SEPTIC ARTHRITIS CAUSED BY *ERYSIPELOTHRIX RHUSIOPATHIAE* 
IN A PROSTHETIC KNEE JOINT 
(CASE REPORT AND REVIEW)

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**Running head:**

*Erysipelothrix* prosthesis infection

**Key words:**

arthritis, *Erysipelothrix rhusiopathiae*, knee, prosthesis infection, review

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SUMMARY

We describe the third case of prosthetic infection due to *E. Rhusiopathiae*. The patient, a 68-year-old woman, had had total knee arthroplasty 12 months before diagnosis. She had been in contact with swine at home. We review the seven previously reports of septic arthritis due to *E. rhusiopathiae*.

[49 words]
CASE REPORT

A 68-year-old woman was referred to the orthopedic ward for total replacement of the right knee, due to severe internal condyle osteonecrosis. She had a medical history of gout, chronic eczema of lower limbs and alcoholism with consequent cognitive disorders. A tricompartmental posterior stabilized cemented knee arthroplasty, containing gentamicin, was performed. The patient did not experience any problems during the first six months of follow-up. The International Knee Scoring (IKS) system was 80/200 before surgery and increased to 163/200 six months after surgery. Soon after, the patient complained of eczema-like skin lesions on the lower limb, involving the site of surgical incision. During this period, neighbors reported seeing the patient feeding her neighbor’s swine through the wire enclosure. The patient’s general practitioner prescribed intra-muscular corticosteroid because of intense itching. Within weeks of receiving this treatment, she complained of swelling and pain in the right knee and received amoxicillin-clavulanate. A radiography of the knee was normal. One month later seropurulent fistulization of the right knee was observed at the distal end of the surgical incision site and the patient was referred to hospital. On admission, flexion of the right knee was reduced to 90°. The patient was not febrile. No cardiac murmurs, skin rash or lymph node enlargement were found. The peripheral white blood cell count was 6,100 cells/mm³ and C-reactive protein concentration was 74 mg/l. Radiography revealed advanced osteolysis of the tibia, femur and patella. Blood cultures remained sterile. Twelve months after right knee arthroplasty, surgical arthrotomy was carried out, yielding a sanguine-purulent ‘chocolate-like’ fluid. Synovial resection was performed revealing large geodes resulting from osteolysis in the femur, tibia and patella. The prosthesis was removed and replaced by a vancomycin- and gentamicin-impregnated spacer. Intravenous rifampin and vancomycin treatment was started. Eleven per-operative samples were sent to the laboratory. All Gram staining tests were negative. Cultures were grown on blood agar plates under aerobic and
anaerobic conditions and on chocolate agar plates incubated under 5% CO2. Cultures were negative on day 2. On day 4, four samples yielded pinpoint colonies. Microscopic observations of these first cultures revealed thin short cylindrical Gram-positive rods. Subcultures were set up for potential confirmation of Lactobacillus or Corynebacterium. These subcultures yielded enterococcus-shaped colonies on day 2. Bacteria were confirmed to be rod-shaped, but were longer and thinner than those observed in initial cultures. On the basis of the patient’s recent surgical history, and in spite of the absence of clusters resembling Chinese letters or palisades, Propionibacterium was suspected. A system for the identification of anaerobic bacteria (API-Ana, bioMérieux®) identified these bacteria as Erysipelothrix. Only subsequent subcultures presented the typical curved morphology. The strain was rough and produced no capsule. Bacteria were definitively identified to be Erysipelothrix rhusiopathiae by amplification and sequencing of the 16S rRNA-encoding gene rrs.

Antibiotherapy was then switched to intravenous imipenem and ofloxacin for two weeks, followed by oral clindamycin and ofloxacin. The patient’s condition improved. C-reactive protein levels decreased. A trans-oesophageal echocardiogram excluded endocarditis. An exo-femoral 30-40 ml abscess-like formation had to be drained two months after removal of the prosthesis. Microbiological cultures and 16S rRNA PCR from drained fluid failed to retrieve any bacteria. Five months after removal of the prosthesis, definitive knee arthrodesis was performed with a “sur mesure” nail Link®. Antibiotics were stopped four weeks later (total duration: 6 months) and osseous fusion of the arthrodesis was observed within six weeks. The patient did not experience any other problems during the rest of the follow-up period, 32 months after knee arthrodesis.
*E. rhusiopathiae* is a ubiquitous, Gram-positive and non-sporing rod. It can exist as a pathogen, a commensal or a saprophyte in a wide variety of wild and domestic animals, affecting both vertebrates and invertebrates (3,5). The major reservoir is generally believed to be domestic swine (5). Humans can pick up infection of this bacterium through contact with animals or environmental sources. Erysipeloïd of Rosenbach is an occupational skin infection. Other rare features have been described in humans: diffuse cutaneous form, bacteremia with or without endocarditis, arthritis, osseous necrosis and intra-cranial infection (3,5).

Whereas arthritis is one of the most common features caused by *E. rhusiopathiae* in mammals, the involvement of a joint is rare in humans (3,5). Previous reports in humans have described the following features: 1- arthritis due to local extension of an adjacent cutaneous infection; 2- polyarthritis or polyarthralgia accompanying systemic infections, such as diffuse cutaneous infection (3,5). However, septic arthritis has rarely been proved by isolation the bacteria. Here we review previous reports of *E. rhusiopathiae* isolation using joint aspiration or surgical procedures. Cases of reactive arthritis are not considered. Only seven additional cases have been previously reported (1,2,4,6-9). The main characteristics observed are summarized in Table 1. Typically, *E. rhusiopathiae* septic arthritis presents as a chronic process (6/8) involving a single big joint (8/8), particularly the knee (5/8). Only two reports described moderate fever. Peripheral white cell count was normal in most patients, with only mild elevation of C reactive protein levels (median concentration = 27 mg/l).

The pathogenesis of joint infection is poorly understood. Most previously described patients had a cutaneous lesion at the site of the infected joint and had carried out occupational or leisure activities that exposed them to a reservoir of infection: working as a butcher, feeding swine, hunting, fishing, cleaning aquariums, knee laceration at the seashore. Thus, *E. rhusiopathiae* infection may have occurred through unrecognized Erysipeloïd or non-specific cutaneous lesions. *E. rhusiopathiae* may also be able to penetrate the safe skin barrier (3).
Although half of the reported cases occurred after a surgical procedure, and could therefore qualify as nosocomially-acquired infections, it is likely that these infections were contracted in the community. Septic arthritis probably resulted from post-operative trans-cutaneous infection in patient G and in the present report (8). In patient F, a pre-operative latent infection of the knee may have been triggered by surgery (7). In patient C, arthroscopic incision through an unrecognised cutaneous infection may have resulted in direct inoculation through the knee (1). Blood cultures, when performed, remained sterile (5/5). No patient showed clinical or echocardiographic signs of infective endocarditis. These findings suggest that septic arthritis is unlikely to result from hematogenous spread. Rather, it may be attributed to a local or regional portal of entry, even through minor skin lesions, or exacerbation of previous latent infection by invasive procedures. Most of the patients underwent surgical lavage of the infected joint (7/8) and received efficient intravenous antibiotic treatment for several weeks (7/8). The overall outcome was favorable: all patients recovered without sequelae, with the exception of the patient reported here, who underwent knee arthrodesis. *E. rhusiopathiae* is naturally resistant to vancomycin and gentamicin. These two antibiotics are frequently used in the empirical treatment of arthritis, particularly to treat post-operative prosthesis infections, and are included in spacers (5).

This review highlights the role of debilitating host factors. Six of eight patients suffered from one or more severe immunosuppressive conditions: terminal renal insufficiency, diabetes mellitus, chronic lymphocytic leukemia, systemic lupus erythematosus or rheumatoid arthritis, systemic and/or intra-articular steroids and alcoholism. Few cases of *E. rhusiopathiae* bacteremia, with or without endocarditis, have been reported in patients who are immuno-compromised or who have a history of alcohol abuse (3,5).
Previous findings regarding possible mechanisms of pathogenicity have been conflicting, with inconsistent data reported for the virulence of smooth (S) and rough (R) colonies and the presence of a hyaluronidase, a neuraminidase and a capsule (3,5).

*Erysipelothrix* is not a fastidious microorganism. However, the diagnosis of this pathogen is difficult if bacteriologists are not aware of clinical suspicion of animal contact (3). The species is rarely found in clinical routine analyses and its initial morphology in culture frequently leads to suspicion of *Corynebacterium, Lactobacillus, Streptococcus* or *Listeria* (3-5). This report provides one such example. Gram staining on clinical samples was positive in only one of eight previously described cases, the result being misinterpreted as Gram-negative rods. Paracentesis cultures were negative for four of six cases, whereas samples obtained under surgical procedures gave rise to *E. rhusiopathiae* in all seven cases where such cultures were established. Bacterial growth was usually slow and definitive identification was often delayed. Gram staining of initial cultures was atypical or confusing in several cases, including the case reported here. *E. rhusiopathiae* is known to yield small colonies, which can be missed, and the typically curved morphology requires several subcultures (3). Important biochemical characteristics allow the identification of *E. rhusiopathiae*: the absence of catalase and H2S production. This bacterium may also be identified by its resistance to vancomycin, but not to penicillin. Amplification of the *rrs* gene encoding 16S rRNA is also a sensitive and useful test to confirm its identification (3).

[1444 words]
AKNOWLEDGMENTS

Authors thank Pr Patrick A.D. Grimont and Dr Anne Le Fleche, from the Molecular Bacterial Identification Centre, Pasteur Institute (Paris, France), who performed the rRNA sequencing of the strain.
REFERENCES


## Table 1: Main characteristics of 8 patients with septic arthritis due to *Erysipelothrix rhusiopathiae*.

<table>
<thead>
<tr>
<th>Patient [ref.]</th>
<th>Sex, age (y)</th>
<th>Debilitating conditions, exposure to animals</th>
<th>Suspected mechanism causing bacteria to spread to joint</th>
<th>Clinical features (duration before diagnosis)</th>
<th>Surgical procedures, Antibiotherapy (duration)</th>
<th>Outcome (follow-up)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C [1]</td>
<td>M, 18</td>
<td>- No debilitating conditions, Septic knee laceration on a rock by seashore</td>
<td>Inoculation during surgery, from pre-operative cutaneous infection</td>
<td>Acute post-operative knee mono-arthritis, 38.5°C (6 days)</td>
<td>- Arthroscopic lavage + debridement + i.v. benzylpenicillin + ciprofloxacin (5 months)</td>
<td>Cured</td>
</tr>
<tr>
<td>D [9]</td>
<td>F, 41</td>
<td>- Oral and intra-articular steroids for SLE, Koi fish</td>
<td>Penetration through minor skin injury while cleaning aquariums</td>
<td>Chronic knee mono-arthritis, no fever (1 month)</td>
<td>- Arthroscopic lavage + synovectomy + i.v. penicillin (4 weeks) then oral ciprofloxacin (12 months)</td>
<td>Cured</td>
</tr>
<tr>
<td>E [6]</td>
<td>M, 76</td>
<td>- Aortic valve replacement, gout, Fishing</td>
<td>Metastasis of an infective endocarditis* (?)</td>
<td>Chronic knee mono-arthritis, no fever (6 months)</td>
<td>- No surgical procedure + i.v. benzylpenicillin (4 weeks) and repeated arthrocentesis</td>
<td>Cured</td>
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<tr>
<td>F M, 76</td>
<td>Long-term high dose steroid for rheumatoid arthritis and lupus nephritis - Pigs while working in a tanning factory</td>
<td>Total knee arthroplasty may have exacerbated pre-operative latent chronic knee infection</td>
<td>Chronic prosthetic knee mono-arthritis**, fever NP (14 months)</td>
<td>- 2-stage exchange revision with lavage, debridement, synovectomy and antibiotic-loaded spacer - i.v. benzylpenicillin + levofloxacin (3 weeks) then oral clindamycin + levofloxacin (7 weeks)</td>
<td>Cured (12 months)</td>
<td></td>
</tr>
<tr>
<td>G F, 73</td>
<td>Idiopathic osteoarthritis - Hunting with his dog</td>
<td>Chronic wound of the heel</td>
<td>Chronic prosthetic hip mono-arthritis**, fever NP (10 months)</td>
<td>- 2-stage exchange revision with lavage, debridement and antibiotic-loaded spacer - i.v. benzylpenicillin + levofloxacin (3 weeks) then oral amoxicillin (8 weeks)</td>
<td>Cured (4 months)</td>
<td></td>
</tr>
</tbody>
</table>

** With radiographic evidence of peri-prosthetic osteolysis.

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Reported case F, 68 - Alcoholism, gout, systemic steroids to treat very itchy skin lesions - Feeding swine | Penetration through self-induced cutaneous abrasions or unrecognized erysipeloid | Chronic prosthetic knee mono-arthritis**, no fever (2 months) | - 2-stage exchange revision with lavage, debridement, synovectomy and antibiotic-loaded spacer - i.v. imipenem + ofloxacin (2 weeks) then oral clindamycin + ofloxacin (24 weeks) | Cured with sequelae (32 months) |

Abbreviations: CLL = chronic lymphocytic leukaemia; i.v. = intravenous; NP = information not provided; PKD = polycystic kidney disease; SLE = systemic lupus erythematosus.

* This hypothesis is very unlikely considering infective endocarditis is “rejected” using modified Duke’s criteria and three hemocultures remained sterile.

** With radiographic evidence of peri-prosthetic osteolysis.