2014

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Journal of Clinical Microbiology

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J. Clin. Microbiol. **2014, 52(4):1290. DOI: 10.1128/JCM.02755-13.**
Published Ahead of Print 29 January 2014.

JCM Journals.ASM.org

CASE REPORT

De Novo Meningitis Caused by *Propionibacterium acnes* in a Patient with Metastatic Melanoma

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***Propionibacterium acnes* is a known cause of postneurosurgical meningitis; however, it is rarely implicated in *de novo* meningitis. Herein we report a case of a 49-year-old male with *de novo* meningitis caused by *P. acnes* with metastatic melanoma as the only identified risk factor for his infection.**

CASE REPORT

A 49-year-old Caucasian male presented to his primary care physician with an 11-week history of bifrontal headaches associated with nausea and emesis but without other symptoms of meningismus. Symptomatic relief was provided with over-the-counter pain medications and antiemetics. Five weeks prior to arrival at our institution, the patient was admitted to an outside hospital for intractable vomiting and headaches. A computed tomography (CT) scan of the head and abdomen were performed, both of which were normal. Two weeks prior to admission, his headache and nausea worsened with the onset of subjective fevers, low back pain, lethargy, and confusion.

Roughly 2 years prior to admission, the patient was diagnosed with stage IIIC melanoma of the right lower extremity, for which he underwent resection and lymphadenectomy. In the intervening period, he was thought to be in remission. Eight weeks prior to admission, a left-lower-extremity skin biopsy specimen demonstrated a melanocytic nevus.

At the time of admission, his vital signs were as follows: temperature, 36.7°C; blood pressure, 168/92 mm Hg; heart rate, 87 beats per minute; respiratory rate, 20 breaths per minute; oxygen saturation of 98% on room air; height, 188 cm (74 in.); and weight, 142 kg (312.4 lb). The physical exam showed a well-developed male in no acute distress, alert, and oriented to place, year, self, and situation. Notable findings included right-lower-extremity swelling, a healed scar at the site of his prior melanoma, and ecchymosis surrounding a left-lower-extremity biopsy site. He did not have signs of meningismus.

Laboratory findings on admission included a hemoglobin level of 14.1 g/dl, hematocrit of 40.3%, white blood cell count of 10,300/mm^3, mildly elevated absolute neutrophil count of 7,600/mm^3 (range, 1,800 to 6,600/mm^3), normal chemistry panel, an alanine transaminase level of 89 U/liter (range, 7 to 53 U/liter) but otherwise normal hepatic function panel, and a normal urinalysis.

A repeat CT scan of the head was obtained on hospital day 2, 5 weeks after the prior scan, which revealed a communicating hydrocephalus. CT myelography was also performed on day 2, which showed clumping of the nerve roots within the lumbar spine and nodular thickening surrounding L2-L3 nerve roots consistent with arachnoiditis versus metastatic disease.

A fluoroscopically guided lumbar puncture (LP) was performed on hospital day 2, which yielded clear, yellow cerebrospinal fluid (CSF) with a glucose concentration of 26 mg/dl (serum glucose, 96 mg/dl), protein concentration of 518 mg/dl, 145 nucleated cells/μl (1% neutrophils, 32% macrophages, 10% monocytes, 6% lymphocytes, and 51% unclassified cells due to poor cell viability), 576 red blood cells/μl, and an opening pressure of 17 cm H_2O. Few polymorphonuclear leukocytes without organisms were visualized in the Gram stain. Less than 10 colonies of a pleomorphic Gram-positive bacillus that was catalase positive and spot indole positive grew on the anaerobic prereduced brucella blood agar plate (Anaerobe Systems, Morgan Hill, CA) after 3 days of incubation in an anaerobic environment. *Propionibacterium acnes* identification was confirmed by matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF MS) using the Bruker Biotyper (Bruker-Daltonics, Billerica, MA) as previously described (1). Biotyper scores of 2.115 and 1.829 (excellent identification to the species level according to internal validation data) were obtained with and without a formic acid overlay, respectively, for an identification of *P. acnes*. Vitek MS analysis was performed according to the manufacturer's specifications and identified the isolate as *P. acnes* with a confidence value of 99.9%. There is no antimicrobial susceptibility profile for this isolate, as susceptibility testing for anaerobic bacteria is not routinely performed in our laboratory. Culture from the initial LP grew *Propionibacterium* species on hospital day 5. Out of concern for contamination, a repeat LP was performed prior to the initiation of vancomycin (1.5 g every 8 h). Cytology showed atypical cells, but flow cytometry was unable to be performed due to low cellular viability.

The patient had gradual improvement in headache, lethargy, and mentation over the ensuing days. Cultures from the repeat LP on day 5 as well as on day 9 grew *P. acnes*. On these subsequent lumbar punctures, the glucose concentration remained low and

Received 2 October 2013 **Returned for modification** 15 December 2013
Accepted 25 January 2014
Published ahead of print 29 January 2014
Editor: B. A. Forbes
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doi:10.1128/JCM.02755-13

the protein concentration remained elevated, while the nucleated cell count rose on day 5 but had decreased significantly by day 9. The Gram stains performed on these specimens demonstrated the presence of polymorphonuclear leukocytes but no organisms.

On hospital day 10, the patient developed altered mental status and acute renal failure. The mental status changes were presumed to be secondary to persistent hydrocephalus seen on repeat CT scan, so an extraventricular drain (EVD) was placed. Moreover, repeat LP on day 9 had demonstrated decreased pleocytosis, and his vancomycin levels were therapeutic, suggesting that his altered mental status was not due to worsening infection. Due to his renal failure, his vancomycin was changed to ceftriaxone dosed 2 g intravenously every 12 h. Subsequent cerebrospinal fluid (CSF) cultures from the EVD failed to grow *P. acnes*.

Pathological examination and flow cytometry of the CSF on days 9 and 12 revealed metastatic melanoma. Repeat CT myelography on hospital day 14 revealed obstruction of CSF flow from T10-L3, consistent with leptomeningeal carcinomatosis. Emergent radiotherapy was performed; however, the patient had worsening mentation and lower-extremity paraplegia and ultimately entered hospice care.

Discussion. We present a rare case of *de novo* meningitis caused by *P. acnes* with leptomeningeal carcinomatosis as a possible underlying risk factor. The patient presented herein did not have any prior neurosurgery.

P. acnes is an aerotolerant anaerobic, non-spore-forming, pleomorphic Gram-positive bacillus that is part of the normal flora of the conjunctiva, external ear canal, skin, mouth, and upper respiratory tract (2). Historically thought of as a common contaminant of blood cultures, numerous reports have implicated *P. acnes* as causing wide-ranging human disease, including endocarditis, endophthalmitis, osteomyelitis, prosthetic joint infections, and postoperative central nervous system infection (PCNSI) (2–6).

P. acnes, classically considered to be a low-virulence organism, has been implicated in a number of PCNSIs, including bone-flap-associated infection, ventriculoperitoneal shunt infection, Ommaya reservoir infection, nosocomial meningitis after craniotomy, and subdural, extradural, and cerebral abscesses (7–12). Without a prior neurosurgical procedure, meningitis due to *P. acnes* is exceedingly rare, with only eight prior case reports identified in the English language literature. However, methods classically used for bacterial cultures of CSF in nonneurosurgery patients would not usually be adequate for the recovery of this organism, so its true prevalence in central nervous system (CNS) disease may be underappreciated.

The eight previously reported cases of *de novo* meningitis caused by *P. acnes* have generally been in younger individuals (median age, 28 years; range, 4 to 72 years), including five males and three females. No significant comorbidities were described in these case reports, and their clinical characteristics are summarized in Table 1 (13–18). The duration of symptoms prior to presentation is nearly equally split between acute presentations (<7 days) and a more subacute process (averaging about 14 weeks). Seven of eight patients presented with the classic signs and symptoms of meningitis (headache, fever, or stiff neck), although one case was in an older man who exhibited confusion as his sole

TABLE 1 Clinical characteristics of the present and previous cases of meningitis caused by *P. acnes*

Case	Reference	Age (yr)	Sex	Comorbidity	Duration of symptoms	Sign(s) or symptom(s) of meningitis	Potential risk factor	Antimicrobials	Duration	Outcome
1	17	11	Female	None	Acute onset	Fever, vomiting, nuchal rigidity	None	Penicillin G	25 days	Recovered
2	16	16	Female	None	Acute onset	Fever, headache, photophobia, nuchal rigidity	None	Penicillin, chloramphenicol, sulfadiazine	3 days	Recovered
3	18	38	Male	None	5 mo	Headache, papilledema	None	Penicillin	6 wk	Recovered
4	18	33	Female	None	Acute onset	Headache, nuchal rigidity	None	Penicillin	6 wk	Recovered
5	18	28	Male	None	2 mo	Headache, altered consciousness, photophobia	None	None		Recovered
6	15	25	Male	None	Acute onset	Headache, photophobia, nuchal rigidity	None	Penicillin G every 6 h then chloramphenicol	63 days	Recovered
7	14	72	Male	CVA[a]	4 mo	Altered consciousness	Chronic lymphocytic leukemia, advanced age	Penicillin G at 2 million units every 4 h	17 days	Residual neurological deficit
8	13	4	Female	Tuberculosis of the foot	Acute onset	Fever, vomiting, nuchal rigidity	None	Chloramphenicol	14 days	Recovered
Present	This report	49	Male	Melanoma	11 wk	Headache, altered consciousness	Melanoma	Vancomycin, ceftriaxone	14 days	Recovered

[a] CVA, cerebrovascular accident.

presenting symptom. This case was complicated by a lack of CSF pleocytosis, which resulted in a delayed diagnosis. In more typical cases, the CSF profile has been consistent with aseptic meningitis with a mononuclear pleocytosis (Table 2).

In reported cases, treatment of meningitis caused by *P. acnes* with penicillin G, chloramphenicol, or vancomycin has resulted in favorable outcomes. Only one patient had residual neurological deficits after finishing treatment. The patient in the case presented herein responded well to treatment with vancomycin, which was switched to ceftriaxone due to toxicities. Although his mentation improved transiently, his CSF cultures became sterile with improvement in his CSF profile.

Since meningitis caused by *P. acnes* typically presents postsurgically, there may be differences in the clinical presentation related to *de novo* meningitis caused by *P. acnes*. Additionally, the type of surgery may also alter the clinical presentation. In a study looking at postsurgical meningitis, overall 79% of cases had fever and 31% had neurologic symptoms, although only 15% of the cases were caused by *P. acnes* (19). A study of ventricular shunt infections in which 9% of cases were caused by *P. acnes* found that overall 36% of patients presented without neurologic signs or symptoms and 78% had fever (7). Unfortunately, these studies do not delineate clinical characteristics of specific postsurgical pathogens; therefore, direct comparison is somewhat limited. *De novo* meningitis caused by *P. acnes* has universally presented with neurological symptoms, but fever remains variable. All 6 adults plus our case lacked fever, while all 3 pediatric cases described fever.

Reasons for the development of *P. acnes*-caused meningitis are unclear, since only two cases have an identifiable risk factor, namely, chronic lymphocytic leukemia and melanoma. Feng and others have hypothesized that matrix metalloproteinases secreted by leukemic cells may facilitate the breakdown of the blood-brain barrier (BBB), which may lead to seeding of the CSF during transient bacteremia (20). Additionally, melanoma is known to disrupt the BBB, and in our patient, disruption of the BBB by metastatic melanoma might have facilitated *P. acnes* to enter the CSF; however, it is unclear why *P. acnes* and not another organism might cause disease in this setting (21, 22). While many scenarios could be hypothesized, one possible explanation is that the patient had a transient *P. acnes* bacteremia after his lower-extremity biopsy 8 weeks prior to admission that resulted in seeding of the CSF. Invasive procedures (e.g., transarterial embolization, radiofrequency ablation, bronchoscopy, cystoscopy, or pericardiocentesis) have been associated with *P. acnes* bacteremia (4). While these types of procedures are more invasive than a skin biopsy, the data may provide a theoretical basis for a transient bacteremia with resultant seeding of the CSF.

P. acnes can be difficult to isolate in the clinical microbiology laboratory due to its preference for anaerobic conditions and low rate of growth. Few laboratories routinely include anaerobic media or culture conditions as part of the workup for CSF specimens in light of the fact that anaerobes are not the organisms classically associated with acute bacterial meningitis. Our patient's *P. acnes* isolate was initially cultured anaerobically on brucella blood agar, and its identification was later confirmed using two matrix-assisted laser desorption ionization–time of flight (MALDI-TOF) mass spectrometry (MS) platforms, the Bruker Biotyper (software version 3.0; Bruker Daltonics, Billerica, MA) and Vitek MS (database version 2.0; bioMérieux) (23, 24). Although details of culture methods are not described in all previous case reports, broth me-

TABLE 2 Laboratory characteristics of meningitis caused by *P. acnes*

					CSF						
Case	Reference	Peripheral leukocytes	Neutrophils (%)	Lymphocytes (%)	Gram stain	WBCs/µl[a]	Differential	RBCs/µl[b]	Glucose concn (mg/dl)	Protein concn (mg/dl)	No. of cultures yielding *P. acnes*
1	17	15,000	86	7	Positive	3,400	Virtually all granulocytes		75	49	2
2	16	13,350	65	28	Negative		Loaded with clumps of neutrophils		20	42	1
3	18	6,800	56	28	Negative	345	90% mononuclear		30	230	3
4	18				Negative	440			37	127	1
5	18				Negative	180			60	134	1
6	15	12,600	86	9	Positive	90	97% mononuclear cells, 3% neutrophils		84	99	6
7	14	23,700	10	90	Negative	2		164	70	64	3
8	13	16,800	90		Negative	750	95% neutrophils		29	108	1
Present	This report	10,300	73		Negative	145	1% neutrophils, 32% macrophages, 10% monocytes, 6% lymphocytes, and 51% unclassified cells	576	26	518	3

[a] WBCs, white blood cells.
[b] RBCs, red blood cells.

dium, such as thioglycolate or Robertson's chopped meat broth, and cysteine Trypticase semisolid agar were used to isolate *P. acnes* from CSF specimens (25). A limitation of a broth-based culture technique is the inability to quantify the number of organisms present in the culture. Cases such as the one described herein call into question if, in the postvaccine era, culture methods for CSF specimens should routinely include medium for cultivation of anaerobic organisms such as *Propionibacterium* spp. Additional microbiological studies are needed to assess whether anaerobic CSF cultures are indicated routinely for patients with possible meningitis.

Conclusion. Our case adds to the small body of literature regarding *de novo* meningitis caused by *P. acnes* and highlights the importance of anaerobic CSF cultures. In disease states that may lead to disruption of the blood-brain barrier, clinicians should be aware of the potential for *P. acnes* to cause clinically significant disease in patients that have not had a previous neurosurgical procedure or an indwelling device.

ACKNOWLEDGMENTS

B.S.T. is supported by Washington University Institute of Clinical and Translational Sciences grant UL1 TR000448 from the National Center for Advancing Translational Sciences.

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

We thank the Barnes-Jewish Hospital Clinical Microbiology Laboratory for assistance with this case.

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