

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

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*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 6-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 and summarize its clinical manifestations, treatment recommendations, and outcomes.

**Keywords.** abscess; HHT; PAVM; *Staphylococcus*.

*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]. *Staphylococcus intermedius* uncommonly may cause human infections ranging from skin and soft tissue infections (SSTIs) to bacteremia [2].

In this study, we aim 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 prediabetes, 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 believed to be related to her underlying HHT (Figure 3). A 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 6-week course.

The patient was re-admitted for vomiting thought to be associated with the antibiotics, specifically the metronidazole. Repeat MRI of the brain, 20 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 (PCR) performed at the University of Washington was positive for *S intermedius* without other identified organisms. Upon further questioning, the patient reported that she was a dog owner. Because no susceptibilities were available given negative culture results, we proceeded with intravenous vancomycin and oral rifampin for 6 weeks based on the available literature.

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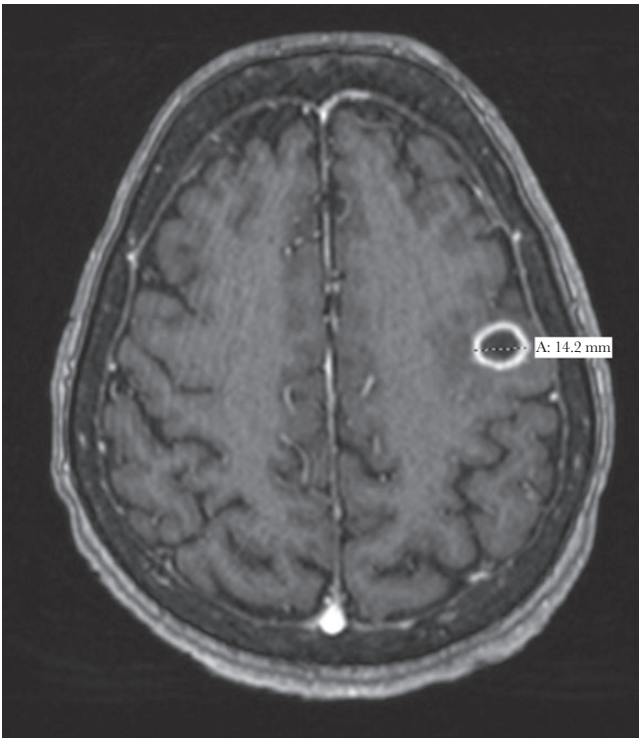
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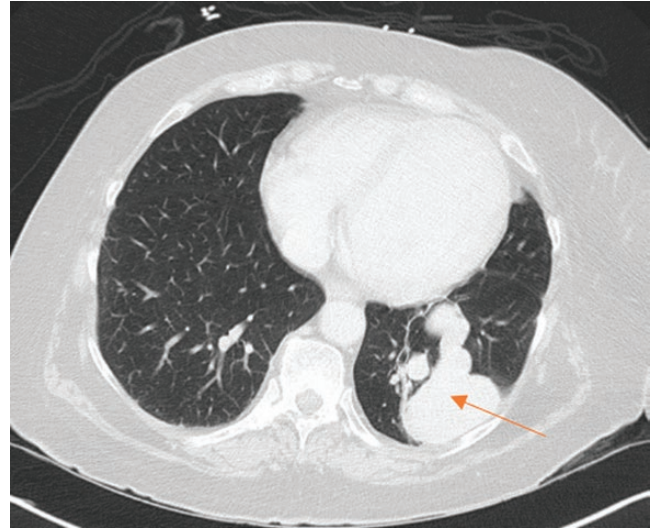
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**Figure 1.** Telangiectasias on tongue as a manifestation of her underlying hereditary hemorrhagic telangiectasia.



**Figure 2.** Magnetic resonance imaging 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 computed tomography showing an enhancing 5.9-cm mass in the left lower lobe that 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.

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 14-mm 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.

#### **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. Before drafting the case report, the medical information was stripped off all 18 Health Insurance Portability and Accountability Act (HIPAA) identifiers. In addition, the re-identification is unlikely because 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.

**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	NR	NR	NR	Dog bite	NR	NR
Lee, 1994	NR	NR	NR	NR	Dog bite	NR	NR
Lee, 1994	NR	Leg Ulcer	NR	Varicose ulcer	Dog owner	NR	NR
Lee, 1994	NR	Leg Ulcer	NR	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 NSC 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	NR	NR	NR	NR
Atalay, 2005	4, M	Brain abscess	Headache, fever, nausea, vomiting, right hemiparesis	None	NR	Vancomycin for 8 weeks	Minimal residual hemiparesis
Kempker, 2009	28, F	Sinusitis	Foul smelling nasal discharge and mild headache	Diabetes insipidus, pituitary adenoma status post transphenoidal resection 8 months prior, CSF leak	Dog owner and licked by dog with recent <i>Staphylococcus intermedius</i> 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 necrotizing fasciitis	Severe chin discharge	1 week postacupuncture	None	Subcutaneous ampicillin; ceftriaxone	Full
Koci, 2015	58, M	Pacemaker lead infection	Fever, chills, headache	Implanted pacemaker	Neighbor's dog licked hand wound	Daptomycin then ceftazolin	Full

**Table 1. Continued**

Author, Year	Age, Sex	Presentation	Infection Site	Risk Factors	Pet Exposure	Treatment	Recovery
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	Foot cellulitis and fever	DM, chronic foot ulcer	Dog owner	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	Beside 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 paresis- thetia

Abbreviations: AVM, arteriovenous malformation; BID, twice daily; CAD, coronary artery disease; CHF, congestive heart failure; CSF, cerebrospinal fluid; DM, diabetes mellitus; HTN, hypertension; IDDM, insulin-dependent diabetes mellitus; IVDA, intravenous drug abuse; NIDDM, noninsulin-dependent diabetes mellitus; NR, not reported; NSC, non-small cell; TID, thrice daily; QID, four times daily.



**Table 2. Reported Antibiotic Susceptibilities**

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

## 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 that included 42 total cases, including this report (Table 1) [2–22].

In terms of demographics, of those with reported data the average age was 46 years ( $\pm 24$ ), 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 SSTIs (25 cases, 69.4%). The remainder were device-associated infections (4 cases, 11.1%) [4–7]; bacteremia (3 cases, 8.3%) [5, 7, 8]; central nervous system ([CNS] 3 cases, 8.3%) (3, 9, this report); sinusitis or mastoiditis (2 cases, 5.6%) [9, 10]; bone or joint infection (2 cases, 5.6% [4, 8]; and pneumonia (1 case, 2.8%) [11]. One case of a pediatric brain abscess caused by *S. intermedius* had been previously reported [12].

Given the presence of *S. intermedius* as part of animal flora, cases were analyzed regarding animal exposure and the majority

of patients reported exposure. Twenty-seven of 33 cases (75.8%) reported exposure to dogs and an additional 2 cases (7.4%) acknowledged exposure to cats.

Twenty-five (59.5%) 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 2 with pacemaker lead infections [6], 1 from a pacemaker site infection [4], and 1 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], 1 patient with chronic foot ulcer, and 1 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 used. 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%) and included uses of amoxicillin-clavulanic acid, penicillin, and ampicillin-sulbactam. Cephalosporins were used in 5 cases (20.0%), including 2 cases each (40.0%) of cefazolin and ceftriaxone, and 1 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 of 10 isolates tested, 90%), and gentamicin and erythromycin each with 7 reports (each with 8 isolates tested, 88%). Rifampin was susceptible in all 3 cases in which testing was performed. Penicillin had the poorest susceptibility (6 cases 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. However, 2 of the 3 CNS cases (9.1%) noted residual neurologic deficits including residual hemiparesis [12] 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 *Staphylococcus aureus* because it produced coagulase, DNases, and had similar growth patterns [23]. *Staphylococcus 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 *Staphylococcus delphini* [15]. The identification of *S. intermedius* serves as a challenge

because it is often misidentified as *S 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* using phenotypic penicillin binding protein 2a (PBP2a) latex agglutination tests [24]. Fortunately, *S intermedius* can be confirmed through additional biochemical tests [1]. For example, in contrast to *S aureus*, *S intermedius* is pyrrolidonyl arylamidase and  $\beta$ -galactosidase positive [3]. Broad-range 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 that may involve atypical pathogens [25]. 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 [25]. There are increased rates of cerebral abscesses in patients with similar right to left shunting including patent foramen ovale and congenital cyanotic cardiopathy [16]. Of note, many patients who present with cerebral abscesses, including our case, were asymptomatic from the PAVM before presentation [26]. Screening methods for pulmonary AVMs include detection of right-to-left shunt by radionuclide perfusion scan or contrast echocardiography. Transcatheter embolotherapy is the current standard treatment for PAVMs [27] 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.

## CONCLUSIONS

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. It is fortunate that 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.

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**Potential conflicts of interest.** All authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

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