**Paediatric brain abscesses: a single centre experience.**

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**ABSTRACT**

**Introduction:** Brain parenchymal abscesses are relatively infrequent but potentially serious infections in the paediatric population. Surgical intervention in addition to ~~a~~ prolonged administration of antibiotics is generally appropriate management. This study presents our centre’s experience of managing such patients in the context of relevant literature.

**Method:** A single-centre retrospective case note review was conducted over a 15 year period (2003-2017). Patients were selected from electronic hospital records using ICD10 code G06.0. Patients < 18yrs of age with a confirmed intra-parenchymal abscess were included. Patient records were reviewed for abscess location, microbiology results, surgical intervention, and outcome using the Glasgow Outcome Score at 3 months.

**Results:** Twenty-four patients were identified (mean age: 7.4 ± 5.3 years, male n=11). Twelve (50.0%) patients had an abscess in the frontal lobe and *Streptococcus* was the most common causative microorganism (n=15). Nineteen patients (79.2%) had an identifiable source which included: ENT infections, congenital cardiac malformations, recent dental surgery and meningitis. All 24 patients underwent surgery with 20 patients having a total of 32 aspirations between them and the other 4 having craniotomy and excision. Twenty patients had 3 month follow-up data of which 18 patients scored GOS: 5, one was GOS: 4 and one was GOS: 3.

**Conclusions:** Brain parenchymal abscess remains an uncommon pathology in the paediatric population. The majority of patients have a preceding infection with *Streptococcus* as the most common causative organism. Antimicrobial therapy should be selected accordingly. All of our patients underwent surgical intervention and received intravenous antibiotics with favourable outcome and no mortality.

# Introduction

Brain abscesses are relatively less common in the paediatric population compared to adults, however, they remain a serious, life-threatening infection (Frazier *et al.*, 2008). The causes of brain abscesses are highly variable in children (Kao *et al.*, 2003; Kao *et al.*, 2008). The major predisposing conditions in children are: an adjacent focus of infection, trauma, haematogenous seeding, neurosurgical procedures, cyanotic heart disease and immunocompromised states (Brook, 1995; Hakan *et al.*, 2006; Frazier *et al.*, 2008; Tandon *et al.*, 2009). Associated sites of infection commonly include sinusitis, mastoiditis, dental infections and chronic otitis media where aerobic bacterial infections such as Streptococci and Staphylococci predominate (Brook, 1995; Shachor-Meyouhas *et al.*, 2010). However the role of ear infections causing abscesses has declined with the introduction of pneumococcal vaccination and the use of antimicrobial therapy (Tandon *et al.*, 2009).

Prognosis is dependent on the efficiency of diagnosis and management (Muzumdar, 2011). The gold standard treatment of brain abscesses continues to be aspiration or excision combined with antibiotic therapy (Hakan *et al.*, 2006; Carpenter *et al.*, 2007). However the outcome has improved dramatically in recent decades due to improvements in diagnostic techniques and broad-spectrum antibiotics (Saez-Llorens, 2003; Patel and Clifford, 2014). The modification of empirical antibiotic regimes to cover anaerobic organisms has also positively influenced outcomes (Keet, 1990). Early diagnosis and prompt use of antibiotic therapy increases prognosis and outcome by preventing the progression from cerebritis to abscess (Saez-Llorens, 2003) and those with a shorter period between symptom onset and surgery have a more favourable prognosis (Kao *et al.*, 2003). Magnetic Resonance Imaging is more sensitive at diagnosing early cerebritis (Mathisen and Johnson, 1997; Saez-Llorens, 2003), and has increased the prognosis of brain abscess by improving the speed of diagnosis (Miller *et al.*, 1988). Despite all of these advances abscesses are still a significant cause of morbidity and mortality (Brook, 1995; Felsenstein *et al.*, 2013).

Following the recent advances in management the aim of this study was to review management and outcomes of paediatric patients with a brain abscess admitted to a single neurosurgical unit.

# Methods

A retrospective review was conducted of paediatric patients with a brain abscess admitted to the Southampton General Hospital Neurosurgery Department, Southampton, UK between 2003 and 2017 (inclusive). Patients were identified from hospital coding records using the International Classification of Diseases, Tenth Revision (ICD-10) code G06.0. G06.0 specifies a diagnosis of “intracranial abscess and granuloma including brain (any part) abscess (embolic), cerebellar abscess (embolic), cerebral abscess (embolic), intracranial epidural abscess or granuloma, intracranial extradural abscess or granuloma, intracranial subdural abscess or granuloma and otogenic abscess (embolic)”.

The case notes were reviewed for demographics, symptoms, inflammatory markers (plasma white cell count and C-reactive protein), abscess location, microbiology results, surgical intervention, complications and functional outcome. White cell count >11 x109/L and/or CRP >5mg/L was classed as raised inflammatory markers. Functional outcome was measured using the Glasgow Outcome Score (GOS) at 3 months from discharge.

The hospital’s radiology database was reviewed and the abscess volumes on admission were measured using the volumetric tool of SectraPACS (Sectra, Linkoping, Sweden). Radiological follow-up was measured from the date of the final surgical intervention to the final follow-up scan. The number of CT or MRI scans (not including routine day one post-operative scans) was also counted.

Inclusion criteria were patients who were less than 18 years of age with a radiologically confirmed intra-parenchymal abscess. Those with isolated subdural empyema, extradural abscess, or an unknown abscess location were excluded from the study.

**Results**

The initial coding search identified 63 patients; 26 with an intra-parenchymal abscess, 17 subdural abscesses, 13 extradural abscesses, 6 with an unknown location and 1 abscess in the scalp. Of the 26 patients with an intra-parenchymal abscess and further 3 patients were excluded due to incomplete data. A further previously published case treated at our institution was added from the authors’ records (Elyas *et al.*, 2011). The final cohort of 24 patients comprised 11 male patients (45.8%) and had a mean age of 7.4 ± 5.3 years.

White cell count and CRP (C-reactive protein) were available for 23 patients in this cohort. Amongst those with a raised white cell count (n=14, 60.0%) the mean value was 17.9 x109/L (95% CI 14.5 to 21.3mg/L) and those with a raised CRP (n=17, 73.9%) the mean was 110.9mg/L (95% CI 54.4 to 168.5mg/L). Twelve (52.2%) patients had both a raised WCC and CRP, and 6 (26.1%) had neither WCC nor CRP raised.

Fourteen (58.3%) patients had documented evidence of headaches, 11 (45.8%) had fevers, 6 (25.0%) had meningism and 6 (25.0%) had focal neurology. The full list of symptoms is shown in **table 1**. The classic triad of headache, fever and focal neurology was only seen in one patient (4.3%). Drowsiness or reduced level of consciousness on presentation was recorded in 8 patients (34.8%)

The frontal lobe was the most common abscess location (n=12; 50.0%). The remainder of the abscesses were in the parietal lobe (n=4; 16.7%), temporal lobe (n=3; 12.5%), cerebellum (n=2; 8.3%), thalamus (n=1, 4.2%), pons (n=1, 4.2%) and the medulla (n=1, 4.2%). Twenty-three patients had a solitary lesion at presentation and the patient with aspergilloma had two lesions in the same location.

*Microbiology*

Nineteen patients (79.2%) had an identifiable source which included; ENT infections (n=8), congenital cardiac malformations (n=5), recent dental surgery (n=2), meningitis (TB and streptococcal) (n=2), pulmonary aspergilloma (n=1), premature rupture of membranes (n=1), and iatrogenic following ICP bolt insertion (n=1). The patient with pulmonary aspergilloma also had a concurrent diagnosis of leukaemia and one patient had a recent dental abscess on a background of congenital cardiac disease.

*Streptococcus* was the most common organism cultured from the abscesses (n=15, 62.5%). The *Streptococcus* species included *intermedius* (n=5), *anginosus* (n=5), Group A (n=2), *constellatu*s (n=1), *non-haemolytic (*n=1), *pneumoniae* (n=1) and *Streptococcus species unspecified* (n=1). Other microorganisms include *Staphylococcus aureus* (n=2), *Coliforms* (n=1), *Aspergillus* (n=1), *Propriobacterium* (n=1), *Mycobacterium tuberculosis* (n=1), Gram negative rods (n=1) and mixed anaerobes (n=2). The abscess following ICP bolt insertion was caused by a *Staphylococcus aureus*. One patient did not grow any organisms from his pus; however this may have been influenced by the antibiotics started before admission. None of the patients had an associated ventriculitis although one patient had positive CSF cultures from an EVD (external ventricular drain) matching her abscess organism.

*Treatment*

All 24 patients underwent surgery. Twenty patients had stereotactic guided burr hole aspirations with a total of 32 burr hole aspirations being performed (1.6 aspirations/patient). The number of aspirations per patient is shown in **Figure 1**. None of the patients initially managed with aspirations subsequently required capsulectomy. Prophylactic anti-convulsant medication was not routinely prescribed in these patients instead the approach was to wait until a patient developed seizures to start them.

Pre-operative imaging was available for 18 patients and volumetric analysis showed an average pre-operative volume of 16.3ml. Amongst those patients with available imaging who underwent burr hole aspiration the average pre-operative volume for those who did not require re-aspiration (n=8, 4.1ml ± 2.2) was significantly lower than those who required repeated aspiration (n=8, 31.4ml ± 17.0) (p=0.001). There was no significant difference in the distribution of abscess locations between those requiring re-aspiration and those treated with a single aspiration only (**Table 2**) (p=0.31). The small number of patients limited analysis of specific micro-organisms associated with re-aspiration. However, amongst patients with a *Streptococcus* species who were managed by aspiration (n=13) there were 7 patients (53.8%) requiring re-aspiration, and of the 7 non-streptococcal infections managed with aspiration, 2 patients (28.6%) required re-aspiration (p=0.37).

Four patients underwent a craniotomy as the initial surgical intervention. One patient was initially treated with 6 weeks of IV antibiotics but developed new headaches with formation of new adjacent daughter abscess. A patient with aspergilloma had a calcified lesion filled with caseous granulomatous material which was deemed not amenable to aspiration. The third patient had a superficial abscess with osteomyelitis following ICP bolt insertion and so underwent abscess resection in the same operation as bony debridement. The final patient had sinusitis and previous subdural empyema evacuation and so had her abscess resected as part of a re-operation for the empyema.

The total antibiotic duration was discernible from the medical notes for 21 of the 24 patients and the mean time was 5.8 ± 2.0 weeks. This comprised a mean of 2.9 ± 1.5 weeks intravenous and 3.0 ± 1.8 weeks oral antibiotics.

The electronic radiology database did not record scans from the early period of the study, so follow-up radiology was only measurable for 17 of the 24 patients. The median number of scans was 4 (range 2-7) and the median radiological follow-up duration was 8 (range 3-106) weeks. The patient scanned at 106 weeks underwent abscess excision for *Aspergillus* and had prolonged follow-up imaging for…..

*Complications and outcomes*

Six (25.0%) patients had a complication either from their abscess or treatment. Three patients developed hydrocephalus, two of which needed to be treated by EVD, however none required long term CSF diversion procedures. One patient had a CSF leak from the wound managed with a lumbar drain and one patient had a transient 3rd nerve palsy secondary to raised intra-cranial pressure. The final patient had cavernous sinus thrombosis associated with their sinusitis requiring long term anticoagulation.

The mean length of stay of a patient was 15.6 ± 9.6 days. Twenty of the 24 patients (83.3%) had follow up clinic letters at 3 months post-discharge. Eighteen (94.7%) patients had a GOS score of 5, one patient had a score of 4 and one patient had a score of 3. There were no deaths.

# Discussion

Brain abscesses are an uncommon diagnosis in the paediatric population and have historically been associated with high rates of morbidity and mortality. The management of paediatric brain abscesses has changed following the widespread use of antibiotics for ENT infections and introduction of CT imaging to aid in timely diagnosis (Goodkin *et al.*, 2004; Tandon *et al.*, 2009). The study reported here contains the results of 15 years’ experience in managing paediatric brain abscesses in the modern era.

The change in practice towards early prescription of antibiotics for oto-sinogenic infections has resulted in a change in the infective aetiologies associated with brain abscess. In studies from the pre-CT era ENT infections were the cause in 38-76% (Idriss *et al.*, 1978; Goodkin *et al.*, 2004) of brain abscesses in children; however this has fallen to 8-36% (Ciurea *et al.*, 1999; Goodkin *et al.*, 2004; Hakan *et al.*, 2006; Gelabert-Gonzalez *et al.*, 2008; Canpolat *et al.*, 2015) in the modern era with congenital heart disease and immunosuppression becoming a more commonly recognised causative factor. The current series reports 30.4% of patients have preceding oto-sinogenic infections, which is at the upper range of reports from the modern era. However the common causes (oto-sinogenic, congenital heart disease, dental treatment, immunosuppression) are all encountered in this series, suggesting that this sample is still representative of the paediatric abscess population, while proportions are likely influenced by the small sample size. Regardless of the changes in aetiology, *Streptococcus* remains the most commonly reported causative microbe both in this series and those published in the literature (Wong *et al.*, 1989; Ciurea *et al.*, 1999; Hakan *et al.*, 2006; Sharma *et al.*, 2009; Felsenstein *et al.*, 2013). Despite the agreement of this series with previous studies the results may not be transferable to the developing world where trauma and HIV factor more heavily in the aetiology, even amongst paediatric abscesses (Nathoo *et al.*, 2011).

The presentation of brain abscesses is non-specific but most commonly includes, headache, fever, altered mental status, meningism and seizures (Chun *et al.*, 1986; Hakan *et al.*, 2006; Gelabert-Gonzalez *et al.*, 2008; Shachor-Meyouhas *et al.*, 2010; Felsenstein *et al.*, 2013; Patel and Clifford, 2014). The classic triad of headache, fever and focal neurology is only found in 8-16% (Shachor-Meyouhas *et al.*, 2010; Canpolat *et al.*, 2015; Sahbudak Bal *et al.*, 2018) and thus is unreliable for diagnosing brain abscess. Those who present with altered mental status and rapid neurological deterioration are more likely to have an increased mortality rate (Mampalam and Rosenblum, 1988; Seydoux and Francioli, 1992). The majority of the patients in this study presented with a good level of consciousness, contributing to the zero mortality rate.

The treatment approach to brain abscesses has classically been either burr hole aspirations or abscess excisions followed by a long course of antibiotics. However, Goodkin *et al.* included cases of treatment using antibiotics alone for abscess <2cm in diameter, multiple abscesses in a neonate or those in multi-system organ failure; however the mortality rate was 42% in this sub-group (Goodkin *et al.*, 2004). Surgically inaccessible lesions, early cerebritis, multiple small abscesses and significant medical comorbidities would also be suitable for treatment with nonsurgical methods only. All of the patients in this series underwent surgical intervention with burr hole aspiration used as the preferred option. The one patient treated with antibiotics only failed medical management and subsequently required a craniotomy for surgical removal of the abscess. The advantage of surgical intervention is the ability to collect pus cultures and achieve a microbiological diagnosis that can inform antibiotic therapy. Despite the consensus for surgical drainage of the abscess, there is no agreement on the post-surgical care for these patients. The duration of antibiotic therapy, the choice between oral and intravenous routes of delivery, and the intervals and duration of surveillance imaging are all still debated (Felsenstein *et al.*, 2013).

The disadvantage of burr hole aspiration compared to excision is that the abscess can re-collect and require multiple operations. Multiple aspirations were associated with a larger initial abscess volume. These will leave a larger cavity that is slower to involute and thus leave a nidus of infection that can re-accumulate. Half of the patients in this series required more than one aspiration and thus patients should be counselled accordingly. Capsulectomy was reserved only for complex abscesses or patients undergoing craniotomy for another purpose. The use of multiple less-invasive operations rather than routine use of capsulectomy is supported by the high rate of good functional outcomes and the absence of any deaths. There are conflicting reports on whether mortality rates have improved in the post-CT era (Tekkök and Erbengi, 1992; Tandon *et al.*, 2009) or remained stable (Goodkin *et al.*, 2004). Modern series report lower mortality rates than the pre-CT era ranging from 8 to 25% (Xiao *et al.*, 2005; Hakan *et al.*, 2006; Auvichayapat *et al.*, 2007; Canpolat *et al.*, 2015) and the large series by Tekkok and Erbengi (Tekkök and Erbengi, 1992) even managed 0% mortality at the end of their study period. Thus whilst the favourable mortality rate in this series is an outlier, there is a precedent for such a result.

One reason for a low mortality rate may be an aggressive approach towards abscess drainage and also sepsis source control. Furthermore, close working relationships between paediatric intensive care and neurosurgery, as well as the proactive approach of the Southampton and Oxford Retrieval Team may result in patients being transferred to specialist centres sooner, before experiencing major neurological deterioration.

Limitations of this study include its retrospective design which is at risk of incomplete data reporting or patient selection. Furthermore, incorrect coding of patients could result in missing patients. The medical and imaging records are incomplete towards the beginning time period of this series and the series itself is relatively small due to the uncommon nature of the condition. Both of these points could be addressed with prospective multi-centre collaborative studies in the future.

**Conclusion**

This study demonstrates that in the modern era with ready access to CT imaging and broad spectrum antibiotics, low rates of morbidity and mortality can be achieved. Surgical drainage/excision of paediatric abscesses remain the mainstay of treatment both to relieve mass effect and provide a microbiological diagnosis. Patients and their families should be counselled to expect multiple procedures however good, anticipated good outcomes should not be overstated based on this study, due to the low patient numbers.

**Declaration of interest**

The authors have no conflicts of interest to declare.

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