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NOVEL ID CASES

A Case of *Burkholderia pseudomallei* Mycotic Aneurysm Linked to Exposure in the Caribbean via Whole-Genome Sequencing

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Melioidosis, an infection caused by *Burkholderia pseudomallei*, has a very high risk of mortality when treated, with an even higher risk of fatality if undiagnosed or not treated appropriately. It is endemic to Asia, Australia, South America, and the Caribbean; however, the number of melioidosis cases reported in the United States has been increasing. Therefore, physicians should be aware of this clinical entity and its possible presentations. Mycotic aneurysms due to *B. pseudomallei* are extremely rare, accounting for ~1%–2% of cases. Here we describe a rare case of melioidosis presenting as a mycotic aneurysm in the United States, highlight the potential for diagnostic challenges and epidemiologic concerns, and provide a review of mycotic aneurysm cases due to *B. pseudomallei* published to date.

Keywords. anneurysm; *Burkholderia*; melioidosis; mycotic; *pseudomallei*

Melioidosis is an infection caused by *Burkholderia pseudomallei*, an aerobic gram-negative rod-shaped bacterium commonly found in surface waters and muddy soils [1]. It is endemic to Asia, Australia, South America, and the Caribbean, with the majority of reported cases from Thailand and northern Australia [2]. Cases outside of endemic regions typically occur in visitors with symptoms arising after departure [3]. Recently, the Centers for Disease Control and Prevention (CDC) described 4 cases of melioidosis in the United States [4]. Whole-genome sequencing revealed these strains to be closely related to those found in South Asia; however, none of these individuals traveled internationally [4]. The source of these infections was ultimately found to be a contaminated aromatherapy spray [5]. As the number of cases reported in the United States has been increasing, clinicians and laboratories need to consider the diagnosis of melioidosis and be aware of its possible presentations. Here, we describe a rare case of melioidosis presenting as a mycotic aneurysm in the United States and highlight the important diagnostic challenges and epidemiological concerns.

CASE

A 58-year-old male with type 2 diabetes mellitus presented to our emergency department on December 21, 2020, with a 3-day duration of acute-onset epigastric and right-sided back pain. He normally resides in Kentucky and works for a large engineering firm specializing in heating, ventilation, and air conditioning (HVAC) systems for commercial buildings. His job entails frequent national and international travel to survey the land for new systems. In August 2020, he traveled to the Dominican Republic for work, where he was frequently exposed to soil. In September 2020, he developed a 1-week duration of fevers, myalgias, and arthralgias, for which he received doxycycline for suspected rickettsial infection. At the end of September, he traveled to Homestead, Florida, where he worked for the next 2 months.

In December 2020, he and his wife traveled across the Southern United States in their recreational vehicle. He had a job in Blythe, California, and there he developed epigastric and right-sided back pain, for which he presented to our emergency department (ED) in Phoenix, Arizona, on December 21, 2020. Blood cultures (BCs) were obtained on admission. A computed tomography (CT) of the abdomen/pelvis with contrast revealed a 2.1-cm penetrating atherosclerotic ulcer of the proximal right iliac artery with marked surrounding inflammatory changes. A mycotic process was considered, and workup was initiated; however, the consensus was that the aortic ulceration was most likely atherosclerotic. He was taken to the operating room (OR) on December 22, 2020, for endovascular repair of the right common iliac artery atherosclerotic ulcer with an endoprosthesis and discharged the following day. BC remained no growth. His serologic workup for infectious etiologies also returned negative.

On December 27, 2020, he developed severe back and lower abdominal pain and presented to an ED in Palo Verde, California, where a CT was performed on December 27, 2020, that did not reveal an endoleak, expansion of the aneurysm, or a ruptured ulcer. However, a repeat CT scan on January 7, 2021, showed an enlarging inflammatory mass around the aortic bifurcation consistent with an abscess and infected stent graft. He returned to the OR on January 11, 2021, for explant of his

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graft and stent, with debridement of the mycotic process, and aortoiliac reconstruction with a rifampin-soaked bifurcated Dacron graft. Intraoperatively, frank caseating purulent material was encountered surrounding the native aorta. Samples were obtained, including a large piece of tissue from the anterior wall of the collection, and sent for culture.

Within 18 hours, aerobic cultures revealed pinpoint growth on sheep blood agar. Gram stain of the growth demonstrated small, gram-negative rods (Figure 1A). Matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry was performed (Bruker Daltonics, Inc.) and provided an unvalidated identification of *Burkholderia thailandensis* on January 16, 2021. Due to concerns for the unvalidated result potentially being suggestive of *B. pseudomallei*, biochemical testing was performed, which demonstrated a negative catalase reaction inconsistent with *Burkholderia* species. However, the isolate was later confirmed as *B. pseudomallei* via polymerase chain reaction specific to *B. pseudomallei* by a public health laboratory. As this is a Select Agent, the clinical laboratories were responsible for destroying all cultures within 7 days of identification or transfer to a certified Select Agent BSL-3 laboratory. The isolate was transferred first to the US Centers for Disease Control and Prevention for susceptibility testing. It was also sent to Northern Arizona University, where susceptibilities were performed using the broth microdilution method as described in the CLSI guidelines with susceptible/resistant breakpoints used from CLSI M45 [6]. The clinical isolate of *B. pseudomallei* demonstrated a typical susceptibility and resistant profile for *B. pseudomallei* with susceptibility to trimethoprim-sulfamethoxazole, doxycycline, amoxicillin/clavulanic acid, and ceftazidime. Growth of *B. pseudomallei* was observed on all culture media including anaerobic, mycobacterial, and fungal cultures, demonstrating classic wrinkled colonies (Figure 1B).

Whole-genome sequencing (WGS) was performed on the isolate. Comparison of the draft WGS with multiple published and several unpublished *B. pseudomallei* genome sequences revealed that this patient's isolate was most closely related to isolates found in the Americas (Figure 2). More specifically, it appeared to cluster with isolates from the Caribbean, sharing the closest identity to an isolate described from a fatal case in Puerto Rico, which was not associated with travel outside of Puerto Rico [7]. Notably, the genome of the infecting strain contained 60 unique genes not present in any other examined *B. pseudomallei* genomes, suggesting a possible adaptation.

The patient was treated with intravenous ceftazidime for an 8-week course for vascular graft infection, followed by life-long oral suppression with oral trimethoprim-sulfamethoxazole. To date, he continues to do well without any further complications.

DISCUSSION

Mycotic aneurysms due to *B. pseudomallei* account for only 1%–2% of cases [8, 9]. To date, 77 cases have been described in the literature, which we have summarized here in Table 1. All cases either lived in, or traveled to, endemic regions. The majority of these were males with underlying medical conditions, such as diabetes or renal disease. Most presented with nonspecific symptoms of fevers and chills (56 out of 77 cases), followed by abdominal and back pain.

B. pseudomallei is a facultative intracellular pathogen capable of survival and replication in phagocytic cells, including macrophages, allowing it to evade clearance from the host [10]. We theorize that our patient was infected with *B. pseudomallei* while in the Dominican Republic, where he was exposed to soil frequently as part of his surveying the land for new HVAC systems. He likely became bacteremic resulting in fever and body aches in September, which was misdiagnosed at the time as rickettsial infection. In the setting of bacteremia, *Burkholderia* likely seeded a site of atherosclerosis. However, the 30-day course of doxycycline he received was enough to suppress his

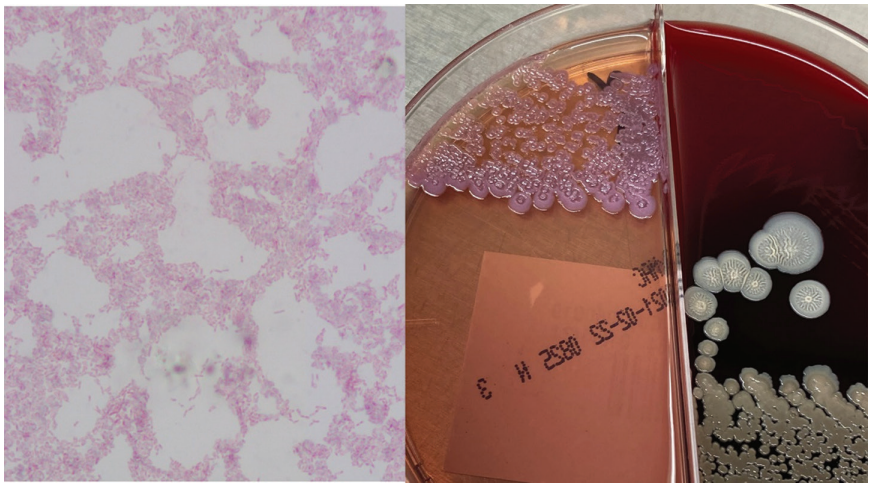

Figure 1. Macroscopic and microscopic morphology of *B. pseudomallei.*

Figure 2. Phylogenetic analysis.

infection, but not fully treat it. Once antibiotics were stopped, *Burkholderia* was able to grow, causing an intense inflammatory response with marked neutrophilic inflammation and giving the appearance of an atherosclerotic ulcer on imaging. Post–surgical intervention, *B. pseudomallei* continued to replicate, developing an abscess on the patient's newly placed aortic graft.

Unfortunately, there were no blood cultures obtained at the time of his initial fevers in September, so there is no way to prove he was bacteremic with *B. pseudomallei*. The authors here also considered the possibility that he may have obtained *B. pseudomallei* while he was in Florida. He did encounter hurricanes during this time when he was wading in water and working in marshy ground. Phylogenetic analysis would also support this as a possibility, as his strain came from the Americas. However, we felt that the more likely explanation was that he acquired *B. pseudomallei* from the Dominican Republic, became symptomatic, and the oral doxycycline suppressed his infection but did not fully treat it. While he travelled extensively throughout the United States and Europe, he had no other travel to melioidosis-endemic areas.

Appropriate specimens for culture are dependent on the clinical presentation. In our case, specimens were obtained from the purulence that was encountered intraoperatively. Growth typically appears quickly; thus routine incubation times for aerobic cultures are sufficient for recovery. The classic wrinkled morphology is not visible before day 3 in culture, leading to difficulties in recognition. Bacterial isolates with morphologic characteristics concerning for *B. pseudomallei* should be referred to public health laboratories if it cannot be ruled out via biochemical testing inside a biosafety cabinet. Although some MALDI-TOF systems either provide or can have spectra added to presumptively identify *B. pseudomallei*, the system used in the case presented would have required full validation of a research use–only spectral database for clinical application under the Clinical Laboratory Improvement

Table 1. Case Reports of *B. pseudomallei* Mycotic Aneurysms

Variable	Case Series of Patients With Mycotic Aneurysms From *B. pseudomallei*			
	Present Review (2021) [16–54] (n = 46)	Wu et al. (2020) [56] (n = 8)	Annunatsiri et al. (2008) [57] (n = 17)	Low et al. (2005) [55] (n = 6)
Age, mean, y	60.7	60.4	61.1	59.7
Male, No. (%)	43 (93.5)	8 (100)	14 (82.3)	6 (100)
Comorbidities, No. (%)				
None	12 (26.1)	1 (12.5)	8 (47.0)	Not reported
Any	30 (65.2)	7 (87.5)	9 (52.9)	6 (100)
Previous melioidosis	6 (13)	Not reported	Not reported	Not reported
Pre/diabetes	15 (32.6)	2 (25)	2 (11.8)	3 (50)
CKD	2 (4.3)	Not reported	4 (23.5)	Not reported
HTN	9 (19.6)	6 (75)	2 (11.8)	2 (33.3)
HLD	2 (4.3)	Not reported	Not reported	1 (16.7)
Atherosclerosis	9 (19.6)	4 (50)	Not reported	1 (16.7)
Location of exposure, No. (%)				
Southeast Asia[a]	31 (67.4)	Not reported	17 (100)	6 (100)
Brazil	1 (2.2)	Not reported	Not reported	Not reported
India	6 (13)	Not reported	Not reported	Not reported
East Asia[b]	4 (8.7)	8 (100)	Not reported	Not reported
Australia	1 (2.2)	Not reported	Not reported	Not reported
Dominican Republic	1 (2.2)	Not reported	Not reported	Not reported
Presenting features,[c] No. (%)				
Fever	35 (76.1)	5 (62.5)	13 (76.5)	3 (50)
Localized pain[d]	23 (50)	8 (100)	17 (100)	6 (100)
Respiratory symptoms	9 (19.6)	4 (50)	6 (35.2)	Not reported
Palpable mass	3 (6.5)	Not reported	15 (88.2)	Not reported
Illness duration, median (range), d	15 (2–180)	60 (30–150)[e]	21 (4–365)	7 (1–21)
Location of aneurysm, No. (%)				
Abdominal aorta	23 (50)	6 (75)	14 (82.3)	5 (83.3)
Thoracic aorta	8 (17.4)	Not reported	1 (5.9)	Not reported
Other[f]	21 (45.6)	2 (12.5)	2 (11.8)	1 (16.7)
Positive cultures, No. (%)				
Blood	27 (58.7)	8 (100)	7 (41.2)	6 (100)
Aneurysm	23 (50)	8 (100)	11 (64.7)	4 (66.7)
Other	14 (30.4)	6 (75)	Not reported	3 (50)
Common inpatient antibiotic therapies, No. (%)				
Ceftazidime	26 (56.5)	4 (50)	Not reported	6 (100)
Meropenem/imipenem	11 (23.9)	5 (62.5)	Not reported	1 (16.7)
TMP-SMX	10 (21.7)	2 (25)	Not reported	2 (33.3)
Other[g]	12 (26.1)	2 (25)	Not reported	2 (33.3)

Table 1. Continued

Variable	Case Series of Patients With Mycotic Aneurysms From *B. pseudomallei*			
	Present Review (2021) [16–54] (n = 46)	Wu et al. (2020) [56] (n = 8)	Annunatsiri et al. (2008) [57] (n = 17)	Low et al. (2005) [55] (n = 6)
Underwent surgery, No. (%)	39 (84.8)	8 (100)	17 (100)	6 (100)
Suppressive antibiotics,[i] No. (%)	30 (65.2)	Not reported	Not reported	6 (100)
Recurrence/aneurysm complications,[h] No. (%)	11 (23.9)	0 (0)	3 (176)	3 (50)
Death, No. (%)	10 (21.7)	2 (25)	4 (23.5)	1 (16.7)

Abbreviations: CKD, chronic kidney disease; HLD, hyperlipidemia; HTN, hypertension; TMP-SMX, trimethoprim-sulfamethoxazole.

[a]Including Thailand, Vietnam, the Philippines, Singapore, Cambodia, Malaysia, and Indonesia.

[b]Including China, Taiwan, and Hong Kong.

[c]Presenting feature at first contact with medical system for mycotic aneurysm. Does not consider symptoms at subsequent encounters for recurrence.

[d]Localized pain, usually at the site of the aneurysm, including headache (intracerebral abscess), chest pain, abdominal pain, back pain, and groin pain.

[e]Durations were reported in months and days in the original document. To ease comparison across case series, we standardized data point month to 30 days and data point year to 365 days.

[f]Including aneurysms of the iliac artery, renal artery, an intracerebral artery in the frontal lobe, subclavian artery, femoral artery, profunda femoris artery, innominate artery, superior mesenteric artery, coronary artery, an intrapulmonary vessel, and splenic artery.

[g]Including doxycycline, amikacin, tetracycline, chloramphenicol, cefoperazone/sulbactam, ciprofloxacin, levofloxacin, and cefixime.

[h]Including perigraft abscess, aorto-enteric fistula, infection of the graft, recurrence of pseudoaneurysm, and, in cases where aneurysm was not resected, aneurysm rupture.

[i]Antibiotics given in the setting of infected graft to suppress infection.

Amendments, and thus was not practical. Additionally, running an isolate on a MALDI-TOF system using routine procedures creates laboratory staff exposures. Ideally, isolates should be referred to public health before manipulation on MALDI-TOF systems, and that was the focus of process improvement in our laboratory as a result of this case. A challenge we encountered was the negative slide catalase reaction intended to rule out *Burkholderia* spp.; however, this was later found to be tube catalase positive by a public health laboratory. This is an unexpected finding, and laboratories should be cautioned to avoid performing slide catalase testing for any suspected select agents due to the potential for aerosol generation if positive, as well as the potential for misleading false-negative results. The patient's isolate also grew in anaerobic, fungal, and mycobacterial cultures, increasing the risk for laboratory staff exposures when growth of this organism was unexpected. This ultimately led to an accidental potential laboratory exposure of 3 employees.

The mainstay of treatment for mycotic aneurysms due to *B. pseudomallei* is surgical resection with repair of the aneurysm [11] followed by antimicrobial therapy. Ceftazidime is the drug of choice for an initial intensive phase, followed by an eradication phase with trimethoprim-sulfamethoxazole (TMP-SMX) for 3–6 months to help prevent recurrence [12]. If surgery requires reconstruction with grafting, it is assumed that the graft will be chronically infected, and thus infection should be suppressed with oral antibiotics for an extended period, often lifelong [11]. In the case presented here, a 2-prong approach to treatment was implemented, first with surgical resection of the mycotic process, followed by an aortoiliac reconstruction with a Dacron graft. Once *B. pseudomallei* was identified, ceftazidime was initiated to complete an initial intensive phase of 8 weeks for vascular graft infection, followed by trimethoprim-sulfamethoxazole to complete an eradication phase of 3–6 months. In the setting of infected graft, the recommendation was made to the patient to remain on trimethoprim-sulfamethoxazole lifelong.

Genomic analysis of this isolate suggests that there are yet uncharacterized reservoirs of *B. pseudomallei* throughout the Caribbean. The case described here is not the first to be associated with the Dominican Republic. In 2011, a 17-year-old native of the Dominican Republic presented in Argentina with a draining nodule, from which samples grew *B. pseudomallei* [13]. With the recent unmasking of endemic regions in Africa, it is evident that there are still many gaps in our knowledge of the global burden of melioidosis [14]. Within the United States, there are likely regions where *B. pseudomallei* resides. There have been at least 2 cases of *B. pseudomallei* thought to be acquired within the United States [15]. Both patients came from the same county in Texas, 1 in 2004 and the other in 2018, both strains related to strains from the Americas [15]. In 1999, a patient from Arizona was also identified; however, where exposure occurred for this

patient is unknown [15]. The isolate from the Arizona patient was closer to the 2 from Texas than to others from Central America, suggesting possible uncharacterized reservoirs in Texas [15].

CONCLUSIONS

Here we describe a rare presentation of *B. pseudomallei* mycotic aneurysm presenting in a nonendemic region likely acquired from traveling. This was successfully treated with surgical debridement in conjunction with ceftazidime followed by lifelong suppression with trimethoprim-sulfamethoxazole for the infected graft. The number of melioidosis cases reported in the United States, especially without travel outside of the Americas, has been increasing. As such, physicians should be aware of this clinical entity and diagnostic challenges when evaluating for possible infectious etiologies of mycotic aneurysms.

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Patient consent. This report does not include factors necessitating patient consent.

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