to these findings, the index case is the least common type of *E. hermannii* infection.

The global distribution of infections due to this microorganism is not fully understood due to the small number of cases. Ioannou P, described 17 human *E. hermannii* case reports in 16 different studies in his review [9]. A total of seven cases have been reported from Europe, and one of them was from southeastern part of this continent. Five other cases were from North America and four cases from Asia. The only *E. hermannii* isolation reported from Southeast Europe was from a case of conjunctivitis in Greece [6]. This microorganism has never been isolated in the Middle East and Cyprus before.

We diagnosed and performed an antibiotic susceptibility test for this rarely isolated microorganism by BD Phoenix™ 100 Automated Microbiology System. Only two previous laboratory studies on the efficacy of this automatic system have been published. Carroll KC et al., tested 251 references Enterobacteriaceae strains, including one-strain of *E. hermannii*, and this microorganism was diagnosed correctly [10]. The author tested only one strain because of its rare isolation. Jin WY et al., compared three automatic diagnostic systems to identify *E. hermannii* reference strains in another study; they found that all three systems correctly identified this microorganism at the species level [11].

This microorganism was isolated from non-living environments such as drinking water pumping systems and metal contaminated soils as well as clinical specimens. Hernandez A et al., suggested that vanadium-containing environmental conditions may cause multiple antibiotic resistance in *E. hermannii* strains [12]. The correlation between environmental conditions and the presence and resistance of this microorganism is still not well known. Cyprus soils are known to be highly contaminated with heavy metals such as copper and nickel [13]. This contamination can lead to the development of MDR in *E. hermannii* as well as in all bacteria.

The demographic and clinical characteristics of the index patient were as follows; he was more than 20 years older than the average age of the reported cases (62 versus 41.5-year-old respectively) [9]. On the other hand, he had a series of underlying diseases such as being an elderly, has a long term uncontrolled diabetes, CAD and PAD. Popescu GA et al., reported a case of *E. hermannii* co-infection in a diabetic patient similar to this patient [4]. Total five days of effective antibiotic treatment and appropriate supportive treatment led to the control of infection and sepsis and allowed safe amputation.

In one of the earliest studies on this subject, this microorganism was found to be susceptible to third generation cephalosporins, aminoglycosides, and cotrimoxazole [14]. On the contrary, our isolate was resistant to cephalosporins, aminoglycosides, and additionally to fluoroquinolones, but still, remained sensitive to cotrimoxazole. All of our antibiotic susceptibility test results showed that the isolate was MDR. These results directed us to use an effective antibiotic such as carbapenem; even ertapenem resistance has been detected. The successful clinical outcome of our patient suggests that the treatment strategy was correct.

CONCLUSION

In this study, *E. hermannii* was isolated for the first time in a patient with diabetic foot infection, in Cyprus. Diabetic foot infections usually develop due to microorganisms present in the environment. Soils in Cyprus is known to be contaminated with heavy metals such as copper and nickel. We still do not know the effect of these conditions on the occurrence of opportunistic and MDR *E. hermannii* infections. This needs to be investigated in further research. Besides the environmental cause, the patient's immunity was also compromised due to severe diabetes and peripheral circulatory system problems.

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