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An in Depth Look Into Intracranial Abscesses and Empyemas: a Ten-year Experience in a Single Institute

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ABSTRACT

Background: As the incidence of intracranial infections increase due to diagnostic procedures improvement, more real-life data is needed to reach a more solid informed management approach. **Objective:** This study aims to describe and analyse clinical features of intracranial abscesses patients treated at a tertiary hospital in North Jordan during a 10-year period. **Methods:** We retrospectively identified 37 patients treated at King Abdullah University Hospital (KAUH) from 2011 to 2020 in Irbid, North Jordan. Treatment consisted of either aspiration, open craniotomy excision (OCE) or conservative therapy. Extracted variables included demographic data such (age, gender), clinical presentation, lab findings, radiological findings as well as management plan. Retrieved data was compared between the patients who underwent a single operation and those who underwent reoperation after the initial procedure. **Results:** Thirty-seven patients with 55 intracerebral abscesses were identified, 29 of whom had intraparenchymal brain abscesses, 4 patients had epidural empyema, and 4 had subdural empyema. The mean age was 28.8 ($\pm$ 20.7) years, with a male predominance (78.4%). Sixteen patients underwent open craniotomy excision (OCE), 14 patients were treated by aspiration and 7 patients were treated conservatively. When comparing the single operation and the reoperation groups, there was no statistically significant difference across variables. **Conclusion:** Our study presents valuable insight from a tertiary hospital in north Jordan on intracranial abscesses and empyemas. Our findings confirm that good recovery can be established after aspiration or OCE in the majority of patients. Similar results were obtained when comparing the SOP and the ROP groups. **Keywords:** Neurosurgery, Brain abscess, Subdural empyema, Epidural aspiration, Open craniotomy excision.

1. BACKGROUND

Intracranial infections caused by bacterial pathogens can occur within the brain parenchyma as brain abscesses, between the dura and arachnoid mater as subdural empyema or between the dura mater and cranial bones as epidural empyema (1). Brain abscess is a focal area of necrosis that develops from a localized cerebritis to a well-vascularized capsule within the brain parenchyma as a result to bacterial or fungal infection while pus collection can also lead to subdural or epidural empyema (2).

For centuries, brain abscesses had high morbidity and mortality rates which dramatically decreased with advances of culturing methods, neuroimaging, neurosurgical techniques, and antibiotic treatments, resulting in an earlier diagnosis, accurate localization and better management (3, 4). However, it still threatens public health with an incidence of 0.4% to 0.9% worldwide, 1% to 2% in western countries and 8% of intracranial insults in developing countries (5, 6).

Vast majority of cases are due to predisposing factors that are consequently spread to the brain either by hematogenous spread through blood vessels in the subarachnoid space or contagiously through venous drainage. Suppurative intracranial infections can also result from direct injury to the skull such as opening or penetrating trauma or as post-operative complication (7). Understanding the aetiology of infection is very crucial in choosing the antimicrobial treatment regimens.

Primary treatment for brain abscess is still not definitively identified as numerous factors have to be considered depending on the patient clinical

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status and abscess stage, size and location (8). Empirical antibiotics are the mainstay of the management plan as they can be sufficient in case of abscesses smaller than 2.5 cm, while those larger than 2.5 cm should be excised or aspirated surgically (9).

Several studies advocate Open Craniotomy Excision (OCE) as it is associated with a lower incidence of recurrence, shorter hospitalization and faster improvement of neurological status (10), while aspiration is can be favoured due to its lower post-operative complications (11). Since craniotomy allows complete evacuation of the abscess and decompresses the underlying cerebral hemisphere, it has been considered superior to aspiration generally.

The status of intracranial abscesses and empyemas is still underreported in the middle eastern region, this leaves our understanding of the current and future trends in incidence and mortality at a vague base. As an attempt to fill this gap, this study presents a 10-year experience from a single tertiary institute in northern Jordan. Herein, we report the demographics, clinical features, microbial findings, management, and outcomes of intracranial suppurative infections. We further highlight the difference in clinical and laboratory findings between patients who underwent a single operation and those who had reoperations after the initial procedure.

2. OBJECTIVE

This study aims to describe and analyse clinical features of intracranial abscesses patients treated at a tertiary hospital in North Jordan during a 10-year period.

3. MATERIAL AND METHODS

Study design and Participants

We retrospectively reviewed patients diagnosed with brain abscess, epidural empyema, and subdural empyema and confirmed via Computed Tomography (CT) and/or Magnetic Resonance Imaging (MRI). at the King Abdullah University Hospital (KAUH) in Irbid, North Jordan from 2011 to 2020. Extracted data from the electronic hospital records included: Demographics data, clinical presentation, Glasgow Coma Scale (GCS) at admission and discharge, microbial and laboratory findings, radiological findings, management plan, recurrence and reoperation, complications, and length of hospital stay. Treatment outcome was assessed using the Glasgow Outcome Scale (GOS) upon last follow up. Favorable outcome was considered in patients achieving good recovery whereas unfavorable outcome was considered in dead, vegetative, moderate, or severely disabled patients.

The study was approved by the research Committee of the Faculty of Medicine and the Institutional Review Board of Jordan University of Science and Technology (JUST). This study was conducted according to the guidelines of Strengthening the reporting of cohort studies in surgery (STROCSS) 2019 (12).

Imaging Techniques

Preoperative CT and MRI with/without enhancement were applied to all patients. Diffusion-weighted imag-

ing (DWI) were conducted to rule out cystic or necrotic tumors and Positron Emission Tomography (PET) scans were used to reflect the degree of inflammatory response in abscesses. For conventional MRI, brain abscesses/empyemas were identified by hypointense signal in T1W1 and hyperintense signal in T2W2, with ring enhancement and extensive surrounding edema (Figure 1). At follow-up, all patients underwent a CT scan and MRI to assess abscess regression and to rule out recurrence.

Laboratory Findings

In all patients, standard laboratory tests were performed, including a White Blood Cells (WBCs) count, Erythrocyte Sedimentation Rate (ESR), C Reactive Protein (CRP), and sepsis workup including urine, sputum, and blood cultures. All intracranial pus samples obtained from aspiration or excision were immediately transferred to the microbiology lab.

Management

Empirical antimicrobial therapy including vancomycin, ceftriaxone, and metronidazole was given to all patients once the diagnosis was suspected. Treatment either remained the same or was changed after conducting susceptibility tests. Antibiotics therapy lasted for 6-8 weeks according to the therapeutic response and neuroimaging follow-up. Primary management consisted of either aspiration, OCE or conservative therapy. Stereotactic guided aspiration was preferred for deep abscesses or for patients that could not tolerate excision. OCE was recommended for [1] superficial abscesses, or [2] >2.5 cm abscesses, or [3] in cases of cerebral herniation signs, or [4] penetrating traumatic brain injury to remove foreign bodies, or [5] in some recurrent cases after aspiration. Conservative therapy was favored in [1] lesions smaller than 2.5 cm or [2] in case of deeply seated abscesses or [3] in patients with poor neurological background or [4] in multiple small abscesses. Corticosteroids were used to reduce cerebral edema and were discontinued in stabilized patients to avoid common side effects such as: intraventricular rupture, decreased antibiotic penetration and delayed capsule formation. Antiepileptic agents were administered prophylactically in case of cortical and subcortical brain abscess, patients presenting with first onset seizures upon admission, or patients undergoing surgical interventions. Reoperation was done in patients with significant abscess recurrence after the first procedure.

Statistical analysis

Summary statistics were demonstrated using means and Standard Deviations (SD) for continuous variables and compared using Student's t-test. Wilcoxon rank-sum test with continuity correction was used as a non-parametric alternative in data that were not normally distributed. Categorical variables were presented using frequency counts and percentages, and χ^2 test was used for associations. Fisher's exact test was used if cell count was less than 5. A two-sided p-value of 0.05 was considered statistically significant. Additionally, we calculated effect measures using Cramer's V for nominal variables and Cohen's D for continuous variables.

Cramer's V was interpreted as described by Kim H.Y.: (0.10–<0.30) as small effect, (0.30–< 0.50) as a medium effect, and (≥ 0.50) as a large effect (13). Cohen's D was interpreted based on recommendations by Rhea M.R. who defines (<0.35) as trivial effect, (0.35–0.80) as small effect, (0.80–1.5) as moderate effect and (>1.5) as large effect (14). All statistical analyses were done using R statistical language, version 4.0.3 (15).

4. RESULTS

Demographics and patient characteristics

Thirty-seven patients with 55 intracerebral abscesses were identified, 29 of whom had intraparenchymal brain abscesses, 4 patients had epidural empyema, and 4 had subdural empyema. The mean age was 28.8 (± 20.7) years, with a male predominance (78.4%). Patients' age ranged from 2 months to 76 years, 12 (32.4%) patients were pediatrics. Secondary immunodeficiency was present in 7 patients (18.9%): 4 had diabetes mellitus and 3 were on chemotherapy for cancer.

Presenting symptoms, diagnosis, and predisposing factors

Focal neurological deficits such as hemiparesis, ataxia, or aphasia, were the most common presenting symptoms (20 patients, 54.1%) followed by fever in 15 patients (40.5%), headache in 13 patients (35.1%) and seizure in 11 patients (29.7%). Classic triad of abscess presentation (fever, headache, and focal neurological deficit) was observed in 2 patients. Details on clinical presentation are provided in Table 1.

All patients underwent CT and MRI with contrast enhancement. The most frequent abscess location was the frontoparietal lobe in 16 patients (43.2%), followed by the temporoparietal and parietooccipital lobes equally (8 patients: 21.6% each). Eleven patients (29.7%) had multiple abscesses and abscesses were complicated by meningitis in 8 patients (21.6%) and ventriculitis in 3 patients (8.1%) and were more common in the pediatric age group. The mean maximum abscess diameter was 2.78 ± 1.99 cm.

The underlying source of the abscess was identified in 26 patients (70.3%), hematogenous spread occurred in 11 patients, 8 patients had a recent trauma, 3 patients had contiguous ear or sinus infection, and 4 patients had a recent cranial surgery.

Laboratory and Microbial Findings

In our cohort, WBCs, CRP, and ESR, were high in 52.9%, 75.9%, and 83.9% of the patients, respectively. Pus culture was positive in 14 patients. The most common species were staphylococcus (5 patients) and streptococcus (3 patients). *Morganella Morganii*, a rare aetiological pathogen, was found in one patient. Fungal infection caused by *Aspergillus Niger* was cultured in one case only. In a pediatric patient with a negative pus culture, post-operative pathological reports indicated an infection with *Toxocara Cati*. Details on cultured microorganisms are presented in Table 2.

Management and Outcomes

In our study, 16 patients underwent OCE, 14 patients were treated by aspiration, and 7 patients were

Patient Characteristics (N=37)	Overall (%)
Age	
Mean (SD)	28.8 (20.7)
Age groups	
0-18	12 (32.4%)
19-39	12 (32.4%)
40-59	11 (29.7%)
60-79	2 (5.4%)
Sex	
Male	29 (78.4%)
Female	8 (21.6%)
Presenting symptoms	
Fever	15 (40.5%)
Vomit	9 (24.3%)
Headache	13 (35.1%)
Loss of consciousness	8 (21.6%)
Focal neurological deficit	20 (54.1%)
WBC	
High	18 (52.9%)
Normal	16 (47.1%)
CRP	
High	22 (75.9%)
Normal	7 (24.1%)
ESR	
High	26 (83.9%)
Normal	5 (16.1%)
Neurological disorders	
Meningitis	8 (27.6%)
Seizure	11 (37.9%)
Epilepsy	3 (10.3%)
Stroke	1 (3.4%)
Tumor	3 (10.3%)
Ventriculitis	3 (10.3%)
Treatment	
Excision	16 (43.2%)
Aspiration	14 (37.8%)
Conservative*	7 (18.9%)
GCS upon admission	
15	26 (70.3%)
9-14	10 (27.0%)
8	1 (2.7%)
GCS upon discharge	
15	31 (86.1%)
9-14	4 (11.1%)
8	1 (2.8%)
Length of hospital stay	
Mean (SD)	35.8 (20.9)
WBC: White blood cells, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, GCS: Glasgow coma scale	

Table 1. Patient characteristics

treated with conservative treatment. After treatment, 34 patients (91.9%) had favorable outcomes based on consecutive MRI/CT scans in last follow-up, while the remaining 3 patients had unfavorable outcomes as they experienced moderate disability (8.1%). GCS upon discharge was 15 in 31 patients (83.8%), (9-14) in 4 patients

(10.8 %) and 8 in one patient (2.7 %). Seizure was the most common post-operative complication (8 patients) and hydrocephalus was observed in 2 patients.

Reoperation versus single procedure patients

Our sample was stratified based on the number of procedures; 19 patients had a single operation and 11 underwent reoperation of which; 5 patients had excision and 6 had aspiration as the initial procedure. Table 3 includes details on comparison between the single operation and reoperation group. The reoperation surgery was aspiration in 9 patients and excision in 2 patients. Male prevalence was slightly higher in the reoperation group but was not significantly different (88.9% vs 68.4%, $P = 1.000$, Cramer's $V = 0.054$ "trivial effect"). Mean age was 3.3 years higher in the single-operation group but was statistically insignificant ($P = 0.634$, Cohen's $D = <0.001$ "trivial effect").

Patients from the reoperation group presented with higher rates of loss of consciousness (36.4% vs. 15.4%; $P = 0.203$) and lower rates of headache (27.3% vs. 38.5%; $p=0.711$) without statistical significance and low trivial effect measures (Cramer's $V = 0.233$ and 0.107 respectively). Rates of other presenting symptoms were remarkably similar for the two groups. We found no difference in the number of patients with elevated ESR, CRP and WBCs count. Twelve of our patients were pediatrics, 4 of them had a reoperation.

The most common location was the frontoparietal lobe in both groups (45.5% and 42.3%). Mean hospital stay was 16.2 days longer in the reoperation group ($P = 0.117$, Cohen's $D = 0.815$ "moderate effect"). Mean maximum diameter of the abscess/empyema was larger in the reoperation group but without statistical significance (3.87 cm vs 2.34 cm; $P = 0.127$, Cohen's $D = .808$ "moderate effect", Figure 2) GCS was notably higher in the single operation group upon admission (GCS 15: 76.9 % vs 54.5%), yet all reoperation patients had GCS 15 upon discharge after the second procedure.

In our cohort, 3 patients (2 males and 1 female) had unfavorable outcome as they had moderate disability as illustrated in table 4. All 3 had a frontoparietal abscess. Two of whom were treated by aspiration and one patient was treated conservatively.

5. DISCUSSION

In this retrospective study we describe our hospital's 10-year experience in the management of brain abscess and empyema patients. Our study describes a cohort of 37 patients with a high percentage of male patients (78.4%) and a young mean age (28.8 years) which is relatively lower than described cohorts

Variables	Reoperation group (%) (N=11)	Single-operation group (%) (N=26)	P-value
Age			
Mean (SD)	26.5 (19.0)	29.8 (21.7)	0.647
Age groups			
0-18	4 (36.4%)	8 (30.8%)	-
19-39	3 (27.3%)	9 (34.6%)	
40-59	4 (36.4%)	7 (26.9%)	
60-79	0 (0%)	2 (7.7%)	
Sex			
Male	9 (81.8%)	20 (76.9%)	1.000
Female	2 (18.2%)	6 (23.1%)	
Presenting symptoms			
Fever	6 (54.5%)	9 (34.6%)	0.685
Vomit	4 (36.4%)	5 (19.2%)	
Headache	3 (27.3%)	10 (38.5%)	
Loss of consciousness	4 (36.4%)	4 (15.4%)	
Focal neurological deficit	6 (54.5%)	14 (53.8%)	
WBC			
High	5 (45.5%)	13 (56.5%)	0.812
Normal	6 (54.5%)	10 (43.5%)	
CRP			
High	8 (88.9)	14 (70)	0.631
Normal	1 (11.1)	6 (30)	
ESR			
High	10 (90.9)	16 (80)	0.382
Normal	1 (9.1)	4 (20)	
Neurological disorders			
Meningitis	2 (20)	6 (31.6)	-
Seizure	3 (30)	8 (42.1)	
Epilepsy	1 (10)	2 (10.5)	
Stroke	1 (10)	0 (0)	
Tumor	2 (20)	1 (5.3)	
Ventriculitis	1 (10)	2 (10.5)	
Treatment			
Excision	5 (45.5)	11 (57.9)	0.781
Aspiration	6 (54.5)	8 (42.1)	
Conservative*			
GCS upon admission			
15	6 (54.5)	20 (76.9)	-
9-14	4 (36.4)	6 (23.1)	
8	1 (9.1)	0 (0)	
GCS upon discharge			
15	11 (100)	20 (80.0)	-
9-14	0 (0)	4 (16.0)	
8	0 (0)	1 (4.0)	
Length of hospital stay			
Mean (SD)	47.2 (29.0)	31.0 (14.8)	0.122

WBC: White blood cells, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, GCS: Glasgow coma scale

Table 2. Patient characteristics upon clinical presentation classified upon reoperation.

in the literature; Lange et al. and Brouwer et al. reported a mean age of 58 and 34 years respectively (16,17). This can be owed to the high percentage of pediatrics in our sample compared to previous studies (18) and due to the

Microorganism	Overall (N=30) (%)
Bacterial	
Staphylococcus aureus	4 (13.3)
Streptococcus milleri	3 (10)
Escherichia coli	2 (6.7)
Coagulase-negative Staphylococcus sp.	1 (3.3)
Klebsiella pneumoniae	1 (3.3)
Morganella morganii	1 (3.3)
Proteus mirabilis	1 (3.3)
Fungal	
Aspergillus niger	1 (3.3)
No growth	16 (53.3)

Table 3. Frequency counts for microorganisms

fact that Jordan has relatively young age group population with a median age of 23.8 (19).

The majority of patients underwent a surgical procedure and the need for reoperation was comparable between both aspiration and OCE cases. In return, this can favor prioritizing aspiration over OCE as the latter is associated with a higher complication rate (6). This is further indicated in a multi-national based study in France and the United Kingdom, as they recommend abscess aspiration as a primary modality of treatment, and excision in case of recurrence (20). Wu et al. showed that patients who underwent aspiration tended to experience reoperation, while OCE was related to surgery complications (6). Another study demonstrated that excision was found to be better than aspiration in terms of length of hospital stay (10). While Gadgil et al. found similar GOS rates between patients who underwent excision and aspiration (21). Overall, the choice of treatment seems to call for a case-by-case decision making, since the available evidence is mainly taken from case series studies rather than well designed clinical trials for the sole purpose of detecting differences in outcomes after taking into account the clinical conditions of patients (22).

In our sample, patients undergoing reoperation did not have clear distinguishable features compared to single operation patients. Maximum abscess diameter was higher in patients who underwent a second procedure which may explain the recurrence of abscess formation in the first place. Wu et al. assured in their study that the surgical method plays a crucial role in predicting post-surgical complications and reoperation (6), they found that reoperation was more likely to be needed in patients who underwent aspiration, and that excision yields better clinical outcomes and more complications. In addition, due to the wide variety in the causative aetiological agents of brain abscesses, all patients need an empirical therapy and are recommended to undergo adjunctive systemic antibiotics management especially in cases of local and remote infections (1,7,17).

In regard to the cultured microorganisms from pus samples, Staphylococcus and Streptococcus species have been the most frequent within our cohort (28.6% and 21.4% from patients with positive cultures), this is in accordance with reported findings in the literature. (2,23). Within Streptococcus species, Streptococcus milleri group (Streptococcus intermedius, constellatus, and anginosus) was found to be the most common isolated microorganism (24), and this is compatible with the outcomes provided by a cohort of 82 patients reported by Zhang et al. and another series done by Carpenter et al. (25). One patient was infected by Morganella Morganii which is an extremely rare pathogen to cause CNS infections via otogenic spread. Similar cases in the literature report similar findings in brain abscesses caused

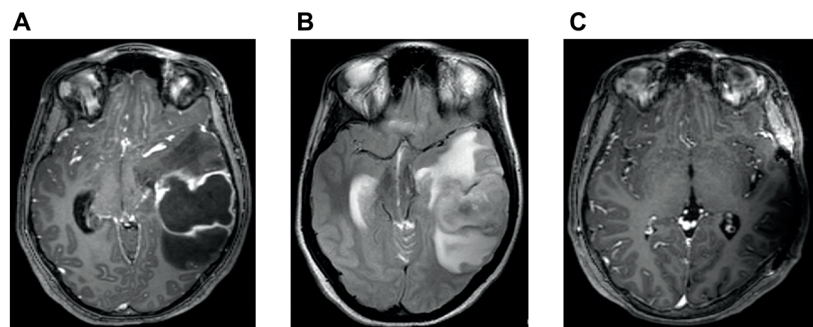


Figure 1. Axial MRI in a patient with a cortical left temporoparietal abscess. A: Contrast-enhanced T1- weighted imaging shows a hypointense necrotic center with pus, ring-shaped enhancement of the abscess wall, and a zone of edema surrounding the abscess. B: T2 weighted imaging showing a hyperintense signal C: A post-operative imaging showing the complete evacuation of the abscess.

by *M. morganii*, all were secondary to otogenic infection (26–28). Hence, in brain abscess patients being treated for otitis media, *M. morganii* must be highly suspected.

Prognostic factors of brain abscess vary across previous studies. A key factor affecting prognosis and mortality in patients suffering brain abscess is the initial Glasgow Coma Score (GCS) (29). A plethora of studies have found that low GCS score at admission is linked with greater likelihood of unfavorable outcomes (30–33). In the present study, patients with unfavorable outcomes had high initial GCS scores. However, their poor outcomes may be attributed to the presenting symptoms they already came with and underlying comorbidities (Focal neurological deficit, Epilepsy). This aforementioned cause was emphasized using Charlson scale in a recent retrospective cohort study conducted by Asquer-Khati et al. on 109 patients (32). A study done in Pakistan concluded that being in the second or forth decade of life makes you more susceptible in terms of post-operative morbidity and mortality (34) and this was in line with two patients whom outcomes were unfavorable in our study. A study done in Denmark found that immuno-compromised status was also an important determinant of poor outcome (18). These findings were also emphasized in Xiao et al. study with 2.8-fold risk in immunocompromised patients (35). Nevertheless, ade-

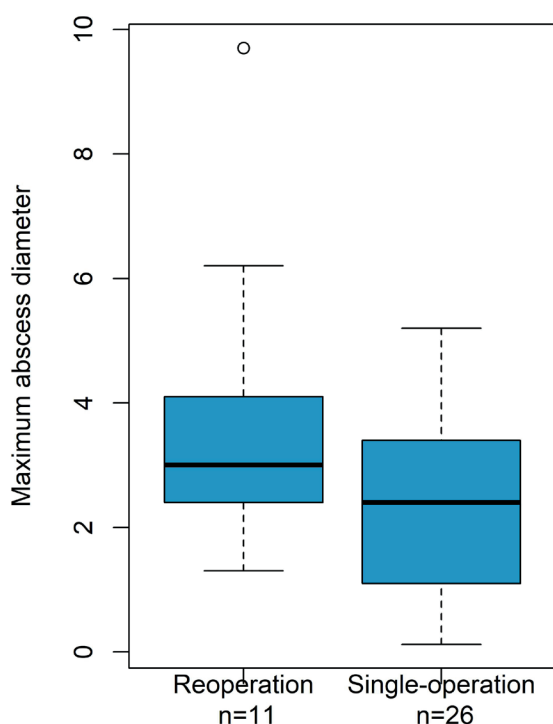


Figure 2. Box-and-whisker plot for maximum abscess diameter across the reoperation and the single-operation groups. Reoperation mean = 3.87 ± 2.58 cm, median = 3 cm; Single operation mean = 2.34 ± 1.55 cm, median = 2.4 cm. Reoperation summary measures remain higher than single-operation even after post-hoc removal of outlier patients who had maximum abscess diameters of 9.7 and 6.2 cm from the reoperation group.

quate management and early diagnosis were believed to result in better prognosis (36).

Our study presents valuable insight on a clinical condition that is poorly reported in the Jordanian population. Some of the limitations of this study include the retrospective nature of the study, and the small sample size which is related to the study being based on a single institution, this makes it hard to generalize our findings to a broader population, therefore future national based multicentric studies with appropriate follow-up periods are needed to reflect a more comprehensive perspective on the landscape of intracranial infections in Jordan.

6. CONCLUSION

Our study presents the first insight from a tertiary hospital in north Jordan on intracerebral infections which can lead to devastating outcomes. Our findings confirm that good recovery can be established after aspiration or OCE in the majority of patients. Identifying the primary infection remains the mainstay of long-term infection control. Comparable results were obtained when

comparing the single operation and multiple operations groups.

- **Declaration of patient consent:** A waiver of patients' consents was approved from the IRB due to the retrospective nature of data collection.
- **Author's contribution:** SJ: Conceptualization, Project Administration, Data Collection, Data Analysis, Draft Writing, and Critical Revision. YA, LMK, HA: Data Collection, Draft Writing, and Critical Revision. SS: Data Analysis, Interpretation. MB, SD, OJ: Conceptualization, Data Collection, Draft Writing, and Critical Revision.
- **Conflict of Interest:** The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.
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