Secondary hand infection with *Eikenella corrodens* and *Staphylococcus aureus* in a patient with Behcet’s disease: a case report

Yaoting Liu¹,*, Jiayun Zhong²,*, Haiqing Hu¹, Qing Hou³, Xianfeng Chen¹, Zhijun Weng¹ and Lin Zhou¹

**Abstract**

We report the first case of a woman with Behcet’s disease (BD) with multiple hand ulcers secondary to coinfection by *Eikenella corrodens* and *Staphylococcus aureus* resulting in necrotizing fasciitis. She had a long history of BD including long courses of prednisone and immunosuppressants. The patient was hospitalized for multiple superficial ulcers, swelling, and infection of the hands. After admission, pus culture examination revealed rare coinfection by *E. corrodens* and *S. aureus*. We administered moxifloxacin and vancomycin to control infection and methylprednisolone to control BD. We performed incision, drainage, and debridement of the ulcer surface on the hands to reduce the pus on the wound surface. *E. corrodens* infections occur in immunosuppressed patients and contribute to coinfections, particularly in patients with BD in whom destruction of the skin immune barrier increases risk to secondary infections. For severe and complicated hand infections, efforts should be made to identify pathogenic microorganisms so appropriate antibiotics and other interventions can be given to control the infection.

¹Department of Laboratory Medicine, Changzheng Hospital, Naval Medical University, Shanghai 20003, PR. China

²Department of Rheumatology and Immunology, Changzheng Hospital, Naval Medical University, Shanghai 20003, PR. China

³Shanghai Key Laboratory of Medical Molecular Mycology, Department of Dermatology, Changzheng Hospital, Naval Medical University, Shanghai 20003, P.R. China

*These authors contributed equally to this work.

**Corresponding author:**
Lin Zhou, Department of Laboratory Medicine, Changzheng Hospital, Naval Military Medical University, No. 415, Fengyang Road, Shanghai 200003, P.R. China. Email: lynzhou36@126.com
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Introduction
BD is a systemic vascular inflammatory disease associated with a high incidence of skin lesions. Patients with BD take prednisone and immunosuppressants for long durations and are thus more vulnerable to complex infections compared with the general population. Because of the complex anatomical structure of the hand, suppurative infections can easily spread and lead to complex severe soft tissue infection. The causative pathogens of such infections are diverse. Eikenella corrodens is part of the normal flora of human mucous membrane surfaces and infections caused by this organism are rare.1,2 E. corrodens infections are usually associated with coinfections by other bacteria and primarily occur in immunosuppressed individuals. Infections primarily occur in the head, neck, pharynx and are associated with conditions such as pleurisy, thyroiditis, meningitis, liver abscesses, hip arthritis, and knee arthritis.3–12 E. corrodens is easily missed from routine cultures because of its biological characteristics. Here, we report a case of a serious secondary hand infection in a patient with BD caused by E. corrodens and Staphylococcus aureus coinfection.

Case report
This study was approved by the Ethics Committee of Changzheng Hospital, Naval Medical University, China. Written informed consent was obtained from the patient for publication of this case report and any accompanying images. The reporting of this study conforms to CARE guidelines.13

A 72-year-old woman was admitted to our hospital on 14 February 2017 complaining of oral cavities and multiple skin ulcers (6 months) as well as swelling and pain in both hands (1 week). The patient had previously experienced shoulder pain with no apparent cause in August 2016 and multiple ulcers in both hands with pain and exudation in October 2016. She was diagnosed with herpes zoster skin infection at a local hospital and received antibiotics (details unknown), but her condition did not improve. The areas of ulceration on both hands gradually expanded, and ulcerations appeared successively on the trunk and oral cavity mucosa. She visited the local hospital again in December 2016 and was diagnosed with BD. She was treated with prednisone 10 mg per os (po) once a day (qd), thalidomide 50 mg po once a night, and methotrexate 10 mg po once a week. After 1 month of treatment, there was no improvement in her condition. A week prior to her admission to our hospital, she experienced swelling of both hands and exudation of pus from the wounds. She had no fever, headache, diarrhea, nausea, chest distress, shortness of breath, or other symptoms. Starting at illness onset, the patient experienced poor mental status, weight loss of about 7 kg, poor appetite, and poor sleep.

The patient had a history of left eye vision loss resulting from retinal
detachment in 2002. Five years prior to admission to our hospital, she underwent cholecystectomy. She had a history of hypertension and took amlodipine irregularly. She was allergic to penicillin and cephalosporin and had no self-reported history of diabetes, tuberculosis, or hepatitis.

On admission, the patient had a body temperature of 36.5°C, a blood pressure of 120/75 mmHg, a pulse of 72 beats per minute, and a respiratory rate of 16 breaths per minute. Physical examination revealed mild anemia. Scattered ulcers (approximately 1 × 1 cm) were observed on the trunk, hands, and feet and had a foul odor with wrapping (Figure 1). Both hands were significantly swollen and showed elevated skin temperature, positive needle puncture response, and limited finger movement.

Initial laboratory results showed low hemoglobin levels and elevated neutrophil count, C-reactive protein (CRP) level, erythrocyte sedimentation rate (ESR), and D-dimer level. In addition, alterations in hepatic and immunological function measures were observed: levels of pro-brain natriuretic peptide and ferritin were elevated, while CD3+CD4+ T-lymphocyte counts, CD3+CD8+ T-lymphocyte counts, total protein level, and albumin level were all decreased (Table 1). Additional laboratory test results were normal. Because the infection had caused severe tissue destruction and decreased hand function, we performed emergency surgery on the patient’s infected hands under brachial plexus anesthesia. The goal of surgery was to incise, drain, and debride the septic infection in both hands. During the operation, the encapsulated pus cavity was opened. The traumatic wound of the left hand and the ulnar side of the forearm wound were completely subcutaneously connected to the skin. After thorough cleaning of the wrapped pus moss and surrounding inflammatory granulation tissue, the tendons of each finger extensor muscle on the back of the hand were observed to be severely compressed, without any elasticity or toughness, and showed necrotizing fasciitis-like changes (Figure 2). The inflammatory fibers were completely removed. Specimens of ulcerated tissue and the necrotic vascular wall were taken for pathological and microbiological examinations. The wound was cleaned with normal saline, hydrogen peroxide and chlorhexidine, then dressed with sterile clean excipients.

Gram-stained smears of wound pus revealed the presence of Gram-positive cocci and Gram-negative bacilli. Within 24 hours, bacterial growth was observed in blood agar cultured at 35°C with 5% CO2. Blood agar cultures were positive for S. aureus as shown by a Vitek 2 system GP card (bioMérieux, Marcy-l’Étoile, France). Based on microscopic examination, Gram-negative bacilli were also detected. After an extended incubation of 48 hours, needle-tip-sized colonies were observed on blood agar (Figure 3). By microscopy, the colonies showed the presence of long and slender Gram-negative bacilli with no spores and capsules (Figure 4) that grew on chocolate agar but not on MacConkey agar. Isolates were further characterized using...
Table 1. Laboratory test results of the patient on admission.

| Variable                                      | Admission | Post-surgery | Normal range          |
|------------------------------------------------|-----------|--------------|-----------------------|
| **Hematology**                                |           |              |                       |
| White blood cells (×10⁹/L)                     | 9.1       | 3.0          | 3.5–9.5               |
| Neutrophils (%)                               | 94.1†     | 60.4†        | 40–75                 |
| Red blood cells (×10¹²/L)                     | 3.02      | 2.89         | 3.8–5.1               |
| Hemoglobin (g/L)                              | 94↓       | 91↓          | 115–150               |
| Platelets (×10⁹/L)                            | 301       | 333          | 125–350               |
| **Biochemistry**                              |           |              |                       |
| Total bilirubin (µmol/L)                      | 17        | 6.5          | 3.0–22                |
| Direct bilirubin (µmol/L)                     | 0         | 1.5          | 0–5                   |
| Total protein (g/L)                           | 56↓       | 53↓          | 63–82                 |
| Albumin (g/L)                                 | 23↓       | 30↓          | 35–50                 |
| Alanine aminotransferase (U/L)                | 78↑       | 42           | 9–52                  |
| Aspartate aminotransferase (U/L)              | 65↑       | 41↑          | 14–36                 |
| Blood urea nitrogen (mmol/L)                  | 8.4↑      | 2.3↑         | 2.5–6.1               |
| Creatinine (µmol/L)                           | 75        | 36↓          | 46–92                 |
| Sodium (mmol/L)                               | 139       |              | 137–145               |
| Potassium (mmol/L)                            | 3.44↓     |              | 3.5–5.1               |
| Chloride (mmol/L)                             | 105       |              | 98–107                |
| Glucose (mmol/L)                              | 6.3↑      | 5.0          | 4.1–5.9               |
| Pro-brain natriuretic peptide (pg/mL)         | 1240↑     |              | 0–125                 |
| Ferritin (µg/L)                               | 795.9↑    |              | 16–300                |
| C-reactive protein (mg/L)                     | 88.14↑    | 7.92         | 0–10                  |
| **Blood coagulation tests**                   |           |              |                       |
| D-dimer (µg/L)                                | 2480↑     |              | <500                  |
| Fibrinogen (g/L)                              | 4.64↑     |              | 2–4.5                 |
| Erythrocyte sedimentation rate (mm/hour)      | 116↑      | 19           | 0–20                  |
| **Infection**                                 |           |              |                       |
| Surface antigen of hepatitis B virus          | Negative  | Negative     | Negative              |
| Anti-hepatitis C virus antibody                | Negative  | Negative     | Negative              |
| Anti-human immunodeficiency virus antibody     | Negative  | Negative     | Negative              |
| Treponema pallidum-specific antibody           | Negative  | Negative     | Negative              |
| Tuberculosis T cell spot assay                 | Negative  | Negative     | Negative              |
| Procalcitonin (ng/mL)                         | 0.18↓     | <0.5         |                       |
| Endotoxin (pg/mL)                             | 8.335     | <10          |                       |
| Plasma (1 3)-beta-D-glucan (pg/mL)            | 38.31     | <60          |                       |
| **Immunology**                                |           |              |                       |
| Antinuclear antibody                          | <1: 100   | <1: 100      |                       |
| Antibody against extractable nuclear antigen  | Negative  | Negative     | Negative              |
| Antineutrophil cytoplasmic antibody            | Negative  | Negative     | Negative              |
| Anticardiolipin antibody                      | Negative  | Negative     | Negative              |
| Anti-double stranded DNA antibodies           | Negative  | Negative     | Negative              |
| Immunoglobulin G (g/L)                        | 11.2      | 8.0–15       |                       |
| Immunoglobulin M (g/L)                        | 1.52      | 0.5–2.5      |                       |
| Immunoglobulin A (g/L)                        | 4.73↑     | 0.85–3       |                       |
| Complement component 3 (g/L)                  | 1.16      | 0.79–1.52    |                       |
| Complement component 4 (g/L)                  | 0.263     | 0.16–0.38    |                       |
| CD3+CD4+T-lymphocytes (×10⁹/L)                | 92↓       | 500–1600     |                       |
| CD3+CD8+T-lymphocyte (×10⁹/L)                 | 36↓       | 320–1250     |                       |
| Acid fast stain smear                         | Negative  |              |                       |

† indicates values below the normal range and †† indicates values above the normal range.
a Vitek 2 system NH card and amplification of 16S rRNA. Sequence analysis of 16S rRNA showed 99.42% similarity to *E. corrodens* (Genbank accession number MT299733.1). Antimicrobial susceptibility of the *E. corrodens* isolate was assessed using the E-test\textsuperscript{\textregistered} gradient diffusion assay (bioMérieux) and that of *S. aureus* was assessed using a Vitek 2 system GP67 card. The results were interpreted based on Clinical and Laboratory Standards Institute criteria. The *E. corrodens* isolate was susceptible to penicillin, ceftriaxone, imipenem, and moxifloxacin, but resistant to clindamycin and amikacin. The *S. aureus* isolate was resistant to methicillin and susceptible to levofloxacin, linezolid, and vancomycin. Thus, we considered this isolate to represent methicillin-resistant *S. aureus*. Postoperative pathology showed mononuclear cell infiltration and fibrinoid necrosis of the intima in the background of suppurative inflammation, which are characteristic manifestations of BD. Subsequently, the patient was treated with 40 mg intravenous (IV) methylprednisolone qd to control BD and with 400 mg IV moxifloxacin qd plus 500 mg IV metronidazole three times a day (tid) to control...
infection. Vancomycin was added (500 mg IV tid) after culture results were available. Albumin supplementation and analgesia were also administered. The patient’s wound surface was significantly reduced. Three days after the operation, blood examinations showed white blood cell counts of $3.0 \times 10^9/L$, neutrophils 60.4%, hemoglobin 91 g/L, ESR 19 mm/hour, and CRP 7.92 mg/L (Table 1). The patient chose to leave the hospital against medical advice and died of sepsis 2 months later. The microorganism causing sepsis and death remains unknown.

**Discussion**

BD is a chronic systemic vascular inflammatory disease associated with a high incidence of skin lesions (up to 80%) and a variety of manifestations, including erythema nodosum, pyoderma, papules, and acne-like rash. The inflammatory manifestations of BD can also mimic infection, making diagnosis and treatment challenging. In the case described here, pathological analysis revealed vasculitis and suppurative infection. Moreover, an increase in CRP indicated that the patient had an infection that could not be explained by BD activity. We speculate that our patient had taken glucocorticoids and immunosuppressive medications for a long duration, and after ulceration destroyed the skin’s immune barrier, *E. corrodens* and *S. aureus* were able to invade deeper tissues and cause a septic infection. The tendon sheath, bursa, and fascial space of the hands usually communicate with each other within a thin space. When suppurative infection occurs, it can easily spread to the whole hand or even to the forearm, leading to complex abscess formation. When hands ulcers in patients with BD do not resolve for long periods because of the presence of high levels of inflammatory factors in the blood, clinicians should remain alert to potential infection by pathogens as *E. corrodens* and *S. aureus*.

Mixed infection with *E. corrodens* and *S. aureus* is rare. Accurate and effective detection of pathogens depends on the relative importance of microscopic examination and pus specimen culture. In our case, we performed Gram staining followed by microscopy and inoculated a plate culture using pus samples simultaneously. Under the microscope, we observed Gram-positive cocci and Gram-negative bacilli. *E. corrodens* was detected based on microscopic examination. *E. corrodens* belongs to the Neisseriaceae family; members of this family grow slowly and have high nutritional requirements. *E. corrodens* requires blood factor X for growth, and thus can only be cultured on blood agar or chocolate agar after comparatively long periods. Therefore, this organism is easily missed in routine cultures, especially when it is mixed with other fast-growing microorganisms with large colony sizes such as *S. aureus*. Based on the results of this case, we appeal to our clinical colleagues to pay close attention to the importance of smear microscopic examinations.

*E. corrodens* is typically sensitive to penicillin, amoxicillin/clavulanic acid, third and fourth generation cephalosporins, fluoroquinolones, and imipenem, but resistant to clindamycin and metronidazole. The *S. aureus* in our patient was methicillin resistant but sensitive to vancomycin. Because our patient was allergic to penicillin, we administered moxifloxacin combined with vancomycin based on drug sensitivity results and performed debridement and drainage of the wound. Blood tests showed that infection markers decreased gradually thereafter (Table 1) and the patient left hospital with stable symptoms. However, she died of sepsis 2 months later. The microorganisms causing sepsis and death remain unknown.
In summary, we report the case of a rare coinfection by *E. corrodens* and *S. aureus* in the hands of a BD patient with multiple ulcers. Early diagnosis, proper drainage, and treatment using fluoroquinolones combined with vancomycin may improve prognosis for other patients with similar condition.

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**Availability of data and materials**

The datasets used and/or analyzed during the current study are available from the corresponding author on request.

**Authors’ contributions**

YTL and JYZ collected the data and wrote the manuscript. HQH, QH, XFC, and ZJW performed the microbiological analysis. LZ critically reviewed the manuscript and supervised the research. All authors read and approved the submitted manuscript.

**Ethics approval and consent to participate**

This study was approved by the Ethics Committee of Changzheng Hospital, Naval Medical University, China.

**Consent for publication**

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent was available for review by the editor of this journal.

The reporting of this study conformed to CARE guidelines.13

**Declaration of conflicting interest**

The authors declare that there is no conflict of interest.

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**ORCID iD**

Yaoting Liu [https://orcid.org/0000-0002-8568-7731](https://orcid.org/0000-0002-8568-7731)

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