Staphylococcus intermedius Brain Abscess as a Complication of Pulmonary Arteriovenous Malformation in a Patient with Hereditary Hemorrhagic Telangiectasia

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Abstract

Staphylococcus intermedius is a rare cause of human infections ranging from skin and soft tissue infections to bacteremia. It is particularly known for its association with exposure to dogs. We report an unusual case of a 73-year-old female with a brain abscess caused by S. intermedius who was recently diagnosed with hereditary hemorrhagic telangiectasia and a pulmonary arteriovenous malformation. The patient underwent debridement of the brain abscess followed by a six-week course of vancomycin and rifampin, after which she made a near complete recovery. This is the first case of a brain abscess in an adult due to S. intermedius in the published literature, and we provide a comprehensive review of the literature of all human infections caused by this pathogen summarizing its clinical manifestations, treatment recommendations, and outcomes.
Introduction

*Staphylococcus intermedius* is an unusual pathogen in humans. Infection is often associated with animal contact and is considered a “zoonotic organism” found as part of the oral and skin flora of dogs, pigeons, foxes, minks and horses (1). *S. intermedius* uncommonly may cause human infections ranging from skin and soft tissue infections (SSTIs) to bacteremia (2).

This paper aims to enhance the recognition of this increasingly important human pathogen by presenting an unusual case of a brain abscess due to *S. intermedius* and providing a comprehensive review of the published English literature summarizing human infections due to this pathogen. Our report also highlights pulmonary arteriovenous malformation (PAVM) as a risk factor for developing unusual infections including brain abscesses.

Case Report

A 73-year-old female with pre-diabetes, congestive heart failure, and recently diagnosed hereditary hemorrhagic telangiectasia (HHT) presented with sudden onset of right-sided lower facial droop, numbness, and slurred speech. Physical examination showed visible telangiectasias on her tongue (Figure 1). Computed tomography (CT) of the brain without contrast revealed a nonspecific low-density lesion of the left posterior frontal lobe cortex. To further evaluate this abnormality, a magnetic resonance imaging (MRI) was performed and demonstrated a 1.2 cm intracerebral ring enhancing lesion consistent with an abscess in the posterior left frontal lobe (Figure 2). The lesion was too small for stereotactic biopsy.

Blood cultures showed no growth, and CT of the chest, abdomen, and pelvis were notable for a large 5.9 cm left lower lobe PAVM and felt to be related to her underlying HHT (Figure 3). CT angiography of the head and neck with contrast did not show intracerebral arteriovenous malformation. The patient was empirically treated for the brain abscess with intravenous vancomycin and ceftriaxone as well as oral metronidazole for a planned six-week course.

The patient was readmitted for vomiting thought to be associated with the antibiotics, specifically the metronidazole. Repeat MRI of the brain, twenty days after initial imaging, showed an increase in the size of the brain abscess, with worsening vasogenic edema. The patient underwent left frontal craniotomy with excision of the brain abscess. Operative findings showed an abscess with a thick capsule with purulent material. Intraoperative bacterial, fungal, and acid-fast bacillus cultures were negative. Broad-range polymerase chain reaction performed at the University of Washington was positive for *Staphylococcus intermedius* without other identified organisms. Upon further questioning, the patient reported that she was a dog owner. Since no susceptibilities were available given negative culture results, we proceeded with intravenous vancomycin and oral rifampin for six weeks based on the available literature.

Due to suspected systemic embolism from the large PAVM and perceived high risk for surgical therapy, she was referred to interventional cardiology for closure of the PAVM. Pulmonary angiography demonstrated a 9 mm patulous pulmonary artery branch to the 5.9 cm AVM sac. The PAVM feeder artery underwent successful obliteration using a 14mm St. Jude Amplatzer AVP2 vascular plug without compromise to adjacent healthy lung tissue. She was treated with baby aspirin and underwent serial surveillance CT imaging that showed a decrease in the size of the AVM. On follow-up, she had experienced no other neurologic or infectious complications and only had mild persistent facial numbness.
Review of the Literature

We searched the English literature from January 1975 to September 2019 through PubMed and Google Scholar using the search terms, “Staphylococcus intermedius” and “S. intermedius.” Only human infections were included. Articles were excluded if the culprit bacterium was “Streptococcus intermedius” or “Staphylococcus pseudointermedius”; or if the article was not in English. The citations of these articles were also examined for additional cases. This yielded a total of 21 articles which included 42 total cases, including this report (Table 1).

In terms of demographics, of those with reported data the average age was 46 years (±24), ranging from 11 months (3) to 78 years old (4). The identified infections were more likely male with a 2:1 predominance (64% male, 36% female).

The majority (36 of 42) of the case presentations reported the type of infection and were predominantly skin and soft tissue infections (25 cases, 69.4%). The infections were device-associated infections (4 cases, 11.1%) (5, 6, 7, 4); bacteremia (3 cases, 8.3%) (5, 7, 8); central nervous system (3 cases, 8.3%) (3, 9, this report); sinusitis or mastoiditis (2 cases, 5.6%) (10, 11); bone or joint infection (2 cases, 5.6% (4, 8); and pneumonia (1 case, 2.8%) (12). One case of a pediatric brain abscess caused by Staphylococcus intermedius had been previously reported (9).

Given the presence of S. intermedius as part of animal flora, cases were analyzed regarding animal exposure and the majority of patients reported exposure. 27 out of 33 cases (75.8%) reported exposure to dogs and an additional 2 cases (7.4%) acknowledged exposure to cats.

Twenty-five (59.5%) of cases reported an underlying medical condition. Of these cases, 6 (24.0%) reported diabetes mellitus and 4 (9.5%) cases reported congestive heart failure. The current case is unique given the underlying history of HHT and PAVM. Four cases noted an association with devices, including two with pacemaker lead infections (6), one from a pacemaker site infection (4), and one catheter-associated bacteremia (7). An additional 4 cases (16.0%) noted overlying soft tissue damage in the area where the S. intermedius infection emerged, including 2 patients with varicose ulcers (13), one patient with chronic foot ulcer, and one patient with a prior foot burn (4) (Table 1). One additional patient had recent acupuncture (14).

With regards to treatment, 25 cases (60.5%) provided the specific antibiotics utilized. Glycopeptides, namely vancomycin, were the most widely chosen among 10 cases (34.0%) using this class, with the vast majority (9 of 10 cases) electing vancomycin versus daptomycin. Penicillins were the second most chosen class of antibiotics with 7 cases (28.0%) comprised of amoxicillin-clavulanic acid, 4 cases (57.1%); penicillin, 2 cases (28.6%); and an additional single case (14.3%) of ampicillin-sulbactam. Cephalosporins were utilized in 5 cases (20.0%), included 2 cases each (40.0%) of cefazolin and ceftriaxone, and one case (20%) using cefotaxime. Rifampin was used as combination therapy in 2 cases (7.7%). Single uses (4.0% each) were also noted for ciprofloxacin, gentamicin, linezolid, neomycin-polymyxin, ofloxacin, and sulfadiazine.
In terms of susceptibilities, 18 cases (42.3%) provided these data and the most common reported susceptibility was to vancomycin (9 cases out of 10 isolates tested, 90%), and gentamicin and erythromycin each with 7 reports (each with 8 isolates tested, 88%). Rifampin was susceptible in all three cases in which testing was performed. Penicillin had the poorest susceptibility (6 cases out of 11 isolates tested, 55%). Additional susceptibilities are noted in Table 2.

Patients had excellent treatment outcomes. Of the 22 cases (52.4%) that reported outcomes, 19 (86.4%) stated that the patient had a full recovery. Yet, two of the three CNS cases (9.1%) noted residual neurologic deficits including residual hemiparesis (9) and facial numbness (current report).

Discussion

*Staphylococcus intermedius* was initially isolated in 1976 from isolates originating from animals including dogs (1). Initially, it was grouped with *S. aureus* because it produced coagulase, DNases, and had similar growth patterns (15). *S. intermedius* was subsequently separated from *S. aureus* when its cell wall composition and guanine-cytosine content were analyzed, ultimately being divided into 3 species, *S. intermedius*, *S. pseudointermedius*, and *S. delphini* (16). The identification of *S. intermedius* serves as a challenge as it is often misidentified as *Staphylococcus aureus* due to its positivity on coagulase testing and its potential pathogenicity. In addition, *S. intermedius* has been falsely identified as methicillin-resistant *S. aureus* (MRSA) using phenotypic penicillin binding protein 2a (PBP2a) latex agglutination tests (17). Fortunately, *S. intermedius* can be confirmed through additional biochemical tests (1). For example, in contrast to *S. aureus*, *S. intermedius* is pyrrolidonyl arylamidase and β-galactosidase positive (3). Broad-range polymerase chain reaction (PCR) is also a useful test to identify *S. intermedius* especially when there is a small specimen obtained or in the presence of prior antibiotic use, and this technology can differentiate this organism from both *S. aureus* and *S. pseudointermedius*. Of note, given the aforementioned difficulties in identifying this organism, it is likely that human infection cases with *S. intermedius* have been underestimated.

An increasing body of literature has implicated an association between HHT, PAVM, and increased rates of infection, in particular cerebral infections which may involve atypical pathogens (18). The increased risk of infection stems from the direct connection between the pulmonary and systemic circulation circumventing the capillary beds, increasing the ability for bacteria to translocate and disseminate to distant sites including the brain (18). There are increased rates of cerebral abscesses in patients with similar right to left shunting including patent foramen ovale and congenital cyanotic cardiopathy (19). Of note, many patients who present with cerebral abscesses, including our case, were asymptomatic from the PAVM before presentation (20). Screening methods for pulmonary AVMs include detection of right-to-left shunt by radionuclide perfusion scan or contrast echocardiography. Transcatheter embolectomy is the current standard treatment for PAVMs (21) and is important for limiting future neurologic and infectious complications. We believe the patient’s PAVM predisposed her to this unusual infection in the setting of exposure to her dog.
Conclusion

To the best of our knowledge, this is the first reported case of a brain abscess stemming from *S. intermedius* in an adult and second report overall. Fortunately, this infection, including this case, is often susceptible to antibiotics such as the vancomycin and rifampin which we chose. Exposure to dogs remains the most consistent and preventable risk factor, with our patient’s PAVM serving as a conduit for this infection to reach her brain. Luckily, cases such as these represent a minority of exposures to dogs; avoidance of these common pets cannot be realistically recommended, but a history of exposure serves as a clue to the possibility of zoonotic organisms such as *S. intermedius*. Furthermore, PAVMs can be a further risk factor for atypical infections in unusual locations.

Conflict of Interest Statement

The authors report no conflicts of interest.

Patient Consent Statement

The patient could not be reached through the contact information provided in her chart to obtain signed authorization to publish the case report. Prior to drafting the case report, the medical information was stripped off all 18 HIPAA identifiers. Additionally, the re-identification is unlikely as no identifying characteristics of the patient are connected to the case and the patient was not aware of the uniqueness of her case. Hence according to 45 CFR 164.514(b), the information is no longer protected health information (PHI) and written authorization is not required for publication of the case report. Of note, Figure 1 was obtained through the hospital’s secure photo upload mechanism of Epic Haiku and cannot be used to identify the patient.
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Figures

Figure 1: Telangiectasias on tongue as a manifestation of her underlying hereditary hemorrhagic telangiectasia.
Figure 2: Magnetic resonance imaging (MRI) of the brain demonstrated a ring-enhancing lesion consistent with a brain abscess in the posterior left frontal lobe with surrounding vasogenic edema.
Figure 3: Chest CT showing an enhancing 5.9 cm mass in the left lower lobe which has a feeding branch from the left lower lobe pulmonary artery and a large draining vein that communicates with the left inferior pulmonary vein. Findings are consistent with a large pulmonary arteriovenous malformation.
Table 1: Cases of Infections due to *Staphylococcus intermedius* Reported in the Literature

| Author, Year | Age, Sex | Presentation | Infection Site | Risk Factors | Pet Exposure | Treatment | Recovery |
|--------------|----------|--------------|----------------|--------------|--------------|-----------|----------|
| Talan, 1989  | 20, M    | Hand, forearm, thigh wounds | Left thumb pain with movement | None | Dog bite | Penicillin V QID for 5 days | Full |
| Talan, 1989  | 34, F    | Forearm wound | Forearm bite and pain | None | Dog bite | Penicillin V QID for 5 days | Full |
| Barnham, 1992| 38, F    | Hand wound | Pain, discharging wound | None | Dog bite | Amoxicillin-clavulanate | Full |
| Lee, 1994    | NR       | NR | NR | NR | Dog bite | NR | NR |
| Lee, 1994    | NR       | NR | NR | NR | Dog bite | NR | NR |
| Lee, 1994    | NR       | NR | NR | NR | Dog bite | NR | NR |
| Lee, 1994    | NR       | NR | NR | NR | Dog bite | NR | NR |
| Lee, 1994    | NR       | Leg Ulcer | Varicose ulcer | Dog owner | NR | NR |
| Lee, 1994    | NR       | Leg Ulcer | Varicose ulcer | Dog owner | NR | NR |
| Lee, 1994    | 13, NR   | Infected suture line | NR | NR | Dog contact | NR | NR |
| Vandenesch, 1995| 63, M | Catheter-associated bacteremia | Fever | Metastatic NS lung carcinoma, chemotherapy, splenectomy | Cat owner | Amoxicillin-clavulanate TID, ciprofloxacin BID for 10 days | Full |
| Gerstadt, 1999| 73, M    | Pneumonia | Fever and secretions | NIDDM, Coronary arterial bypass graft | None | Vancomycin | Full |
| Talan, 1999  | NR       | Wound | NR | NR | Dog bite | NR | NR |
| Talan, 1999  | NR       | Wound | NR | NR | Cat bite | NR | NR |
| Tanner, 2000 | 38, F    | Otitis Externa | NR | NR | Dog owner | Topical neomycin, polymyxin B | Full |
| Kikuchi, 2004| 51, F    | Mastoiditis | Irritation and otorrhea of the Right ear | Tympanoplasty, radial mastoidectomy | Dog lick | Ofloxacin ear drops | Full |
| Pottumarthy, 2004| 60, F | Nail bed infection | Inflamed nail bed | Breast cancer, chemotherapy | NR | NR | NR |
| Pottumarthy, 2004| 37, M    | Cellulitis | Left leg cellulitis | None | NR | Vancomycin for 8 weeks | Full |
| Atalay, 2005 | 4, M     | Brain abscess | Headache, fever, nausea, vomiting, Right hemiparesis | None | NR | Minimum residual hemiparesis | Full |
| Kempker, 2009| 28, F    | Sinusitis | Foul smelling nasal discharge and mild headache | Diabetes insipidus, pituitary adenoma S/p transphenoidal resection 8 months prior, CSF Leak | Dog owner and licked by dog with recent S. Intermedius pyoderma | Bilateral sphenoidotomy, vancomycin then linezolid for total 6 weeks | Full |
| Chuang, 2010 | 6, M     | Catheter-associated bacteremia | Intermittent high fever | Hemophilia B | Dog owner | Vancomycin then oxacillin for 18 days | Full |
| Durdik, 2010 | 0, M     | Meningitis | Persistent fever | None | Dog owner | Cefotaxime | Full |
| Kelesidis, 2010| 43, M    | Forearm abscesses | Chills after injecting intravenous cocaine | IVDA | None | Amoxicillin-clavulanate for 2 weeks | Full |
| Hatch, 2011  | 76, M    | Bacteremia, septic arthritis, iliacus abscess | Generalized rash | DM | Dog owner | Vancomycin for 52 days | NR |
| Wang, 2013   | 73, F    | Elbow wound | Fever, pain, swelling of Left elbow | Recent left elbow total arthroplasty | Dog owner | Cefazolin daily then rifampin for 4 weeks | Full |
| Choi, 2014   | 32, F    | Cervical | Severe chin | 1 week post- | None | Sulbactam-ampicillin; | Full |
| Author, Year | Age, Gender | Diagnosis | Symptoms | Treatment | Follow-up |
|--------------|-------------|-----------|----------|-----------|-----------|
| Koci, 2015   | 58, M       | Pacemaker lead infection | Fever, chills, headache, Implanted pacemaker, Neighbor’s dog licked hand wound | Daptomycin then cefazolin | Full |
| Viau, 2015   | 78, M       | Hallux osteomyelitis | Blood-filled blisters on his left foot, DM, prior foot burn | None | Doxycycline then vancomycin | Full |
| Viau, 2015   | 74, M       | Hand cellulitis | Pain and clear exudate on the left hand | CHF, NR | Topical silver sulfadiazine | Lost to follow-up |
| Viau, 2015   | 77, M       | Pacemaker site infection | Purulent drainage from pacemaker site | DM, cirrhosis, CHF, NR | "Antibiotics" | Full |
| Viau, 2015   | 59, M       | Foot cellulitis and fever | DM, chronic foot ulcer, Dog owner | Topical silver sulfadiazine | Ceftriaxone for 4 weeks | Full |
| Viau, 2015   | NR          | Foot osteomyelitis | NR | NR | NR | Toe amputation then (cefazolin or amoxicillin/clavulanic acid) | NR |
| Viau, 2015   | NR          | Foot osteomyelitis | NR | NR | NR | Toe amputation then (cefazolin or amoxicillin/clavulanic acid) | NR |
| Viau, 2015   | NR          | Foot osteomyelitis | NR | NR | NR | Toe amputation then (cefazolin or amoxicillin/clavulanic acid) | NR |
| Viau, 2015   | NR          | Foot osteomyelitis | NR | NR | NR | Debridement then vancomycin for 6 weeks | NR |
| Viau, 2015   | NR          | Foot infection | NR | NR | NR | Vancomycin | NR |
| Viau, 2015   | NR          | Foot infection | NR | NR | NR | Bedside debridements then topical neomycin-polymyxin | NR |
| Lainhart, 2018 | 46, M     | Toe ulceration | Left toe ulceration, IDDM, CHF, CAD, HTN | Dog owner | Doxycycline and gentamicin topical | Full |
| This Report, 2019 | 73, F     | Brain abscess | Right-sided facial droop and slurred speech, Hereditary hemorrhagic telangiectasia, Pulmonary AVM, CHF | Dog owner | Vancomycin and rifampin for 6 weeks | Mild residual paresthesia |

NR, not reported; NIDDM, non-insulin dependent diabetes mellitus; CABG, coronary artery bypass graft; DM, diabetes mellitus; IVDA, intravenous drug abuse; IDDM, insulin dependent diabetes mellitus; CHF, congestive heart failure; CAD, coronary artery disease; HTN, hypertension; NSC, non-small cell; HHT, Hemorrhagic hereditary telangiectasia; AVM, arteriovenous malformation

Table 1. Reported cases of *S. intermedius* in the English Literature
Table 2: Reported Antibiotic Susceptibilities.

| Antibiotic Class | Number of Isolates Susceptible | Number of Isolates Tested |
|------------------|---------------------------------|----------------------------|
| **Macrolides**   |                                 |                            |
| Erythromycin     | 7                               | 8                          |
| **Aminoglycosides** |                               |                            |
| Gentamicin       | 7                               | 8                          |
| Kanamycin        | 1                               | 1                          |
| **Cephalosporins** |                               |                            |
| Cefazolin        | 5                               | 7                          |
| Cefoxitin        | 1                               | 1                          |
| **Glycopeptides** |                                 |                            |
| Vancomycin       | 9                               | 10                         |
| **Lincosamides** |                                 |                            |
| Clindamycin      | 6                               | 8                          |
| Lincomycin       | 1                               | 1                          |
| **Penicillins**  |                                 |                            |
| Ampicillin-Sulbactam |                           | 3                          | 4                          |
| Oxacillin        | 10                              | 14                         |
| Penicillin       | 6                               | 11                         |
| **Quinolones**   |                                 |                            |
| Ciprofloxacin    | 2                               | 3                          |
| Levofloxacin     | 5                               | 6                          |
| Pefloxacin       | 1                               | 1                          |
| **Rifamycins**   |                                 |                            |
| Rifampin         | 3                               | 3                          |
| **Streptogramins** |                               |                            |
| Pristinamycin    | 1                               | 1                          |
| **Tetracyclines** |                                 |                            |
| Doxycycline      | 2                               | 3                          |