ORIGINAL ARTICLE

Propionibacterium Acnes Infections After Cranial Neurosurgery

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ABSTRACT: ***Background:*** *Propionibacterium acnes (P. acnes)* is a relatively avirulent organism that is part of the normal skin flora. Most patient isolates are considered contaminants but, in a small subset of patients, particularly in the post-neurosurgery setting, the organism can cause significant infections. We reviewed our experience with the occurrence and management of *P. acnes* infections after cranial neurosurgical procedures over a five-year period. ***Methods:*** Patients with positive cultures for *P. acnes* between 1996 and 2001 were identified by review of the Saskatoon Health Region microbiology laboratory database. Of the 141 positive cultures, a review of hospital records identified six patients with *P. acnes* infections after neurosurgical procedures. A review of the literature related to *P. acnes* associated CNS infections was conducted. ***Results:*** All patients had undergone a craniotomy or burrhole placement, and one patient had received prior radiotherapy. There were no *P. acnes*-related ventriculoperitoneal shunt infections. All patients presented with scalp swelling and three had purulent discharge. Symptoms occurred more than two months after the initial surgery in five of six patients, while one patient developed symptoms three years post-operatively. Management for all patients included removal of the craniotomy flap and treatment with parenteral antibiotics, followed in most cases by oral antibiotics. A good response without relapse of infection was seen in five patients; one patient had recurrent infection after cranioplasty. ***Conclusions:*** *P. acnes* is a rare but important cause of infection after craniotomy. Wound debridement, removal of the bone flap and adequate antibiotic coverage result in cure in the majority of patients.

RÉSUMÉ: Infection à Corynebacterium acnes après une neurochirurgie crânienne. ***Contexte :*** Le Corynebacterium acnes est un organisme relativement avirulent qui fait partie de la flore cutanée normale. On considère que la plupart des isolats de patients sont des contaminants. Cependant chez un petit sous-groupe de patients, particulièrement après une neurochirurgie, ce microorganisme peut causer des infections importantes. Nous revoyons notre expérience sur une période de 5 ans de l'infection à C. acnes et de son traitement après une neurochirurgie crânienne. ***Méthodes :*** Nous avons identifié les patients dont la culture démontrait la présence de C. acnes entre 1996 et 2001 au moyen d'une revue de la base de données du laboratoire de microbiologie de la région sanitaire de Saskatoon. 141 cultures positives ont été identifiées, dont six provenaient de patients ayant subi une neurochirurgie. Nous avons effectué une revue de la littérature sur les infections à C. acnes du SNC. ***Résultats :*** Tous les patients avaient subi une craniotomie ou un trou de trépan et un patient avait reçu de la radiothérapie avant l'intervention. Il n'y avait pas de cas relié à une dérivation ventriculo-péritonéale. Les patients ont tous présenté un gonflement du cuir chevelu et trois présentaient un écoulement purulent. Les symptômes sont survenus plus de 2 mois après la chirurgie chez cinq des six patients alors que chez l'autre ils sont survenus trois ans plus tard. Tous les patients ont reçu le même traitement, soit l'ablation du volet osseux avec antibiothérapie par voie parentérale suivie, dans la plupart des cas, d'antibiothérapie par voie orale. Cinq patients ont bien répondu au traitement, sans récidive. Un patient a eu une récidive après une cranioplastie. ***Conclusions :*** Le C. acnes est une cause d'infection rare mais importante après la craniotomie. Le débridement et l'ablation du volet osseux ainsi qu'une antibiothérapie adéquate assurent la guérison chez la majorité des patients.

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Propionibacterium acnes (P. acnes) is an anaerobic gram-positive bacillus found as a normal component of the bacterial flora of the skin, hair follicles and sebaceous glands. Although the majority of patient isolates are thought to be contaminants, *Propionibacterium acnes* does cause significant disease in a small subset of patients after neurosurgical procedures.[1] Ventriculoperitoneal shunt infections are the most commonly reported type of *P. acnes* infection in the neurosurgical literature.[2,3] However, several reports describe *P. acnes* infections after craniotomy[4-8] and it has been suggested that central nervous system infections caused by *P. acnes* are more important than previously recognized. We report on our single center experience and present one of the largest series of post-craniotomy *P. acnes* infections; we also reviewed the relevant literature.

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METHODS

A search of the Saskatoon Health Region Laboratory Information System identified 141 cultures positive for *P. acnes* at our institution over five years (June 1, 1996 to May 31, 2001). Review of the hospital records revealed 13 patients with positive *P. acnes* cultures after neurosurgical interventions. Patient data including age and gender, procedure performed, type of surgical skin preparation, laboratory data including culture results, infection-related symptoms, medical and surgical management, and clinical outcome were collected. Positive cultures were classified as contaminants if the patient had no clinical symptoms. Based on a medical chart review, six patients were determined to have had definite clinical *P. acnes* infections.

For the literature review, an English-language Medline search was conducted using the key words "propionibacterium", "acnes" and "neurosurgery". Additional references were identified from citations in the papers found in the search.

RESULTS

Patient and treatment data are summarized in Table 1. There were four male and two female patients with a mean age of 48.5 (range, 11-67) years. Surgical procedures preceding the infection included placement of burrholes for a chronic subdural hematoma in one case, and craniotomy in the other five patients. Two patients had craniotomies for management of ruptured intracranial aneurysms, one for an acute subdural hematoma, one for decompression of bilateral optic nerve meningiomas, and one for a brain metastasis. The latter patient had received whole brain radiation therapy (50 Gray) one month prior to the onset of symptoms.

An iodine based skin preparation had been used prior to all of the surgical procedures, and all patients had received prophylactic intravenous cefazolin intra-operatively and for the first 24 hours post-operatively.

The mean time to symptom onset in five patients was 8.4 (range 4-14) weeks postoperatively. Patient 6 who had been treated for optic nerve meningiomas was unique in that symptoms did not develop until 192 weeks after surgery.

All six patients underwent repeat surgery after they presented with symptoms suggestive of infection. The five patients with prior craniotomies had removal of the infected bone flap. The patient with initial burrhole placement (Case 3) underwent craniotomy at the time of repeat surgery to facilitate drainage of a subdural empyema. Cultures were obtained from the surgical site in all patients. In five cases, *P. acnes* was isolated from both fluid and solid culture media incubated under anaerobic conditions. In one patient, (Case 4) *P. acnes* was isolated only

Table 1: Clinical characteristics of six patients with P. acnes infections after cranial neurosurgical procedures

Case no.	Age	Sex	Underlying Disease	Initial Surgical Procedure	Onset of Symptoms (weeks)	Antibiotic treatment	Surgical treatment	Reconstruction
1	62	F	Brain metastasis (lung cancer)	Craniotomy	8	Vancomycin IV x 6 wks	Removal bone flap	Cranioplasty at 6 mos
2	45	F	Aneurysm	Craniotomy	8	Ciprofloxacin po, metronidazole po, vancomycin IV x 6 wks	Removal bone flap	Cranioplasty at 6 mos
3	55	M	Chronic subdural hematoma	Burrholes	8	Cefazolin IV x 5 wks	Craniectomy and evacuation of subdural empyema	Cranioplasty at 5 mos
4	51	M	Acute subdural hematoma	Craniotomy	4	Cefazolin IV X 1 wk, then cephalexin po x 8 wks	Removal bone flap	Cranioplasty at 7 mos
5	67	M	Aneurysm	Craniotomy	14	Clindamycin po x 3 wks	Removal bone flap	Cranioplasty at 6 mos
6	11	M	Bilateral optic nerve meningioma	Craniotomy (bilateral)	192	1) Piperacillin/tazobactam IV x 2 weeks then ceftriaxone IV x 8 wks 2) Ceftriaxone IV x 4 weeks 3) Piperacillin/ tazobactam IV x 8 wks	Removal bone flap, 2 failed cranioplasties	3 recurrent infections, no final cranioplasty

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from fluid media; this patient was included in the series because he clearly had infection-related symptoms.

Following surgical drainage and adjunctive antibiotic therapy, five of the six patients had complete resolution of infection and underwent cranioplasty six months later without further incident. A number of different antibiotic regimens were used for these patients (Table 1). Two patients, one of whom also received concurrent oral ciprofloxacin and metronidazole, were treated with intravenous vancomycin for six weeks. Two patients received intravenous cefazolin, although one patient was stepped down to oral cephalexin after one week. One patient was treated with a three week course of oral clindamycin. The patient with relapsing infection (Case 6) had two attempts at cranioplasty; *P. acnes* infection recurred each time, necessitating removal of the cranioplasty material and multiple courses of parenteral antibiotics: piperacillin-tazobactam (two weeks) followed by ceftriaxone (eight weeks) for the first episode, a four week course of ceftriaxone for the second, and a final eight week course of piperacillin-tazobactam.

Discussion

This study accounts for 6 of 25 patients (in 9 studies including our own) published in the literature.[4-6, 8-12] To our knowledge, it is the largest published series on this topic. Our study summarizes the early management plans and outlines our recommendations based on these findings. This study is also unique because there were no cases of ventriculoperitoneal shunt infections.

Propionibacterium species are non-spore forming anaerobic gram positive bacilli. *Propionibacterium acnes*, the species most commonly isolated from human specimens, is part of the normal bacterial flora of the skin, conjunctivae and oropharynx. In the majority of cases, *P. acnes* strains isolated from humans represent clinically insignificant contaminants. In a comprehensive review of *Propionibacterium* species recovered over 10 years at the National Naval Medical Center, 94 of 816 (12%) isolates were determined to have caused infection based on review of medical records. Eleven of these patients had central nervous system infections.[1] A similar review of *Propionibacterium* species isolates from pediatric patients at seven US hospitals over a 15-year period showed similar results: 50 of 386 (13%) were considered to be causing infection, including five involving the central nervous system.[13] In both reviews, approximately 70% of the patients had predisposing conditions such as prosthetic material at the site of infection or preceding surgery.

Propionibacterium acnes can be recovered in highest concentrations from areas with high densities of hair follicles such as the scalp.[14] Kamme et al[7] conducted a study in which skin at neurosurgical operative sites was cultured just before incision in patients who had received pre-operative skin cleansing. They demonstrated that *P. acnes* was isolated more frequently and in larger quantities than other members of the normal skin flora. Subsequently, van Ek et al[15,16] analyzed the effect of cloxacillin prophylaxis on the bacterial flora of craniotomy wounds in a randomized, placebo-controlled trial. *Propionibacterium* acnes and *Staphylococcus epidermidis* were the two most frequently isolated organisms from wound cultures taken at the time of initial surgery. Analysis of culture results showed a statistically significant reduction in *S. epidermidis* infections with cloxacillin prophylaxis, while the initial percentage of cultures positive for *P. acnes* did not differ between the placebo and cloxacillin -treated groups. The two studies described above illustrate the ability of *P. acnes* to survive surgical wound preparation and antibiotic prophylaxis, providing a potential mechanism for entry into wounds during neurosurgical procedures.

Successful management of *P. acnes* infections of the central nervous system requires surgical drainage followed by appropriate antibiotic treatment. Antibiotic choice should be based both on in vitro activity and central nervous system (CNS) penetration. Penicillin G and cephalosporins such as cefotaxime and ceftriaxone would be preferred choices based on these criteria. Clindamycin is an active drug in vitro but it has poor CNS penetration, and metronidazole penetrates the CNS well but is less active against *P. acnes* than it is against most other anaerobic bacteria. Interestingly, several successfully treated patients in our series and in the previously published reports that we reviewed received antibiotic regimens that might not be predicted to be successful based on the spectrum and/or pharmacokinetics of the drugs that they received. This suggests that thorough surgical evacuation of infected material may be more important to the outcome than the post-operative antibiotic regimen. Based on our experience and the literature review, it is

Table 2: Summary of P. acnes infections after craniotomy reported in the literature

Author	Findings	Management
Barazi et al.[9]	1 case of brain abscess 18 months after craniotomy for tumor excision	Removal of abscess cavity Cefotaxime IV x 2 weeks, then clindamycin po x 10 weeks
Bruce and Bruce .[10]	4 cases of *P. acnes* infection (including 1 coagulase negative *Staphylococcus* co-infection) without intradural involvement after craniotomy for tumors	Debridement with betadine scrubbing and soaking of bone flaps; bone flap preservation Antibiotics chosen based on susceptibility results: 1 week IV, then 2-4 weeks po
Chu et al.[11]	2 cases of brain abscess after craniotomy for tumor	Surgical drainage Nafcillin IV x 6 weeks Penicillin G IV x 6 weeks
Critchley and Strachan[4]	2 cases of subdural empyema after burr hole evacuation of chronic SDH (1 co-infection with *Lactococcus* species)	Craniotomy (1 delayed), evacuation of subdural empyemas Vancomycin/ceftriaxone IV x 6 weeks, Penicillin/cefotaxime IV x 6 weeks
Jakab et al.[5]	3 patients with *P. acnes* infections after craniotomy	Removal of infected bone flap in two patients and aspiration brain abscess in one patient All received intravenous therapy between 3-8 weeks (exact antibiotics not specified)
Jallo et al.[6]	3 cases after duraplasty: 2 epidural collections, 1 subdural	Drainage (all 3), flap removal (2) Levofloxacin IV x 2-4 weeks, then po x 4-8 weeks
Maniatis and Vassilouthis[8]	1 case of infected hematoma after craniotomy for SAH	Infected extradural hematoma evacuated Cephacetrile + gentamicin IV x 10d
Richards et al.[12]	2 cases of intracerebral abscess after aneurysm clipping	Operative drainage Ampicillin/gentamicin/metronidazole IV

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not possible to determine a minimum effective antibiotic duration. We recommend a minimum of three weeks of intravenous antibiotic therapy followed by oral step down therapy for three to six more weeks. Although some authors have advocated preservation of the bone flap in patients with post-craniotomy infections,[8,10] in our experience removal of the craniotomy flap for *P. acnes* infections is needed because this organism is difficult to eradicate without removal of foreign material and necrotic debris. Before considering cranioplasty for reconstruction of the skull defect, an adequate amount of time must pass in order to ensure that the infection has resolved. In all but one patient (Case 6), we had had uniformly good cranioplasty outcomes with a delay of six months. We are uncertain why this patient had a poor outcome. However, this case illustrates an unusually aggressive presentation of a relatively indolent skin organism with significant patient morbidity.

Most early publications regarding *P. acnes* infections in neurosurgical patients were reports of shunt infections.[3,17-20] More recently, several articles describing *P. acnes* infections after craniotomy have been published.[4-12] Table 2 is a summary of 19 previously reported cases of non-shunt related *P. acnes* infection following neurosurgical interventions for which details regarding management were published. The antibiotic regimens and surgical treatment are shown if they were reported in the original manuscript.

Propionibacterium acnes is a relatively indolent member of the normal skin flora. Human infections are rare, but they are being recognized with increasing frequency following neurosurgical procedures. Based on our experience with post-craniotomy CNS infections caused by *P. acnes*, we recommend surgical debridement including bone flap removal followed by minimum of three weeks of intravenous antibiotic therapy followed by oral step down therapy for an additional three to six weeks.

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