Comparison of medical and/or surgical management of 23 cats with intracranial empyema or abscessation

Sophie Martin[1], Randi Drees[1], Balazs Szladovits[2] and Elsa Beltran[1]

[1]Department of Clinical Science and Services, [2]Department of Pathobiology and Population Sciences, Royal Veterinary College, Hatfield, UK

Corresponding author:
Elsa Beltran Ldo Vet, DipECVN, MRCVS
Department of Clinical Science and Services, Royal Veterinary College, Hawkshead Lane, Hatfield, Hertfordshire, AL9 7TA, UK
Email: ebeltran@rvc.ac.uk
Phone number: 01707 666333

Key Words:
Intracranial empyema, intracranial abscessation, feline, otitis media, otitis interna, craniectomy

Objectives

Feline intracranial abscessation or empyema is infrequently reported in veterinary literature, to date the largest study is based on a population of 11 cats with otogenic infection. The aim of this study is to review a larger population of cats with intracranial empyema from multiple aetiologies and document their signalment, imaging findings, treatment protocols including medical and/or surgical management and compare outcomes.

Methods

Cases presenting to a single referral centre over a ten-year period with compatible history, neurological signs and imaging findings consistent with intracranial abscessation and empyema were reviewed retrospectively.

Results

Twenty-three cats met the inclusion criteria. Advanced imaging (CT and/or MRI) was performed in 22/23 cats, one case was diagnosed via ultrasound. Ten cases underwent medical and surgical management combined, ten underwent solely medical management and 3 were euthanised at the time of diagnosis. Short-term outcome showed that 90% of surgically managed and 80% of medically managed cats were alive at 48 hours post-diagnosis. Long-term survival showed that surgically managed cases and medically managed cases had a median survival time of 730 days (range 1-3802 days) and 183 days (range 1-1216 days) respectively. No statistical significance in short or long-term survival ($P>0.05$) was found between medically and surgically managed groups.

Conclusions and relevance

Feline intracranial abscessation and empyema are uncommon conditions that have historically been treated with combined surgical and medical management. This study documents that in some cases, intracranial abscessation and empyema can also be successfully treated with medical management alone.

Introduction

Intracranial abscessation (intra-axial collection of purulent material, IA) and intracranial empyema (suppuration within a pre-existing anatomical cavity, IE) arise as a consequence of bacterial infection within the cranial cavity.[1,2] IA and IE is infrequently seen in cats. Infection originating from local extension (eg, adjacent spread from the eyes, ears and sinuses), haematogenous spread, secondary to trauma (eg, skull fractures, penetrating foreign bodies) and iatrogenic infection are reported in the literature.[3–7] These cases present with a wide range of neurological deficits due to the inflammatory response induced by the bacteria and/or secondary mass effect. Both aerobic and anaerobic bacteria have been isolated, with culture results typically yielding polymicrobial growth.[3,7–9]

IA and IE are severe and life-threatening diseases requiring emergency intervention; mortality rates as high as 100% have been reported.[8,10] Treatment modalities consist of medical treatment with broad-spectrum antibiotics and supportive care, or combined medical and surgical intervention via craniectomy.[3–5,11] Little information is currently available as to which treatment modality carries the most favourable prognosis.

The aim of this study is to describe medical and surgical treatment protocols for IA and IE and compare their effect on short and long-term survival in feline patients.

Materials and Methods

Ethical approval was granted by the Clinical Research Ethical Review Board at the Royal Veterinary College (RVC). Cats presenting to the RVC Queen Mother Hospital between April 2008 and August 2017 that had been diagnosed or treated for possible IA and/or IE were reviewed retrospectively. Terms entered into the search engine database included: 'intracranial empyema', 'intracranial abscess', 'meningoencephalitis' and 'otitis media/interna'.

Cats were included in the study if they had complete clinical records with MR images, CT or ultrasound findings consistent with IA and/or IE. Data was collected regarding signalment, history and previous treatment prior to referral. All cases were required to have full medical records and a documented neurological examination upon presentation. Pyrexia was defined by a rectal temperature over 39.2^{o}C.[12] Disease progression, imaging findings, additional diagnostics and therapeutics were recorded for the study. Where available, ancillary test results such as feline immunodeficiency virus (FIV) and feline leukaemia virus (FeLV) status, cerebrospinal fluid (CSF) analysis and CSF and surgical swab culture and sensitivity results were collected.

CT images were obtained using a Philips MX8000 16 MDCT unit, with 1.5mm slice thickness for brain and 1-2mm slice thickness for head sequences. Pre- and post-contrast exams were performed, with bone and soft tissue recons. All MRI images were obtained using a 1.5 Tesla Intera System (Philips Medical Systems). Each cat had a minimum series including pre- and post-gadolinium contrast T1-weighted (T1W) series and T2-weighted (T2W) series in transverse and sagittal planes and fluid-attenuated inversion recovery (FLAIR) sequences.

All images were independently reviewed by a board-certified veterinary neurologist and board-certified veterinary radiologist. A diagnosis of IA and/or IE was described further by location (intra/extra axial lesion and corresponding area of the brain), heterogenous or homogenous contrast enhancement, demarcation to surrounding tissues and secondary overlying soft tissue changes. Evidence of skull fractures and raised intracranial pressure such as midline shift, herniation through a craniotomy defect, caudal transtentorial, subfalcine and foramen magnum herniation were recorded.[13]

Cats were subsequently divided into solely medically treated or combined surgically and medically treated groups. Only those cases treated via craniectomy were defined as surgically treated, cases undergoing any other form of surgery (e.g. ventral bulla osteotomy) were therefore categorised as medically managed.

Information regarding outcome was obtained via telephone consultation with the referring veterinarian and/or owner, combined with the referring vet clinical records and findings of re-examination appointments at the RVC. Short-term outcome was reviewed at 48 hours (h) and one month after diagnosis, longer-term outcome was assessed at three and six months. Outcome was classified as alive or dead, but where available, survival was further categorised with a 1-3 grading system alongside neurological examination findings. The grading system is as follows; Grade 1 was given if cats returned to being neurologically normal, Grade 2 was defined as persistent mild neurological deficits that did not affect the normal ambulation and behaviour of the cat, Grade 3 was defined as persistent neurological abnormalities that significantly affected the patients' ability to ambulate and display normal behaviours.

The two-tailed Fisher's Exact Test was used to ascertain the significance of short and long-term survival between surgically and medically managed groups. Other variables assessed included the effect of empyema location, use of steroids, and the development of seizures upon outcome.

Results

A total of 27 cats presented to the Queen Mother Hospital for Animals between April 2008 and August 2017. One cat was excluded as initial diagnostics and surgery were performed at an alternative referral centre, a second cat was excluded due to a lack of

pre-operative imaging. A further two cats were excluded as they failed to fulfil the imaging criteria of IA and/or IE. Twenty-three cats were included in the study population.

The included cats had a median age of 7.4 years at presentation (range 7 months-16 years) and had a male predominance with 15 neutered males (65.3%), two entire males (8.7%), five neutered females (21.7%) and one entire female (4.3%). Male cats were overrepresented in comparison to the hospital population over the same time period. Cats encompassed a range of breeds including Domestic Shorthair (n=13), Domestic Mediumhair (n=1), Domestic Longhair (n=4), Bengal (n=2), British Shorthair (n=1), Siamese (n=1) and Exotic Shorthair (n=1).

Clinical Signs at Presentation

Cats had a variable duration of clinical signs prior to presentation reflecting the underlying aetiology and location of the IA and/or IE. Cats presenting with IE due to otitis media/interna (OMI) generally had a longer history (median duration 34 days, range 7-183 days) compared with other aetiologies such as trauma (median duration 6 days, range 2-21days). A history of cat bites and associated abscessation was the most common finding, reported in 13/23 cases, 11 of which were male.

Only two cats had normal clinical examination findings on presentation. Nine cats had

visible wounds on their heads with two of these still actively discharging purulent material. Six cats had concurrent grade II-III/IV (n=5) heart murmurs or a gallop rhythm (n=1) on auscultation. These cats did not have a history of cardiac disease and no further cardiac assessment was performed at the time of presentation. Two cats had unilateral serous nasal discharge and one cat bilateral purulent nasal discharge with stertor. One cat had aural discharge and otitis externa noted on clinical examination, with concurrent Horner's syndrome ipsilateral to the otitis.

Other clinical examination findings included tachycardia (n=10), tachypnoea (n=3), pale mucous membranes (n=2) and a dull or quiet demeanour (n=9). Rectal temperature was recorded in 21/23 cats; two cats were pyrexic at presentation, a further five cats had pyrexia documented prior to referral but had recently received anti-inflammatory medication (non-steroidal anti-inflammatory drugs (NSAIDs) or anti-inflammatory doses of steroids).

Neurological Examination Findings at Presentation

All cats had a history of progressive, multifocal neurological dysfunction that reflected the location of their IA and/or IE. The most common neurolocalisation was to the forebrain, commonly described examination findings included altered mental status and an absent menace response (Table 1). Seizure activity was infrequently reported; two cats exhibited generalised seizures and one partial seizures prior to referral.

Table 1 Neurological exam findings

Imaging

MR images were available for 21 cats. Fourteen cats had extra-axial lesions consistent with IE, four intra-axial IA and three had findings compatible with IA and IE (Table 2). Distribution was classified as forebrain (13), brainstem (4), cerebellar (1) or multifocal (3); and localisation further described by affected lobes of the cerebrum. Specifically the temporal (14) and frontal (10) lobes were the most affected. Solitary and well-defined lesions were the most common finding in 18/21 cats. Nine cats had concurrent overlying bite wounds, of these seven had associated skull fractures. In two cases nasal infection with associated sinus pathology was visible.

Lesions had an overall mixed homogenous and heterogeneous appearance on T1 and T2W images. All lesions were hyper-intense to normal grey matter on T2W series and partially suppressed on FLAIR series. Post-gadolinium contrast uptake was present in all cases and heterogeneous in all but 3/21 cases, eight cats had evidence of rim enhancement. Changes consistent with mass effect suggestive of raised intracranial pressure were visible in all cases.

Figure 1 MR T2-weighted transverse image

Table 2 MR imaging findings of 21 cats

CT exams were available for four cases, lesion location included the forebrain (1), cerebellum (1) and brainstem (2) and was further defined as extra-axial (3) or mixed intra and extra-axial (1). All lesions were hypo-attenuating pre-contrast, with heterogeneous rim enhancement post contrast. Three of the cats had well demarcated lesions with concurrent mass effect. Concurrent findings included otitis media (n=2) and abscessated overlying soft tissues.

Figure 2 Transverse CT images

One case was diagnosed via ultrasonography; flocculent material was observed passing between the subcutaneous space and the cranium via a defect in the overlying skull (Figure 3).

Figure 3 Ultrasound image

Ancillary Tests

Haematology results were available for 12 cats; only two had mild to moderate inflammatory neutrophilias with evidence of mild left shift and/or toxicity, six had leukograms most consistent with glucocorticoid response and four had values all within

reference intervals. FIV and FeLV status was available for seven cats, all of which were negative for both diseases.

Cerebrospinal Fluid Analysis

Four out of 23 cats had CSF analysis (three from the cerebellomedullary cistern and one from the lumbar cistern) performed, all of which demonstrated neutrophilic inflammation. Two out of 4 cats had increased total nucleated cell count (TNCC 1005/uL, 1310/uL) and total protein concentration (0.79 g/L, 2.21 g/L). Intracellular bacteria were identified on cytology in 2 cats (Figure 4) When cultured in enrichment medium, one cat had a growth of coagulase-negative *Staphylococcus spp.*, the second cat had insufficient sample for culture however a polymicrobial infection with gram-positive organisms was identified from direct smears.

Figure 4 Cytology image of cerebrospinal fluid

Culture Results

Bacterial culture yielded growth in 1/3 CSF samples and 6/9 samples taken at the time of craniectomy. Isolated bacteria encompassed both aerobic and anaerobic species including *Escherichia, Corynebacterium, Bacteroides, Streptococcus, Staphylococcus, Actinomyces, Nocardia* and *Enterococcus* species. Polymicrobial growth occurred in two cases.

Treatment

Prior to referral, 13/23 cats had been treated with a range of both broad and narrow spectrum antibiotics for variable duration. Eight of which had also been given either NSAIDs, or anti-inflammatory or immunosuppressive doses of steroids (dexamethasone) but exhibited no improvement in their clinical signs.

Treatment groups consisted of solely medically treated (10/23) or combined medically and surgically treated (10/23) cats. Three out of 23 cats were euthanised at the time of diagnosis but were included for descriptive purposes. Surgically managed cases and medically managed cases were hospitalised for a median duration of 6 and 5 days, respectively.

Antibiosis

All treated cases received broad-spectrum antibiosis; amoxicillin clavulanic acid (20mg/kg q12h) was the most common agent used (17/20 cases). Metronidazole (10-25mg/kg q12h) was the most common second agent used and was administered to 10 cats. Antibiosis chosen was clinician dependant or influenced by antibiosis given prior to referral, with a combination of up to four types of antibiotic used for a variable duration of 4 to 16 weeks.

Steroids

Twelve out of 20 cats received anti-inflammatory doses of dexamethasone ranging from 0.1-0.3mg/kg intravenously (median dose 0.15mg/kg) as either a single intra-operative dose or up to three days.[14]

Anti-epileptics

Seven cats received anti-epileptic medication consisting of phenobarbital (2-3mg/kg q12h) and/or levetiracetam (20mg/kg q8h followed by 20mg/kg q12h dosing) post-operatively. Four cats were treated for seizure activity and three received prophylactic anti-epileptic medication.

Outcome

Of the surgically managed group, most (90%) cats had a good short-term prognosis (survived 48 h post-operatively). One case failed to regain spontaneous ventilation after surgery and was euthanised. All 9/10 remaining cats were alive 6 months post-operatively and had a Grade 1 neurological status. The median survival time for surgically managed cases was 730 days (range 1-3802 days). One cat was euthanised 7 years after diagnosis due to development of seizures and deterioration to status epilepticus; repeat imaging was not performed prior to euthanasia.

The medically managed group had a similar short-term prognosis, with 80% of cases surviving the first 48 h after diagnosis. Of the two cases that did not survive, one had

cardiopulmonary arrest whilst receiving treatment and another was euthanised after 24 h of medical therapy due to financial constraints. Six-month survival information was available for the eight remaining medically managed cats. Six out of 8 cats had good long-term outcome, all of which were reported to be neurologically normal (grade 1). Medically managed cases had a median survival time of 183 days (range 1-1216 days).

It is important to note that two cats, one of each treatment group, were still alive at the time of writing this paper.

Figure 5 Kaplan Meier curve

Two-tailed Fisher's Exact Test demonstrated no statistical significance in short or long-term survival ($P>0.05$) between surgically and medically managed groups. The empyema location, use of steroids, and the development of seizures were also not statistically significant when compared to outcome.

Discussion

To the authors' knowledge, this study is the largest of its kind in cats. Six studies and four case reports within the literature describe IA and/or IE in 47 cats in total, with variable aetiologies including cat bites, haematogenous spread, fungal infection and OMI. Of these, 11 cats were treated surgically and 35 medically with overall short-term mortality

of 27% and 26%, respectively. The outcomes of each treatment group in this paper demonstrate a lower mortality rate than that of the literature.[3–11,15]

Interestingly, the described treatment regimens for IA and IE in the human literature typically involve a surgical approach.[16] Human patients are treated via burr holes, a small craniectomy or craniotomy to facilitate drainage of pustular material and irrigation with antibiotics.[17,18] Published reports evaluating solely medical management in humans do exist, with some reporting a favourable prognosis comparable to that of surgical intervention.[19] The over-representation of males in this study was also found to be a consistent finding with human literature.[16,17] Male cats typically presented with IA and/or IE secondary to cat bite abscesses overlying their calvarium; we hypothesised this finding may be due to the increased likelihood of entire male cats to fight and roam larger areas.

The absence of prominent inflammatory leukogram changes (marked neutrophilia or neutropenia) on haematology, and absence of pyrexia upon physical examination in the majority of cases is consistent with previous reports.[4,6,7] This may reflect a lack of systemic response to intracranial infection; it is important therefore that IA and IE is still considered as a differential in normothermic cases without peripheral neutrophilia .

As with other case reports, CSF analysis was rarely undertaken, likely due to a greater risk of complications when performing this procedure in cases with increased intracranial pressure.[5] When performed, CSF results consistently demonstrated neutrophilic inflammation and were diagnostic (exhibited intracellular bacteria or had positive culture results) in two cases with empyema. Intracellular organisms are less frequently seen with intra-axial abscesses unless they have ruptured into the subdural space.[8] When available, CSF analysis provides valuable diagnostic information. It may be argued that these results are of more use in medically managed cases, as intra-operative findings and the ability to culture direct swabs taken at the time of craniectomy may make CSF findings redundant in surgical cases.

Reports of predisposition to both aerobic and anaerobic bacteria exist within the literature.[8] A mixed cohort of both aerobic and anaerobic isolates were identified in this study. This likely reflects the underlying aetiology of the IA and/or IE as both OMI and cat bite abscesses can yield polymicrobial growth.[20,21] In this study only 33% of CSF samples and 67% of surgical swabs yielded positive culture results; this finding is consistent with the existing literature.[22] A likely explanation for the high incidence of negative culture results may be that many cases were exposed to antibiotics prior to referral. Additionally, species such as *Actinomyces* and *Nocardia* often require extended cultures and therefore may give false negative results.[23]

Potentiated amoxicillin and metronidazole were the two most commonly prescribed antibiotics whilst pending culture and sensitivity results. These broad-spectrum antimicrobials provide activity against aerobic and anaerobic bacteria. When selecting antibiotics in these cases, consideration must be given to penetration of agents across the blood-brain barrier to allow therapeutic concentrations to be reached within the CSF. High intravenous doses of beta-lactam antibiotics and metronidazole both readily penetrate the blood-brain barrier and therefore are suitable choices for intracranial infections, a likely explanation for their frequent use in this study.[24] Consideration should also be given to the duration of antibiotics prescribed, as our results showed a large variation from four to 16 week courses. A minimum course of 6-8 weeks is advised to treat IA within humans, alongside surgical drainage of the abscess.[25,26]

In this study, IA and/or IE was typically localised to the forebrain, likely due to the overlying tissues being a common site of cat bite injury. Of the 11 cases that received treatment, eight were managed surgically. Perhaps, the comparative ease of a craniectomy to access the forebrain led to surgical treatment being the favoured choice.

Brainstem IE was infrequently documented and associated with infection spread from OMI or retrobulbar disease. Conversely, these cats were all managed medically, likely due to the challenging nature of a craniectomy at the skull base. Two out of 4 cases died

399 or were euthanised within three months. Our findings demonstrated a more favourable
400 50% mortality than those of Klopp *et al.* 18 years previously, who found 100% mortality
401 in two cats with brainstem abscessation.[10]

402

403 Limitations of this retrospective study include a possible inherent bias between treatment
404 groups as cases were not randomly allocated. Information regarding decision making
405 between different treatment modalities was not available for all cases. Those cases
406 managed medically may have had other prognostic factors associated with their
407 treatment choice; such as advanced disease, patient instability or financial limitations.

408

409 Analysing IA/IE secondary to multiple aetiologies may also make interpretation of
410 results challenging, as analysis of one aetiology alone may have yielded different results.
411 Furthermore, treatment regimens varied widely with inconsistent use of steroids, anti-
412 epileptic medication and type and duration of antibiotics. Follow up examination was
413 not always performed by a board-certified neurologist, therefore return to a
414 neurologically normal status was sometimes based upon referring veterinarian reports
415 or owner communication. This means milder persisting neurological deficits (Grade 2)
416 may have been missed in some cats.

417

418 Our results found no significant difference between survival of those cases managed
419 medically and those cases managed with combined surgical and medical therapy. These

results are however based upon a relatively small sample size. A larger study population will increase the statistical power and may yield different results; therefore, future work in the form of a multi-centric retrospective study is required. A prospective randomised control trial would provide the most reliable data, however due to the low prevalence of this disease would be challenging to conduct.

Conclusions

IA/IE is an uncommon disease in cats and often presents a challenging diagnosis due to its non-specific and variable clinical signs; if not diagnosed early it can prove fatal. This study suggests that IA/IE can be successfully treated with medical management alone.

Conflict of interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

Author Note

This paper was presented in part at the 2018 BSAVA conference

References

1. Tsou T-P, Lee P-I, Lu C-Y, et al. **Microbiology and epidemiology of brain abscess and subdural empyema in a medical center: a 10-year experience.** *Journal of microbiology, immunology, and infection* 2009; 42: 405–412.
2. Das AK, Jumani K, Kashyap RC. **Subdural empyema: A rare complication of chronic otitis media.** *Med J Armed Forces India* 2005; 61: 281–283.
3. Costanzo C, Garosi LS, Glass EN, et al. **Brain abscess in seven cats due to a bite wound: MRI findings, surgical management and outcome.** *J Feline Med Surg* 2011; 13: 672–680.
4. Cardy TJA, Lam R, Peters LM, et al. **Successful medical management of a domestic longhair cat with subdural intracranial empyema and multifocal pneumonia.** *J Vet Emerg Crit Care* 2017; 27: 238–242.
5. Sturges BK, Dickinson PJ, Kortz GD, et al. **Clinical signs, magnetic resonance imaging features, and outcome after surgical and medical treatment of otogenic intracranial infection in 11 cats and 4 dogs.** *J Vet Intern Med* 2006; 20: 648–656.
6. Barrs VR, Nicoll RG, Churcher RK, et al. **Intracranial empyema: Literature**

review and two novel cases in cats. *J Small Anim Pract* 2007; 48: 449–454.

7. Moore SA, Bentley RT, Carrera-Justiz S, et al. **Clinical features and short-term outcome of presumptive intracranial complications associated with otitis media/interna: a multi-center retrospective study of 19 cats (2009–2017).** *J Feline Med Surg* Epub ahead of print 2018. DOI: 10.1177/1098612X18764582.

8. Dow SW, LeCouteur RA, Henik RA, et al. **Central Nervous System Infection Associated With Anaerobic Bacteria in Two Dogs and Two Cats.** *J Vet Intern Med* 1988; 2: 171–176.

9. Blauvelt M, Weiss D, McVey A, et al. **Space-occupying lesion within the calvarium of a cat.** *Vet Clin Pathol* 2002; 31: 19–21.

10. Klopp LS, Hathcock JT, Sorjonen DC. **Magnetic resonance imaging features of brain stem abscessation in two cats.** *Vet Radiol Ultrasound* 2000; 41: 300–7.

11. Wouters EGH, Beukers M, Theyse LFH. **Surgical treatment of a cerebral brain abscess in a cat.** *Vet Comp Orthop Traumatol* 2011; 24: 72–75.

12. Quimby JM, Smith ML, Lunn KF. **Evaluation of the effects of hospital visit stress on physiologic parameters in the cat.** *J Feline Med Surg* 2011; 13: 733–737.

13. Lewis MJ, Olby NJ, Early PJ, et al. **Clinical and Diagnostic Imaging Features of Brain Herniation in Dogs and Cats.** *J Vet Intern Med* 2016; 30: 1672–1680.

14. Plumb DC. *Plumb's Veterinary Drug Handbook*. Eigth edit. Wiley Blackwell, 2015.

15. Espino L, Barreiro JD, Gonzalez A, et al. **Intracranial epidural empyema due to Cryptococcus neoformans in a 5-year-old neutered male European short hair cat.** *Vet Q* 2015; 35: 51–55.

16. Nathoo N, Nadvi SS, Van Dellen JR, et al. **Intracranial subdural empyemas in the era of computed tomography: A review of 699 cases.** *Neurosurgery* 1999; 44: 529–536.

17. Bok AP, Peter JC. **Subdural empyema: burr holes or craniotomy? A retrospective computerized tomography-era analysis of treatment in 90 cases.** *J Neurosurg* 1993; 78: 574–578.

18. Joubert MJ, Stephanov S. **Computerized tomography and surgical treatment in intracranial suppuration. Report of 30 consecutive unselected cases of brain abscess and subdural empyema.** *J Neurosurg* 1977; 47: 73–78.

19. Leys D, Destee A, Petit H, et al. **Management of subdural intracranial empyemas should not always require surgery.** *J Neurol Neurosurg Psychiatry* 1986; 49: 635–639.

20. Love DN, Malik R, Norris JM. **Bacteriological warfare amongst cats: What have we learned about cat bite infections?** *Veterinary Microbiology* 2000; 74: 179–193.

21. Cook LB, Bergman RL, Bahr A, et al. **Inflammatory polyp in the middle ear with secondary suppurative meningoencephalitis in a cat.** *Vet Radiol Ultrasound* 2003; 44: 648–651.

22. Menon S, Bharadwaj R, Chowdhary A, et al. **Current epidemiology of intracranial abscesses: A prospective 5 year study.** *J Med Microbiol* 2008; 57: 1259–1268.

23. Markey, BK Leonard, FC Cullinane, A Maguire, D Archambault M. *Clinical Veterinary Microbiology*. 2nd ed. Elsevier, 2013; 147–160.

24. Nau R, Sörgel F, Eiffert H. **Penetration of drugs through the blood-cerebrospinal fluid/blood-brain barrier for treatment of central nervous system infections.** *Clinical Microbiology Reviews* 2010; 23: 858–883.

25. Lu CH, Chang WN, Lui CC. **Strategies for the management of bacterial brain abscess.** *Journal of Clinical Neuroscience* 2006; 13: 979–985.

26. Black P, Graybill JR, Charache P. **Penetration of brain abscess by systemically administered antibiotics.** *J Neurosurg* 1973; 38: 705–709.