Case Report

Giant Actinomyces brain abscess in an immunocompetent child: A management strategy

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INTRODUCTION

Intraparenchymal brain abscesses have been recognized since the early days of modern medicine, with the first recorded treatment of a brain abscess in 1768 by French Surgeon Monrand. Brain abscesses occur in all populations, with approximately 1500–2000 cases/year in Western nations and in greater numbers in developing nations. They occur approximately 2–3 times more in men than women. Abscesses within the pediatric population (patients under 15 years of age) are relatively uncommon and have an incidence between 15 and 50%. The most common bacterial causes of brain abscesses identified in the pediatric population are Streptococci, Staphylococcus, and Enterobacteriaceae.
Diagnostic evaluation for possible brain abscess is critical and should include a medical workup with complete blood count, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR). Blood cultures should be obtained in febrile patients, especially those with concern for concomitant extra-axial infection.\textsuperscript{[9]} Lumbar culture is generally not utilized in the setting of brain abscess due to limited yield of cerebral spinal fluid cultures and more importantly because of the significant risk for herniation.\textsuperscript{[9,16]} Brain abscesses once identified, should be staged radiographically from cerebritis stage to late capsular formation, offering opportunity for surgical planning and prognostic advice for the patient and their families.

Management of a brain abscess utilizes a multifocal approach. The medical antibiotic therapy can be guided by operatively collected positive cultures with susceptibility testing of recovered microbes, to deescalate broad empiric pharmacotherapy. When one or more organisms are identified and developed abscesses are <2.5 cm in diameter, they are commonly treated with antibiotics alone, guided by a hypothesis that the minimum inhibitory concentration at abscess center is sufficiently toxic to the microorganism.\textsuperscript{[3,4,9]} However, when abscesses grow despite therapy or have a diameter >3 cm, surgical strategies, including craniotomy for excision or stereotactic aspiration, should be performed.\textsuperscript{[24]} All surgical approaches have potential corridor associated morbidity, and goals of surgery should correlate with invasiveness of the procedure. Large, multiloculated, superficial abscesses in noneloquent areas may benefit from a definitive procedure such as craniotomy and drainage, with or without postsurgical drain placement.\textsuperscript{[9,7,16]} Conversely, deep abscesses, like those in the thalamus, that fail conservative therapy would benefit from a stereotactic needle aspiration with or without postsurgical drain placement.\textsuperscript{[9,16]}

There is a high degree of variability in both the antibiotic and surgical strategies for brain abscesses, but overall there are some commonalities, as follows;\textsuperscript{[28,6,14]}

- Treatment is often prolonged, lasting a minimum of 6 weeks
- Selected antibiotics should possess bactericidal properties
- Selected antibiotics must be able to cross the blood–brain barrier
- In nonoperative or culture-negative cases, the antimicrobial spectrum of activity should cover, at minimum, common Gram-positive and anaerobic organisms.

We present a 2-year-old female patient who presented to our practice with a giant right frontal Actinomyces abscess. This presentation of Actinomycosis is highly unusual as there were no identified risk factors, and development of an abscess without risk factors is not frequently reported in literature.

Due to the giant size of the abscess, it required multiple surgical strategies and interventions, ultimately resolving successfully without neurologic complication. The variability in operative approach further demonstrates the immense variability required in management of even one patient, to have resolution of symptoms, and the unusual nature of this case.

CASE REPORT

History

Our 2-year-old patient is the product of a 40-week gestation born through induced vaginal delivery to a Group B Streptococcus agalactiae negative mother. She developed normally, without infections, until age 8 months when she developed a febrile urinary tract infection from Escherichia coli that was managed with daily prophylactic trimethoprim-sulfamethoxazole for 1 year without recurrence of UTI.

Examination

The patient presented to our emergency department at the age of 2 years 10 months with 3 weeks of headaches, lethargy, malaise, and following 2 days of vomiting before admission. She was afebrile without chills, rashes, recent infections, or on the infectious disease team’s evaluation without dental carries. She had only recent domestic travel, without international trips or exposures.

Her vital signs on presentation were normal and her clinical examination reflected an awake, alert but low-energy female with the left lower facial droop. Urine culture on presentation falsely recovered >100,000 colony-forming units/mL of E. coli, as a repeat culture before starting antibiotics returned negative. Her total white blood cell count was elevated at 15,000, with a neutrophil predominance (66%). She had an elevated ESR of 53 mm/h, as well as CRP which was increased at 6.3 mg/dL. Her preantibiotic therapy admission blood cultures did not recover E. coli and were finalized as negative. The symptom of facial droop prompted brain magnetic resonance imaging (MRI) [Figure 1].

Operation

Consequently, the child underwent right frontal burr hole craniectomy and ultrasound-guided needle aspiration with removal of 50 mL of purulent material, a with a Gram stain detecting Gram-positive cocci. Initially, the patient was empirically treated with broad-spectrum intravenous (IV) triple antimicrobial therapy using vancomycin, cefepime, and metronidazole. Promptly, Actinomyces grew in the operative anaerobe culture within 48 h and was found to be pansusceptible. Subsequently, a peripherally inserted central catheter (PICC) was inserted and the child was converted to...
a continuous IV penicillin G (6,000,000 units/day), infused over 22 h, with oral metronidazole 120 mg every 6 h.

Postoperative course

The patient was discharged home on postoperative day (POD) 6 with a 2-week Decadron taper given her cerebral edema and prophylactic levetiracetam therapy. Eleven days later, she returned to the emergency department with a PICC-associated nonocclusive thrombus with a white blood cell elevation to 19,000, but an ESR of 5 (peak 60) and CRP of <0.5 (peak 6.3). Her PICC line was replaced in the opposite arm.

Seventeen days postoperatively, she represented to the emergency department with fever, emesis, and return of the left lower facial droop and continued headaches. Despite compliance with the prescribed antibiotic therapy, and in the absence of symptoms consistent with an alternative localizing infection, the white blood cell was found to be 11,800, with interval increases in ESR (70) and CRP (3.6). MRI, at this time, demonstrated a larger abscess in all dimensions. Due to radiographic worsening, recurrent symptoms, and worse inflammatory markers, the child was taken back to the operating room for aspiration and placement of an intra-abscess drain, and briefly provided IV vancomycin, changing penicillin to ceftriaxone. [Figure 2] demonstrates pre- and immediate postoperative representative sections from MRI. The drain had daily decreased output from 30 mL, 19 mL, 11 mL, 8 mL, 5.5 mL, 3 mL, 2 mL, and 1.5 mL and was discontinued on POD 9. Antibiotic therapy was limited to ceftriaxone and oral metronidazole and since there was no growth of organism from any operative specimen collected during this third admission.

After 13 weeks of ceftriaxone and metronidazole following her second, and definitive, surgery, she is neurologically normal without developmental delay. [Figure 3] demonstrates representative images from multiple time points in the postoperative period throughout 3 months of antimicrobial therapy. The PICC and antimicrobial therapy were discontinued at this time with resolution of abscess on imaging.

One month following treatment cessation, she developed fever and abdominal pain with transaminitis not previously seen during antimicrobial therapy. She was diagnosed with cholelithiasis, to which her prolonged ceftriaxone therapy likely contributed, and underwent an uncomplicated cholecystectomy. Surgical pathology demonstrated a gallbladder with some irregular cholelithiasis but was otherwise normal. The patient is currently in preschool and learning to be potty trained.

DISCUSSION

Otto Bollinger first discovered Actinomyces in 1877 in cattle, with subsequent recovery of the bacteria in soil by Eugen
By 1878, Actinomyces as a human pathogen had been appreciated due to the works of J. Israel and M. Wolff. Actinomyces is an anaerobic branching filamentous Gram-positive bacillus. Most commonly, actinomycosis infections present as cervicofacial, abdominopelvic, and respiratory infections. Central nervous system (CNS)
| Case Year | Source/Author | Age | Sex | Procedure | Antibiotic Regimen | Duration | Resolution/ Follow Up |
|-----------|---------------|-----|-----|------------|-------------------|----------|----------------------|
| 1963      | Heineman Braude | 14 years | M | Craniotomy and drainage | IV 10 million units penicillin | 16 days | Resolved; unknown follow up |
|           |                |      |     |            | IV Sulphisoxazole |        |                      |
|           |                |      |     |            | IV Tetracycline 1 gm TID |        |                      |
|           |                |      |     |            | IV Penicillin 20 million units/day |        |                      |
|           |                |      |     |            | IV Tetracycline 2 gm/day |        |                      |
| 29 years  | F              | Craniotomy and drainage | | | IV Penicillin | 2 weeks | Recovered with relapse 2.5 years later, attributed to incomplete surgical evacuation |
| 2007      | Mylonas Tzerbos Rologis Boutsikakis | 54 years | M | Craniotomy and resection of abscess | IV Ceftriaxone 200 mg BID | 23 days | Resolved with complete recovery of hemiparesis within 29 months |
|           |                |      |     |            | IV Metronidazole 50 mg QID | 23 days |                      |
|           |                |      |     |            | IV Vancomycin 500 mg TID | 23 days |                      |
|           |                |      |     |            | IV Ofloxacin 200 mg TID | 5 weeks |                      |
|           |                |      |     |            | IV Teicoplanin 400 mg BID | 5 weeks |                      |
| 2007-2009 | Akhaddar Elouennass Baallal Boucetta | 18 years | M | Burr hole craniotomy | IV Metronidazole | 1 month | Resolved; unknown follow up |
|           |                |      |     |            | Oral Erythromycin | 2 months |                      |
|           |                |      |     |            | IV Ciprofloxacin | 1 month |                      |
|           |                |      |     |            | IV Ceftriaxone | 10 days |                      |
|           |                |      |     |            | IV Gentamicin | 10 days |                      |
|           |                |      |     |            | IV Metronidazole | 10 days |                      |
|           |                |      |     |            | Oral Ciprofloxacin | 2 months |                      |
|           |                |      |     |            | 1 gm/day | Unknown |                      |
|           |                |      |     |            | IV Ceftriaxone | 2 months |                      |
|           |                |      |     |            | 1 gm/day | Unknown |                      |
|           |                |      |     |            | IV Gentamicin | 4 weeks |                      |
|           |                |      |     |            | IV Metronidazole | 4 weeks |                      |
|           |                |      |     |            | Oral Ciprofloxacin | 2 months |                      |
|           |                |      |     |            | 1 gm/day | Unknown |                      |
|           |                |      |     |            | IV Cefotaxime | Unknown | Resolution of neurological symptoms in 6 weeks; unknown follow up |
|           |                |      |     |            | IV Gentamicin | Unknown |                      |
|           |                |      |     |            | IV Metronidazole | Unknown |                      |
|           |                |      |     |            | Oral Ciprofloxicin | Unknown |                      |
|           |                |      |     |            | 1 gm/day | Unknown |                      |
| (Contd...) | | | | | | | |
### Table 1: (Continued)

| Case Year | Source/ Author                  | Age   | Sex | Procedure                                                                 | Antibiotic                  | Duration | Resolution/ Follow Up                      |
|-----------|---------------------------------|-------|-----|---------------------------------------------------------------------------|------------------------------|----------|--------------------------------------------|
| 2010-2016 | Ravinda Sadashiva Mahadevan Bhat Saini | 1.5 months | M | Surgical excision                                                       | Cloxacillin                 | 7 days   | Resolved; follow up 54 months             |
| 14 years  | M | Stereotactic aspiration       | Injected Penicillin Amoxicillin Penicillin | 6 weeks 10 months 6 weeks | Resolved; follow up 11 months |
| 15 years  | M | Craniotomy and removal bone flap with orbital de-roofing excision | Rifampicin Amoxicillin Unknown | 6 weeks 1 year 4 weeks | Resolved; follow up 32 months |
| 18 years  | F | Craniotomy and excision      | Ceftriaxone               | 4 weeks            | Resolved; follow up 30 months |
| 21 years  | M | Re-exploration of excision    | Ceftriaxone               | 2 weeks            | Resolved; follow up 10 months |
| 24 years  | M | Bi-frontal craniotomy and excision | Unknown               | Unknown            | Unknown follow up |
| 29 years  | M | Bi-frontal craniotomy and decompression | Unknown               | Unknown            | Unknown follow up |
| 30 years  | M | Craniotomy and decompression of lesion | Amoxicillin             | 2 months           | Resolved with nondependent ataxia; follow up 54 months |
| 35 years  | M | Craniotomy and excision      | Ceftriaxone               | 2 weeks            | Resolved; follow up 10 months |
| 36 years  | M | Re-exploration and removal of bone flap | Cloxacillin Metronidazole Unknown | 2 weeks 2 weeks | Unknown follow up |
| 39 years  | F | Craniotomy and excision      | Cefotaxime               | 2 weeks            | Resolved; follow up 120 months |
| 40 years  | F | Craniotomy and excision      | Amikacin Olloxacin       | 2 weeks 4 weeks    | Resolved with non-associated hemiparesis; follow up 80 months |
| 45 years  | F | Craniotomy with tapping of abscess | Amikacin Metronidazole Unknown | 4 weeks 2 weeks | Unknown follow up |
| 51 years  | M | Endoscopic Transsphenoidal removal  | Amikacin Metronidazole Unknown | 2 weeks | Unknown follow up |
| 52 years  | M | Re-exploration of excision    | Unknown               | Unknown            | Unknown follow up |
| 65 years  | M | Stereotactic aspiration      | Ceftriaxone Amikacin Metronidazole | 1 week 1 week | Resolved; follow up 22 months |

(Contd...)
| Case Year | Source/ Author | Age | Sex | Procedure | Antibiotic | Duration | Resolution/ Follow Up |
|-----------|----------------|-----|-----|------------|------------|----------|----------------------|
| 2014      | Valour Senechal Dupieux Karsenty Lustig Breton Gleizal Boussel Laurent Braun Chidiac Ader Ferry | 50 years | M | Stereotactic aspiration | Unknown | Unknown | Unknown follow up |
| 2015      | Clancy Ronayne Prentice Jackson | 55 years | F | Craniotomy and drainage | Vancomycin | 11 days | Resolved with seizure prophylaxis (levetiracetam); follow up ongoing |
| 2017      | Guillament Malinis Meyer | 29 years | M | Stereotactic drainage | Oral TMP-SMX BID | Post-operatively | Resolved within 6 months; unknown follow up |
| 2017      | Corcione Curtoni Paolucci Perri De Rosa Cavallo | 21 years | | | | | Resolved; unknown follow up |
| 2018      | Hwang Lee Hong Kim Kim | 51 years | F | Craniotomy with stereotactic guidance and evacuation | IV Moxifloxacin 400 mg daily | 6 weeks | Resolved within 12 months of follow up |

*Table 1: (Continued)*
Actinomyces infection is an uncommon presentation, occurring in <5% of infected individuals and can manifest as a brain abscess, meningitis, meningoencephalitis, epidural abscess, or subdural empyema.[19,26] These varied CNS presentations develop through hematogenous spread or direct extension from an adjacent infection.

The low rate of confirmed Actinomyces diagnosis is likely confounded by the difficulty of recovering this microbe in the laboratory, on account of slow growth and strict anaerobic metabolism. Growth on the enriched medium of chocolate blood agar can take anywhere from 5 to 20 days and cannot be reasonably excluded without a minimum 10 days of “no growth” to be considered negative.[26] Classification of this infectious agent was previously reliant on branching filamentous features, although observing sulfur granules on microscopy which form once the bacteria have induced a chronic granulomatous infection, can aid in diagnosis.[7] Modern technologies, such as polymerase chain reaction of 16S ribosomal RNA gene sequencing and matrix-associated laser deionization-time of flight, have proven helpful in identifying Actinomyces infection utilizing samples from pus from a brain abscess, and cultures from CSF, blood, urine, and sputum.[7,26] These more modern techniques will optimistically lead to earlier identification of infection, and thus earlier and more successful intervention.

Typically, cerebral abscesses from Actinomyces affect adults with predisposing factors including congenital heart defects, chronic otitis media, otologic surgery, chronic sinus infections, dental infections, alcoholism, IV drug use, and infected intrauterine device.[5,6,8,10,11,12,13,19] In the pediatric population, the most common causes include direct extension from chronic otitis media or dental abscess and hematogenous seeding with concomitant congenital heart disease.[5,6] These brain abscesses manifest clinically with symptoms as sequelae of local mass effect by compression of adjacent neural tissue including the venous sinuses, global mass effect by increasing intracranial pressure, or development of hydrocephalus.[2,14] Clinically, these symptoms manifest as generalized malaise, lethargy, fever, and seizures.[5,18,26] Recognition by a clinician through thorough examination is vital, as rupture of the brain abscess and spilling of purulent contents into the patient's ventricular system may precipitate a sudden clinical decompensation and is a dreaded complication with a mortality rate >40%, reaching even as high as 80%.[20]

On recognition of these abscesses, the management of CNS Actinomyces infection is multimodal. Despite the acquisition of susceptibility data, the antibiotic regimen for Actinomyces specific has immense variability. [Table 1] summarizes the variations in antibiotic choice, duration of treatment, as well as operative approach. Most reported cases resolved by an average 18 months, with one case with long-term failure 2½ years posttreatment. Initially, due to the culture results and susceptibility data, our team selected the combination of IV penicillin G, with oral metronidazole. However, her clinical course and persistently elevated infectious markers, ultimately required broadening to the combination of ceftriaxone and metronidazole to best optimize coverage of unrecovered conventional pathogens, and the outcome for our patient. The surgical management of Actinomyces infection also has tremendous variation. Initially, we performed a burr hole craniectomy with ultrasound-guided aspiration which is a widely accepted intervention particularly in deep parenchymal abscesses; however, due to a combination of radiographic worsening and recurrent symptoms, with worsening inflammatory markers despite compliance with prescribed antimicrobial therapy, our patient underwent a subsequent ultrasound-guided aspiration of her abscess, with placement of an intra-abscess drain that was successfully discontinued on day 9 of her readmission.

CNS Actinomyces infections are found in patients of all ages, although more cases reported in literature, are in the adult population. Within the pediatric population, there are a limited number of reported cases, and exceedingly rare, are those in an immunocompetent child without notable risk factors. We found no such cases in our literature review of an immunocompetent pediatric patient, like ours, developing an Actinomyces brain abscess. The common tie between pediatric and adult cases is the variability in the management of both antimicrobial and surgical approaches. In the case of a 2-year-old patient who uniquely had no risk factors, we found success utilizing a minimal access surgery with placement of intra-abscess drain and 3 months of antibiotics using ceftriaxone with metronidazole. We recommend this management in the future for pediatric patients with CNS Actinomyces abscesses.

**CONCLUSION**

Brain abscess is a rare consequence of hematogenous spread or direct extension of adjacent infection, and without appropriate often combinatorial treatment can frequently prove fatal. Successful treatment depends on organism and location. The even more uncommon giant intraparenchymal abscesses can be managed with minimal access and prolonged antibiosis, especially when slow-growing organisms are identified. Long-term follow-up should be employed to mitigate missed late failures.

**Declaration of patient consent**

Patient’s consent not required as patients identity is not disclosed or compromised.

**Financial support and sponsorship**

Nil.
Conflicts of interest

There are no conflicts of interest.

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