

Brain abscess induced by *Propionibacterium acnes* in a patient with severe chronic sinusitis

Lorenzo Zaffiri, Rasha Abdulmassih, Shafik Boyaji, Imad Bagh,
Amanda R. Campbell, Mark E. Loehrke

Department of Internal Medicine, Western Michigan University Kalamazoo Center for Medical Studies,
Oakland Drive, Kalamazoo, Michigan

SUMMARY

Propionibacterium acnes has long been considered a contaminant organism. However, recently the isolation of this emerging pathogen has become a more difficult clinical challenge. Infections of the central nervous system caused by *P. acnes* have been strongly associated with neurosurgical procedures. We describe a patient with *Propionibacterium acnes* cerebral abscess developed as consequence of a severe chronic sinus disease.

KEY WORDS: *Propionibacterium acnes*, Brain abscess, Chronic sinusitis.

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INTRODUCTION

Propionibacterium acnes (*P. acnes*) is an anaerobic Gram positive bacilli mostly present in human skin and hair follicles. It is involved in the pathogenesis of *acnes vulgaris* and has often been considered a common contaminant of blood and fluid cultures. However, recently several case reports have shown that *P. acnes* can be the causative agent of infections following arthroplasty, cerebrospinal shunts and spinal instrumentations (Brook *et al.*, 1991). We describe a rare case of *P. acnes* brain abscess in a 79-year-old man with chronic sinusitis without prior neurosurgical intervention. In conclusion, *P. acnes* should be considered an emergent pathogen in central nervous system infections.

CASE REPORT

A 79-year-old Caucasian male presented with altered mental status and fever. During the pre-

ceding four weeks, the patient had complained of a persistent headache affecting mostly the right frontal and temporal regions. Despite lack of fever, change in vision or leukocytosis, the presence of elevated sedimentation rate and his clinical findings were worrisome for giant cell arteritis (GCA). He was therefore empirically started on prednisone 40 mg PO daily for two weeks. However, a temporal artery biopsy was found to be negative and prednisone was discontinued a few days before the hospitalization.

His medical history was significant for type 2 diabetes mellitus, hypertension and chronic kidney disease. On examination, the patient was afebrile and hemodynamically stable. He appeared confused, somnolent but easy to arouse. He was disoriented in time, place and with impairment of short memory. Head was normocephalic and atraumatic. Pupils were equal, round and reactive to light and accommodation. There was no papilledema and extraocular muscles were intact. The remaining cranial nerves were intact. There was neither meningism nor gross focal deficit with preserved strength and sensation bilaterally. Nasal examination shows a severe septal deviation anteriorly with complete obstruction of the anterior right nasal cavity. The patient had very poor mandibular dentition with thick mucoid postnasal drainage. Hematological investi-

Corresponding author

Lorenzo Zaffiri, M.D., Ph.D.

Department of Internal Medicine, MSU/KCMS

1000 Oakland Drive, Kalamazoo, Michigan 49008

E-mail: lorenzozaffiri@gmail.com

lzaffi@kcms.msu.edu

gations revealed a hemoglobin level of 11.6 g/dl and a white cell count of 12.3×10^9 /liter. Creatinine was 2.2 mg/dl, hemoglobin A1C was 8%. In view of the history and clinical presentation, blood sputum and urine cultures were taken. The patient was initially treated with ceftriaxone and vancomycin intravenously for possible bacterial meningitis. Computed tomography (CT) scan without contrast of paranasal tissue and head demonstrated pansinus disease with subtotal opacification of paranasal sinuses with areas of cortical defect involving the posterior wall of right frontal sinus (Figure 1 a-c). Cerebrospinal fluid (CSF) studies demonstrated white cell count 115/mcl with 92% neutrophils, glucose 65 mg/dl and protein 138 mg/dl. Bacterial, mycobacterial and fungal stain and culture were then negative. Initial sinus culture grew normal flora in spite of a gram stain with few Gram-positive bacilli. The antimicrobial regimen was subsequently modified to vancomycin, piperacillin/tazobactam and anidulafungin in order to cover most common pathogens for sinus infection in patients with uncontrolled diabetes mellitus. Brain magnetic resonance imaging (MRI) confirmed a complicated sinusitis with direct intracranial extension, cerebritis and diffuse leptomeningitis (Figure 2 d-f). The patient underwent bilateral endoscopic sinus surgery including: ethmoidectomies, frontal sinusotomies with balloon sinuplasty, maxillary antrostomies bilaterally and septoplasty. A conspicuous amount of mucopurulent secretions were aspirated from the sinuses especially from the right frontal sinus and maxillary sinus bilaterally.

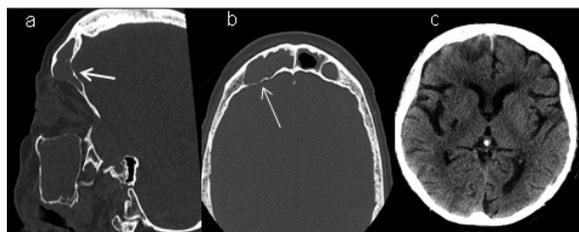


FIGURE 1 - CT scan of paranasal tissue and head on admission. CT of paranasal tissue disclosed pansinus disease with subtotal opacification of the frontal sinus and thinning of the posterior wall of the right frontal sinus with permeative-type appearance (a, b). Head CT demonstrated an abnormal low density in the anterior right frontal lobe involving the anterior pole extending to the right frontal cortex (c).

Samples were sent for Gram stain, bacterial, mycobacterial and fungal culture. *Propionibacterium acnes* grew from right frontal and right maxillary sinus cultures. Treatment was therefore de-escalated to vancomycin and meropenem.

The patient showed clinical and laboratory signs of improvement. He was discharged to a nursing skill facility to continue a physical rehabilitation program along with intravenous antimicrobial treatment for six weeks. Given the relevant clinical progress and the lack of imaging findings consistent with a brain abscess, a follow-up brain MRI was scheduled at end of four weeks of antibiotic treatment. Following 24 days of continuous intravenous antibiotic treatment, he developed an abrupt change in mental status characterized by confusion and dysphasia associated with fever and leukocytosis. He was confused, disoriented and unable to follow commands. Due to lack of collaboration his neurologic examination was only partially completed. Cranial nerves appeared to be intact. Pupils were equal, round and reactive to light and accommodation and extraocular muscles were intact.

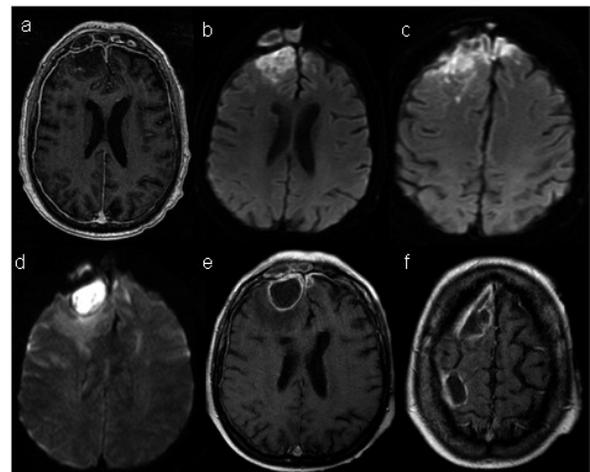


FIGURE 2 - Brain MRI images at admission (a-c, upper row) and 30 days later (d-f, lower row). Diffusion brain MRI images at admission (a-c) confirmed cerebritis involving right and left frontal parenchyma with most pronounced involvement of the anterior right frontal lobe associated with diffuse leptomeningeal and pachymeningeal enhancement as for meningitis. Follow-up brain MRI demonstrated the formation of right frontal lobe abscess formation measuring 2.9x3.0x3.9 cm (d). This collection extended extra-axially over the right superior frontal convexity and was associated with increased adjacent parenchymal signal abnormality (e,f).

However, he demonstrated weakness of the left upper and lower extremities but conserved deep tendon reflex. His brain MRI revealed a 2.9x3.0x3.9 cm abscess in the right superior frontal convexity with increased adjacent parenchymal signal abnormality and persistence of severe paranasal sinus disease (Figure 2). Despite an attempt at stereotactic burr hole evacuation of the right frontal abscess and change in antibiotic regimen to linezolid and levofloxacin, the patient's clinical condition continued to deteriorate requiring prolonged mechanical ventilation. His laboratory tests showed progressive leukocytosis and worsening renal failure. Following discussion with the family due to the lack of clinical improvement, requirement of respiratory support and possible renal replacement therapy, patient was made comfortable and died on day 20 of hospitalization.

DISCUSSION

Propionibacterium acnes is a Gram positive, anaerobic bacillus that is part of the normal human skin flora and involved in the development of *acnes vulgaris*. Although it has been considered a common contaminant with low clinical relevance, it has recently been associated with frequent clinically significant infections in the setting of neurosurgical procedures (Brook *et al.*, 1991). In particular, several reports described indolent CNS infections caused by *P. acnes* following craniotomy and cerebrospinal shunt placement even several years after surgery (Richards *et al.*, 1989; Hall *et al.*, 1994). Biofilm production and high concentrations of *P. acnes* in sebaceous glands of the scalp and forehead play an important role in the development of infections following cerebrospinal fluid shunts and craniotomy (Brook *et al.*, 1991; Jakab *et al.*, 1996; Bayston *et al.*, 2007). However, we found few reports of CNS infection in adults without previous surgical procedures (Ramos *et al.*, 1995; Schlossberg *et al.*, 1980).

Characteristically, *P. acnes* presents as a delayed and indolent infection. Our patient presented with typical stigmata of a subacute infection. He had suffered from persistent headache for four weeks affecting mostly the right frontal region. Interestingly, his clinical findings and laboratory

evaluation were initially worrisome for possible giant cell arteritis (GCA). GCA or temporal arteritis is a chronic vasculitis affecting medium and large vessels that occurs in individuals older than 50 years of age. It is characterized by persistent headache, tenderness to palpation of the temporal artery and elevated ESR (Smetana GW, *et al.*, 2002). These symptoms were also present in our patient before his hospitalization. Due to the high incidence of vascular complications in patients with GCA, treatment with prednisone was prophylactically started before temporal artery biopsy. However, his clinical condition eventually worsened developing altered mental status and requiring hospitalization.

CSF studies were consistent with a picture of aseptic meningitis with pleiocytosis, normal glucose and elevated protein. His CT scan and brain MRI images clearly demonstrated extensive sinus disease, a right frontal sinus defect, representing the port of entry for the infection, as well as cerebritis. These culprit findings guided our antimicrobial regimen in consideration of the most common pathogens in patients with sinus disease and uncontrolled diabetes. Although *Aspergillus* spp. and *Pseudomonas aeruginosa* are the most common pathogens isolated in neutropenic patients (Decker CF, 1999), it has been shown that in patient with diabetes mellitus the most common isolates are represented by *S. aureus*, streptococci, gram-negative enteric bacteria and fungi (Jackson *et al.*, 1987). Despite the lack of the typical clinical findings of disseminated rhino-orbital- cerebral infection such as nasal ulceration, facial swelling or ophthalmoplegia, treatment for mucormycosis was also considered. However, the fungal stain and culture were subsequently negative. *P. acnes* was the only pathogen isolated from sinus culture obtained during sinus surgery. The failure to isolate any pathogen from the brain abscess cultures is most likely due to the prolonged and broad antibacterial treatment the patient underwent before the surgical intervention.

Interestingly, *P. acnes* is also considered an important pathogen in the development of acute and chronic sinusitis (Brook, 2006). It has been hypothesized that chronic inflammation and lack of sinus drainage may induce a low oxygen tension environment supporting colonization and growth of anaerobic organisms (Niederfuhr *et al.*,

2009). In our opinion the presence of chronic sinusitis could represent one of the predisposing conditions for the development of CNS infection in our patient. However, the history of uncontrolled diabetes mellitus and recent treatment with prednisone could have allowed the growth of this pathogen (Ramos *et al.*, 1995). Several reports have suggested that an acquired immune defect could increase the risk of intracranial infection with *P. acnes* (Barazi *et al.*, 2003, Lyons *et al.*, 2012).

Microbiological identification of *P. acnes* is complicated because it grows slowly and is a difficult pathogen to isolate correctly. It is therefore recommended to prolong the incubation time for longer than the usual five days (Richards *et al.*, 1989). The management of *P. acnes* CNS infections includes a combination of surgical procedures and prolonged intravenous antibiotics. Several reports highlight the need for extensive curettage and removal of infected bone and prosthetic devices (Brook *et al.*, 1991; Brook 2009; Jakab, 1996).

The antibiotic regimen should be chosen on the basis of *in vitro* activity and blood-brain barrier penetration (Mory *et al.*, 2005). Although several antibiotics such as vancomycin, linezolid and fluoroquinolones are active *in vitro* against *P. acnes*, failure of treatment in the course of multiple brain abscesses has been described (Senneville *et al.*, 1997). Mory *et al.* demonstrated that *P. acnes* strains isolated from CNS sources were susceptible to vancomycin, ceftriaxone and penicillins. However, an optimal treatment is not yet clear. A minimum of three weeks of intravenous antibiotics followed by six weeks of oral antibiotics has been proposed as a regimen to increase the eradication. Although our patient received more than three weeks of intravenous antibiotic regimen with demonstrated efficacy, the delay in a more aggressive surgical debridement could have affected the outcome. Once a diagnosis of brain abscess is made, then a combination of surgical drainage and prolonged antimicrobial therapy is mandatory (Arlotti *et al.*, 2010). Moreover, serial MRI or CT should be obtained to document resolution of the abscess. It is suggested brain imaging be repeated twice a month or in case of clinical deterioration to allow rapid intervention with aggressive surgical procedures (*Mampalam* combination of surgical drainage

and prolonged antimicrobial therapy is mandatory (Arlotti *et al.*, 1988).

In conclusion, this case underscores the emergent role of *P. acnes* as an important pathogen for CNS infection. Chronic sinusitis should be considered an additional risk factor for the development of *P. acnes* infection, especially when associated with other clinical conditions that can cause an impaired immune response.

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