Summary: We report a case of bloodstream infection due to *Staphylococcus intermedius*—a bacterium typically associated with zoonotic infections—with prolonged bacteremia and invasive and metastatic sequelae that required extended antimicrobial therapy.

Running title: Metastatic *S. intermedius* infection

Keywords: Staphylococcal infections; bacteremia; zoonoses

**Metastatic Complications From *Staphylococcus intermedius*, a Zoonotic Pathogen**

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Abstract: Metastatic infection is an infrequent complication of non-aureus staphylococcal infection. Here we report a case of bloodstream infection due to *Staphylococcus intermedius*. To our knowledge, ours is the only known case of metastatic infection with *S. intermedius*.

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Case Report

A 76 year old man with Type II diabetes mellitus and myelodysplastic syndrome was admitted to our hospital with a generalized rash. Four months prior, he was diagnosed with new-onset psoriasis and received acitretin for 3 weeks. The rash had varying morphology, including a morbilliform eruption intermixed with papules coalescing into plaques on the back and chest, plaques with scaling and fissuring on the arms and upper thighs, and thick hyperkeratotic scaling of both soles.

His past medical history was also significant for diabetic retinopathy and osteomyelitis requiring amputation of the right 4th and 5th toes five years previously. He lived at home with his wife and dog. He denied any recent dog bites.

He was admitted with the diagnosis of drug hypersensitivity. He was afebrile on admission, with a slight leukopenia (3700 cells/µl). He initially improved on treatment with intravenous corticosteroids but subsequently developed arthralgias of multiple joints, generalized weakness and confusion.

On hospital day 14, he first developed fever (38.6°C). Examination showed a grade III/VI systolic murmur at the left sternal border (consistent with a baseline exam), a 3 mm non-purulent, dry ulcer on the plantar surface of the left first metatarsophalangeal joint and hyperkeratotic lesions and deep fissuring of the foot. All extremities and joints were tender. Blood cultures (BacTAlert® blood culture system, BioMérieux) yielded gram-positive cocci in 4 of 4 bottles; a staph latex test (Staphaurex®, Remel) was negative, leading to the identification of the organism as staphylococcus not-aureus (SNA). Isolate testing in manual antibiotic dilution revealed a vancomycin MIC of <2 µg/ml, and intravenous vancomycin was administered. Blood cultures remained positive for SNA from hospital days 14 through 22. He developed septic arthritis of both shoulders and both elbows and an abscess of the right iliacus muscle. He underwent multiple aspirates and incision and drainage
procedures; all cultures yielded a heavy growth of SNA. He received intravenous vancomycin for 52 days, and was discharged to a rehabilitation facility after a 9-week hospitalization.

All the blood and fluid cultures were initially reported by the hospital laboratory as SNA. Subsequent manual biochemical testing took place in our reference laboratory. The colony morphology was described as large, white beta-hemolytic colonies, appearing as large gram positive cocci in clusters and tetrads on Gram stain, growing on both aerobic and anaerobic media with a better aerobic growth. The biochemical tests performed revealed a positive reaction to catalase, tube coagulase, arginine utilization at 48 hours, urease, nitrate, trehalose, mannitol, mannose, sucrose, maltose, weak positivity to PYR, novobiocin susceptible and a negative reaction to oxidase, acetoin production (Voges Proskauer test), ornithine, esculin, xylose, cellobiose, lactose, arabinose and raffinose. These biochemical tests led to the species identification of the isolate as *Staphylococcus intermedius*.

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*Staphylococcus intermedius* is a coagulase-positive staphylococcus first described in 1976 (6). It is a commensal, living in the oral cavity and on the body surfaces of various animals, including dogs, pigeons, minks, cats, foxes, raccoons, gray squirrels, goats, and horses (3). Moreover, it is a recognized pathogen in animals, causing infections of skin, bone, respiratory tract, genito-urinary tract and central nervous system (14).

*S. intermedius* was first identified as a human pathogen in 1989, when a case series of dog bite-induced cellulitis revealed *S. intermedius* as the causative organism in 3 of 14 cases (15). In a one-year study of 144 veterinary staff who were exposed to dogs, only one person had *S. intermedius* cultured from the nasopharynx, whereas 30 persons (21%) carried *S. aureus* (15). Our patient may have acquired this organism through animal contact prior to admission.

Excluding outbreaks of gastroenteritis in which *S. intermedius* was implicated (9), only 17 human cases of *S. intermedius* infection have been reported (Table). Of these, only 4 cases had non-
cutaneous infection, including single cases each of endocarditis and brain abscess. To our knowledge, ours is the first report of metastatic infection involving S. intermedius. The clinical manifestations in our patient were similar to the well-recognized complications of S. aureus bacteremia.

Approximately half of S. intermedius isolates possess protein A and clumping factor (bound coagulase) (4). As a result, latex agglutination tests, which rely on detection of clumping factor or protein A, may be negative and can lead to an initial identification as SNA, as in the initial identification of our isolate, although subsequent manual testing did indicate the isolate was coagulase-positive.

In summary, we report an unusual case of S. intermedius bacteremia with multiple metastatic complications requiring surgical intervention and an extended course of vancomycin. This case illustrates the potential for SNA strains to cause invasive infection.

Potential conflicts of interest: none.
References
7. Kelesidis, T., and S. Tsiodras. Staphylococcus intermedius is not only a zoonotic pathogen, but may also cause skin abscesses in humans after exposure to saliva. Int J Infect Dis 14:e838-41.
<table>
<thead>
<tr>
<th>Case number</th>
<th>Year reported</th>
<th>Description</th>
<th>Site of infection</th>
<th>Immune deficiency/underlying illness</th>
<th>Drug susceptibility</th>
<th>Antibiotic treatment</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>1-3</td>
<td>1989</td>
<td>Case series- canine inflicted cellulitis (13)</td>
<td>Skin/soft tissue</td>
<td>None</td>
<td>Two isolates – S to PCN, One isolate – R to PCN</td>
<td>PCN, amoxicillin/ clavulanate</td>
<td>Recovered</td>
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<td>4</td>
<td>1992</td>
<td>Case report (11)</td>
<td>Endocarditis</td>
<td>HIV</td>
<td>N/A</td>
<td>Cefoxitin, gentamicin followed by oral ciprofloxacin &amp; rifampin</td>
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<td>5</td>
<td>1992</td>
<td>Case report (2)</td>
<td>Skin/soft tissue</td>
<td>None</td>
<td>R- PCN, tetracycline</td>
<td>S- amox/clav, erythromycin, flucloxacin, gentamicin, sodium fusidate</td>
<td>Amoxiclav Recovered</td>
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<td>6-8</td>
<td>1994</td>
<td>Case series of canine- inflicted and non-canine inflicted wounds (17)</td>
<td>Skin/soft tissue</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
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<td>1999</td>
<td>Case report (5)</td>
<td>Pneumonia</td>
<td>Diabetes</td>
<td>R- PCN, oxacillin, clindamycin, erythromycin, ofloxacin</td>
<td>S- TMP/SMX, gentamicin, vancomycin</td>
<td>Vancomycin Recovered</td>
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<td>11</td>
<td>2000</td>
<td>Molecular phylogenetic analysis (16)</td>
<td>Otitis externa</td>
<td>None</td>
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<td>N/A</td>
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<td>2004</td>
<td>Case report (10)</td>
<td>Mastoiditis</td>
<td>None, but s/p mastoidectomy</td>
<td>Pan-sensitive, including PCN</td>
<td>Ofloxacin</td>
<td>Recovered</td>
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<tr>
<td>13, 14</td>
<td>2004</td>
<td>Case series (12)</td>
<td>Skin/soft tissue</td>
<td>Case 1: breast cancer on chemotherapy; Case 2: none</td>
<td>Case 1 isolate was pan-sensitive except to PCN and produced B-lactamase; Case 2 was sensitive to all but PCN and tetracycline</td>
<td>Case 1: disk</td>
<td>Not reported</td>
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<tr>
<td>15</td>
<td>2005</td>
<td>Case report (1)</td>
<td>Brain abscess</td>
<td>None</td>
<td>R- PCN, methicillin, clindamycin</td>
<td>Vancomycin</td>
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<td>16</td>
<td>2005</td>
<td>Case report (8)</td>
<td>Sinusitis</td>
<td>None</td>
<td>R- ceftazolin, oxacillin, levofloxacin, cotrimoxazole, tetracycline, l. gentamyacin</td>
<td>Vancomycin, linezolid</td>
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<tr>
<td>17</td>
<td>2011</td>
<td>Case report (7)</td>
<td>Skin abscesses</td>
<td>Hepatitis C</td>
<td>S- oxacillin, ampicillin/sulbactam, cefazolin, TMP/SMX, vancomycin</td>
<td>Vancomycin, amoxiclav</td>
<td>Recovered</td>
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