Dorsal midbrain encephalitis caused by *Propionibacterium acnes*

Report of two cases

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A syndrome of dorsal midbrain dysfunction in association with a central nervous system anaerobic diphtheroid infection is described. Two cases of infection with *Propionibacterium acnes* manifested as shunt malfunctions with a clinical dorsal midbrain syndrome. Magnetic resonance images showed increased signal in the midbrain tectum which has decreased slowly over time. The evidence suggesting that this syndrome represents bacterial midbrain encephalitis is discussed.

**KEY WORDS**
- brain-stem encephalitis
- *Propionibacterium acnes*
- hydrocephalus
- cerebrospinal fluid shunt

ENCEPHALITIS of the brain stem is most frequently presumed to be of viral etiology; however, there are at least 60 reports of bacterial inflammation of the brain stem with abscess formation. Streptococcus and *Staphylococcus* are most commonly found in brain-stem abscesses, while *Listeria* and *Mycoplasma* have been shown to cause inflammation with and without abscess.

We have found only four cases of magnetic resonance imaging of brain-stem encephalitis, bacterial or viral, in the literature. In this report, we present two strikingly similar cases of what we believe to be mesencephalic encephalitis caused by the anaerobic diphtheroid, *Propionibacterium acnes*.

**Case Reports**

**Case 1**

This 14-year-old boy with headaches was diagnosed as having hydrocephalus in January, 1984, after an ophthalmological examination revealed papilledema, and a computerized tomography (CT) scan demonstrated massive lateral and third ventricular enlargement. Physical examination was remarkable for a large head and a slightly wide-based gait. A right frontal ventriculoperitoneal (VP) shunt was placed. Six weeks later, he began to complain of back and neck pain after jumping on a trampoline, contrary to the advice of his parents and physicians. A CT scan demonstrated collapsed ventricles and bilateral subdural hematomas. The subdural hematomas were drained, and the shunt was revised without complications. He underwent two more shunt revisions over the next several months.

In November, 1984, the patient presented with a several-day history of decreased level of consciousness, slurred speech, and loss of upward gaze. His peripheral leukocyte count was 15,800/cu mm with 89% neutrophils. A CT scan showed interval ventricular enlargement, and his shunt was revised. The peritoneal catheter was found to be occluded. A cerebrospinal fluid (CSF) cell count showed 2 white blood cells (WBC's)/cu mm and 50 red blood cells (RBC's)/cu cm. His neurological syndrome persisted, and the peritoneal catheter was again revised 5 days later. He slowly improved, although the paresis of upward gaze persisted. A postoperative shunt tap showed good function and an intracranial pressure (ICP) of 0 mm Hg. A CT scan showed a slight decrease in ventricular size. Two CSF cultures taken during his hospitalization grew *P. acnes* 4 and 7 days after collection and following the patient’s discharge. These growths were initially believed to be contaminants. The patient did well clinically; outpatient examination 1 month later showed full extraocular move-
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Six weeks later the patient presented at the emergency room with increased lethargy, abdominal pain, slurred speech, dilated sluggishly reactive pupils, and a paresis of convergence and upward gaze. His WBC count was 10,600/cu mm with a normal differential. The shunt was explored, peritoneal insufficiency diagnosed, and the catheter replaced. A CSF cell count showed 1 monocyte/cu mm. After 2 days of no improvement, a shunt tap indicated high pressure, and a ventriculostomy was placed to maintain ICP at 5 to 10 mm Hg. Three days after admission, *P. acnes* began growing from the initial culture and a course of intravenous cephalothin was instituted. The entire shunt system was externalized at this time, but the patient continued to be minimally responsive with persistent downward deviation of gaze. He had marked hypertonia, resting tremors, diaphoresis, and decerebrate posturing. Magnetic resonance (MR) images obtained at this time showed an area of increased intensity on first-echo (Fig. 1A) and 

![Fig. 1. Case 1. A: Sagittal intermediate weighted magnetic resonance (MR) image (spin-echo (SE) 1900/35 msec) of the midbrain at time of infection. B: Computerized tomography scan without contrast enhancement obtained at the same time as A. C and D: Sagittal (C) and axial (D) MR images (SE 1500/35 msec) 3 months after presentation. E and F: T2-weighted MR images obtained at the 3-year follow-up visit: with gadolinium (SE 850/17 msec) (E) and intermediate-weighted image (SE 700/35 msec) (F).](image)
Case 2

This 19-year-old man was referred to the University of Minnesota in March, 1985, after a series of shunt malfunctions. He was initially diagnosed in July, 1981, as having hydrocephalus, presumed due to aqueductal stenosis. He did well following placement of a right parietal VP shunt until January, 1985, when he presented with symptoms of shunt malfunction including somnolence, headache, and confusion. He also had paresis of upward gaze. The ventricular catheter was found to be obstructed by choroid plexus and was revised. Cerebrospinal fluid studies including cultures were unremarkable. Ten days later, his upward gaze paresis remained and he again became more lethargic. ACT scan indicated large lateral and third ventricles, and the shunt was again revised. Examination of CSF obtained at the time of surgery again showed it to be sterile.

A left-sided shunt was placed 1 month later when the patient's gait and alertness deteriorated. A CT scan again showed large ventricles. His upward gaze paresis remained and he again became more lethargic. A CT scan indicated large lateral and third ventricles, and the shunt was again revised. Examination of CSF obtained at the time of surgery again showed it to be sterile.

A left-sided shunt was placed 1 month later when the patient's gait and alertness deteriorated. A CT scan again showed large ventricles. His upward gaze paresis persisted after surgery, although CT scans showed decreased ventriculomegaly. Four weeks later his complaints included 2 weeks of abdominal pain, persistent upward gaze paralysis, headache, nausea, lethargy, and fever. A CT scan of the head demonstrated massive ventriculomegaly; an abdominal CT scan was unremarkable. His admission WBC count was 16,500/cu mm with a left shift. After blood samples were drawn for culture, intravenous tobramycin and cefalothin were instituted. His shunt was urgently revised and, when no clinical improvement was seen, a ventriculostomy was placed without clinical change. The CSF contained 13 WBC's (8% neutrophils) and 550 RBC's/cu cm. It was at this point that he was transferred to our care.

The patient was obtunded with no speech, and he followed commands intermittently. His pupils were sluggishly reactive, and he had no upgaze on oculo-vestibular testing. Between episodes of decerebrate posturing, he would move his extremities purposefully to pain. He had a peripheral WBC count of 15,400/cu mm with a marked left shift. Electrolytes were within normal limits. A CSF cell count showed 149 WBC's/cu cm with 61% neutrophils. A CT scan showed enlarged ventricles and a radionuclide shunt study showed a functioning shunt on the left.

Ventricular drainage was maintained to keep ICP below 5 mm Hg for 4 days, yet the patient showed no clinical improvement and his ventricles did not decrease in size. At this point, a CSF culture obtained 2 days prior to transfer began growing out diptheroids. Both shunts were externalized. Five days later, when several CSF cultures had been reported negative after 72 hours,
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A new shunt was placed and the old systems were removed. Subsequently, all preoperative cultures including one obtained on the day of surgery grew diphtheroids. No postoperative cultures were positive.

The patient continued to receive cephalothin, and serial CT showed a steady decrease in size of the ventricles. Clinically, he remained un arousable with a downward deviated gaze. A CT scan showed a swollen quadrigeminal plate which did not enhance with contrast material (Fig. 2A and B). An MR image showed an increased signal in the expanded tectal plate, which was thought might represent a glioma or inflammation (Fig. 2C and D). Electroencephalography showed diffuse slowing, and CSF studies sent for myelin basic protein and counter-immunoelectrophoresis were normal. When CT scans again demonstrated increased ventricular size, the shunt was revised to a VA shunt. Over the next several weeks the patient slowly improved to the point where he could follow one-step commands and verbalize two-word phrases. He was markedly bradykinetic and hypertonic, with tremors and a persistent upward gaze paresis. Six months later his only deficit was mild fine motor incoordination. He had normal extraocular movements and convergence. Multiple modality evoked responses were normal. Neuropsychometric testing revealed above-average intelligence, reduced attentional capacity, and a slight recent memory dysfunction in the midbrain arousal structures.

The patient continued to improve and was able to return to college classes. An 18-month follow-up MR image demonstrated a persistent increased signal in the midbrain with enlargement of the quadrigeminal plate (Fig. 2E and F). Studies at the 3-year follow-up review continued to show an abnormal signal in this area, although decreased in intensity (Fig. 2G and H).

**Discussion**

*Propionibacterium acnes* are Gram-positive, anaerobic, non-motile rods found in abundance on human skin. They are often referred to as diphtheroids because they are technically part of the Corynebacterium genus, and because of their similarity to *C. diphtheriae*. These bacteria, thought to play a part in the etiology of C. diphtheriae, are Gram-positive, anaerobic rods found in abundance on human skin. They are particularly prevalent in areas containing a large number of sebaceous follicles, namely the forehead, scalp, prefrontal area, and upper back. The unsaturated fatty acids secreted onto the skin provide an ideal environment for these strict anaerobes.

The infectious spectrum of *P. acnes* is well documented in the neurological literature. It has been recognized as a common cause of shunt infection, colonization, and ultimately malfunction. It has been shown to cause a disabling chronic meningitis in previously healthy patients without previous surgery. It has also been implicated in acute, fulminant meningitis, postoperative wound infections, subdural fluid infection, intracerebral abscess, and immune complex-mediated shunt nephritis. These are the first cases suggesting a role of *P. acnes* in the pathogenesis of a midbrain inflammatory process.

*P. acnes* has been incriminated in the pathogenesis of CSF shunt infections. The actual number of infections caused by these bacteria is probably greater than reported for several reasons. First, the organism is so fastidious in routine aerobic CSF cultures because it is a fastidious anaerobe. Unless specimens are routinely sent for separate culture and transported in anaerobic media, they will often fail to grow out. Even then, it is common for growth to be delayed as long as 1 week. Second, because the organism is so prevalent on the skin, when it grows in small amounts on routine culture medium it is frequently reported as a contaminant.

Third, the clinical central nervous system (CNS) infection produced by *P. acnes* can range from an asymptomatic colonization to fulminant meningitis. The CSF cell count has been reported to show mild to prominent leukocytosis.

These two cases appear to be typical of other cases of *P. acnes* infection both from our institution and from the literature in several respects. The isolation and recognition of *P. acnes* as a pathogen in each of these examples were delayed by late growth and by labeling of the culture result as a "contaminant." Several shunt system malfunctions and revisions were required before the problem was recognized and finally brought under control.

These cases are unique in several respects. The slow development and persistence of upward gaze paresis in combination with pupillary abnormalities and obtundation in these patients seems to point to the midbrain as the site of pathology. The appearance of MR images of an area of increased signal in the midbrain tectum of each patient would seem to confirm this. Increased ICP was initially considered to be responsible for the Parinaud's syndrome. However, the syndrome persisted despite normalization of ICP. In both of these patients the initial diagnosis was hydrocephalus secondary to aqueductal stenosis.

Both cases were brought to medical attention in mid to late adolescence, a time when *P. acnes* skin colonization is at its peak. The CSF cell count was for the most part unremarkable despite the repeated presence of the diphtheroid bacilli in cultures. This characteristic of a slow, indolent infection of low virulence is reflected in the literature and can account for the pattern of repeated shunt malfunction/obstruction in the absence of an overt, purulent infectious process.

The location of abnormalities seen on MR imaging corresponds well to the clinical syndrome. Although a neoplastic process, such as a glioma, was entertained as a possible diagnosis, the likelihood that this is the case is small given the recovery of each patient following a course of antibiotics, and the improvement on follow-up MR images. We believe that the clinical and imaging evidence suggests a structural dorsal midbrain lesion.
occurring in conjunction with documented CSF infection, and is most consistent with midbrain encephalitis caused by *P. acnes*.

In her classic treatise, Russell \(^\text{30}\) demonstrated luminal areas denuded of ependyma in cases of aqueductal stenosis due to gliosis. This gliosis in the aqueduct of Sylvius is more frequently found in non-myelomeningesc cerebrospinal fluids than in normal brains. \(^\text{33}\)

The ependymal lining of the aqueduct in these brains has been shown to be often defective with islands of ependyma buried beneath the lumen. Experimental evidence using the congenital murine hydrocephalus model showed similar denuded areas in the aqueduct, although this was not extensive. \(^\text{24}\) These luminal defects may represent an avenue by which bacteria would gain easier access to midbrain parenchyma.

Brain-stem encephalitis is a rare disorder and can present with a variety of symptoms including cranial-nerve and bulbar dysfunction and obtundation. \(^\text{1,2,38}\) In the classic description, Bickerstaff \(^\text{3}\) reviewed eight cases with ophthalmoplegia, other cranial nerve palsies, and ataxia. The clinical picture progressed from nonspecific prodromal symptoms to neurological signs indicative of brain-stem pathology. Patients became severely lethargic and disabled neurologically; however, they generally recovered over the course of several weeks to months. Interestingly, several of his cases developed a transient Parkinson-like symptom complex (resting tremor, masked facies, bradykinesia) during the course of their recovery. Since that report, other similar cases have been reported, \(^\text{4,31,42}\) most describing a viral-type prodromal symptomatology.

Bacterial invasion of the brain stem is less frequently reported. *Listeria monocytogenes* appears to have a particular predilection for the brain stem, being implicated in several cases of abscess or encephalitis. \(^\text{5,6,23,37}\) Although other bacteria have been reported to cause brain-stem abscess, low-grade chronic inflammation has been almost universally ascribed to infection with virus. *P. acnes* has been described as a pathogen with low virulence and has been shown to be responsible for subclinical and chronic CNS infections, it seems likely that it could be implicated in brain-stem encephalitis.

There are only four reports of MR imaging characteristics in brain-stem encephalitis, \(^\text{8,15,18}\) and several cases with normal MR studies. \(^\text{8,28}\) However, none of these cases presented specifically with the dorsal midbrain syndrome. \(^\ast\) There are two reports in the literature of Fisher's syndrome (the specific symptom complex including ophthalmoplegia, ataxia, and hyporeflexia) with a tegmental lesion seen on CT scanning. \(^\text{5,36}\) The MR images of our two patients showed areas of increased signal on intermediate and T2-weighted images very similar to those reported in the literature. None of the cases reported previously has shown images obtained years after the lesion was diagnosed. Our patients would suggest that the lesion will lessen in signal intensity over time, but may not completely disappear.

It might be argued that the present cases represent typical Bickerstaff encephalitis or atypical cases of Fisher's syndrome, in which complete recovery is most often the case and the cause is probably viral. If that were so, the hydrocephalus and shunt infections caused by *P. acnes* would have occurred simultaneously. Because of the extreme rarity of the entity itself, and the coincidental association in these cases with shunt infections caused by *P. acnes*, we believe this scenario to be unlikely.

In summary, we believe that untreated CSF infections with *P. acnes* can progress to parenchymal involvement producing structural lesions visible on MR imaging that cause virulent, life-threatening disease. *Propionibacterium acnes* isolated from the CSF, especially in association with a shunt, must be treated seriously and not viewed as a contaminant without exhaustive investigation.

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**References**

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