STUDY OF CLINICORADIOLOGICAL PROFILE AND SURGICALLY MANAGED 41 CASES OF INTRACRANIAL INFECTIONS IN A TERTIARY CARE INSTITUTE OF NORTH KERALA

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ABSTRACT Aims: The aim of our study were to present last 3 years case series of intracranial infections, its major clinical manifestation, radiological distribution and surgical management **Background:**Intracranial infections are serious and life threatening medical conditions. Spectrum of intracranial infections includes meningitis, encephalitis, ventriculitis to cerebritis/brain abscess and subdural empyema. **Methods:**We included 41 patients in our studies out of 45 total cases between 2017(Jan) to 2020(May). Patients information were found from department records and operative register. These patients were confirmed after surgical procedures. In our studies, 11 patients were female and 30 patients were male. The mean age distribution was 7month to 67 years. Out of 41 patients 33 had intracerebral abscesses (21 solitary abscesses and 12 having multiple abscesses) and 8 had subdural empyemas. All patients were underwent craniotomy and some craniectomy as surgical procedures followed by antibiotic regimen average 4-6 weeks including at-least 2weeks injectable based on culture or empirical. **Results:**Our results showing more predominant in male gender and most age group involved were third and fourth decade. Majority cases no definite infectious agents identified which constitute about 56%. Fungus and tubercular cause constitute 2.4% and 9.7%. Most common lobe involved was temporal lobe and the majority of patients underwent craniotomy with complete/partial capsule excision. Predominate clinical manifestations were headache(78%), fever(53.6%), Nausea/Vomiting(29.2%), Neurological deficits(19.5%), Seizure(19.5%). Different location of intracranial infections as follows Solitary brain abscess in 21%, multiple brain abscess in 12% and subdural empyema in 19.5%. Following surgery 63.4% were complete symptomatic free and 24.3% clinically improved and death in 12.1% **Conclusion:**Surgical treatment is the gold standard treatment available for brain abscess and craniotomy still holds the best method to address brain abscess and in particular to developing countries like India in terms of feasibility and cost effective.

KEYWORDS Brain abscess; subdural empyema; craniotomy; intracranial infection

Introduction

Spectrums of intracranial infection include meningitis, ventriculitis, encephalitis, Cerebritis/brain abscess, subdural or epidural empyema. Intracranial infection can extend from infection of contiguous structures (e.g., acute or chronic suppurative otitis media, osteomyelitis, dental infection, mastoiditis, sinusitis, etc.), secondary to hematogenous spread from a remote site (cyanotic congenital heart disease, lung infection, skin infection), after skull trauma or surgery and majority cases cryptogenic origin. We included brain abscess and subdural empyema in our study.

The incidence of brain abscess is approximately 8% of intracranial masses in developing countries and 1-2% in western countries. [1] At some centres, pediatric cases of Brain abscess account for almost 25% of all patients with brain abscess. [1] Infectious diseases are usually common in tropical countries. [1] Clinical presentations of intracranial infection vary significantly. Brain abscess is a focal, intracerebral infection that begins with a localized region of cerebritis, evolving into a discrete collection of pus surrounded by a well-vascularized capsule.[2]

Imaging features of a brain abscess depend on the stage at the time of imaging and the aetiology of infection. [3] Brain

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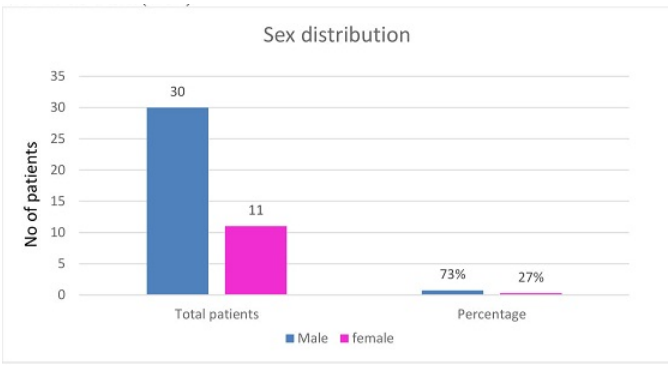

Figure 1 Sex distribution(n=41)

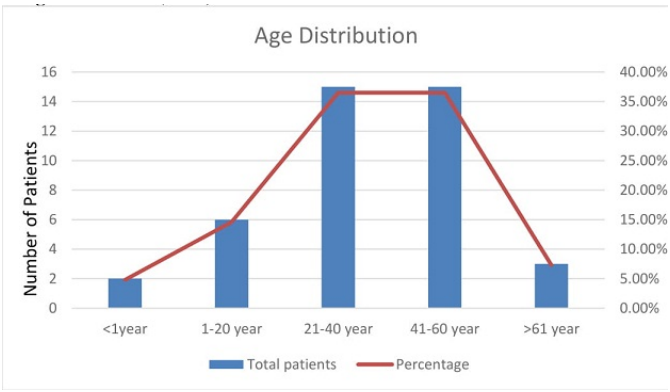

Figure 2 Age distribution(n=41)

abscess development can be divided into four stages: 1) early cerebritis (1 to 4 days); 2) late cerebritis (4 to 10 days); 3) early capsule formation (11 to 14 days); and 4) late capsule formation (>14 days) [26]. The majority of abscesses demonstrate considerable surrounding oedema, which generally presents during the late cerebritis or early capsule formation stage, secondary to mass effect. Hematogenous abscesses, which can be seen in the setting of endocarditis, cardiac shunts, or pulmonary vascular malformations, are usually multiple, identified at the grey-white junction, and located in the middle cerebral artery territory.

The most frequent brain abscess locations are the frontotemporal, frontoparietal, parietal, and occipital lobes and the cerebellum. Subdural empyema is also a pyogenic infection but is located between the dura and arachnoid maters. It is an uncommon condition, representing 15%–20% of confined intracranial diseases. [4] The most common cause is a previous neurosurgical procedure, such as a tumor or subdural hematoma surgery. Previous skull trauma and meningitis may also be responsible for subdural empyema. [4,5] Although brain abscesses are mostly

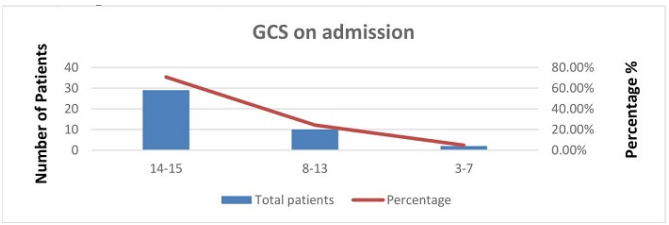

Figure 3 GCS (Glasgow Coma Scale) on admission(n=41)

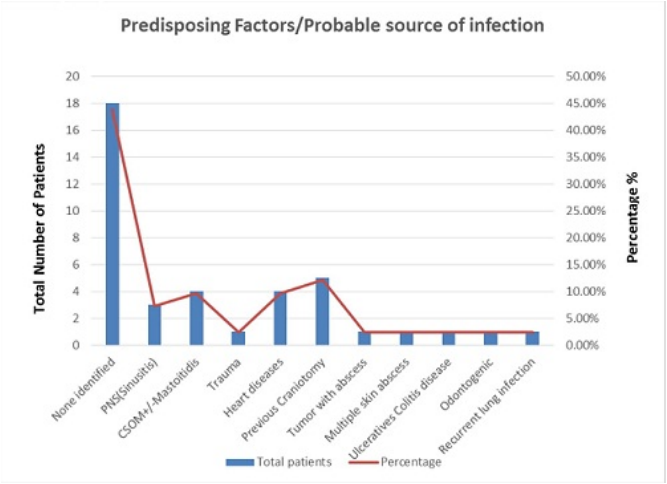

Figure 4 Predisposing factors (n=41)

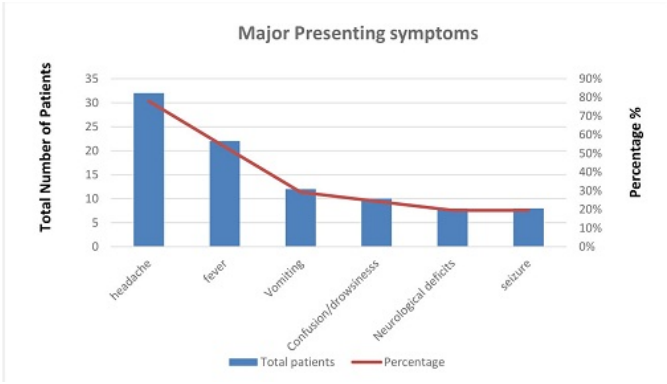

Figure 5 Major Presenting symptoms (n=41)

seen in adults, they may also present in childhood. [3] Major predisposing factors for developing a brain abscess are a close infection focus, hematogenous spread from a distant focus, and previous trauma. [1,6]

The microbiological aetiology of the abscess depends on many factors such as the site of primary infection, a patient's age and immunological condition, underlying diseases, and the geographic location of the patient. [7]

CT scanning and MRI are the two primary radiological modalities used for the detection of intracranial infections [1,8]

MRI is more sensitive, especially for evaluating CSF involvement, leptomeningitis, empyema, ventriculitis, vasculitis, and abscess. [2,7,9] Metastatic brain tumors and radiation necrosis are the most common conditions in the differential diagnosis of intracranial infections[7,10]

In our setting, we use CT scan brain with or without contrast investigation of choice as an emergency basis. However, in an elective setting, we prefer contrast MRI scans to differentiate other differential diagnoses viz; Metastasis, Cystic high-grade tumor, radiation necrosis, parasitic infection, etc. Current surgical treatment methods include craniotomy for resection or stereotactic aspiration of the abscess material.[11,12] In most instances, drainage of the purulent material is enough to initiate the healing of the intracranial infection. Also, there is no significant difference between excision and drainage alone regarding patient morbidity and mortality. However, excision is better than

Table 1

Study authors	Total cases studied	M: F	Meanage(age ranges)	No pre-disposing factors identified	Identified probable source (Predominant)
Tanon, et al[15]	100		49.06 (range 6-84)	32%	Iatrogenic=28% Haematogenous=17%
Chowdhury, et al [16]	162	3.37:1	42.5(3-72)	54.94%	CSOM/Mastoiditis=13.58% Sinusitis(F+E)=9.87%
Kural, et al [17]	52	2.68:1	40.46(10-75)	17%	Sinusitis 25% Prev craniotomy=20%
Kothari, et al[18]	715				Otogenic 67.5%(out of280) CHD=17.85% Post traumatic=5%
Our study	41	3.66:1	36.5(7m-67)	46.30%	Previous craniotomy=12% CSOM+/Mastoiditis=9.7% Sinusitis =9.7% Heart disease=9.7%

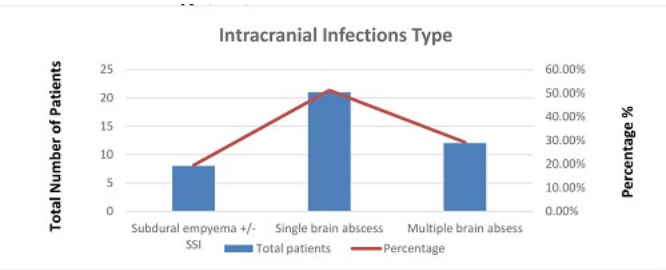

Figure 6 Intracranial infections type(n=41)

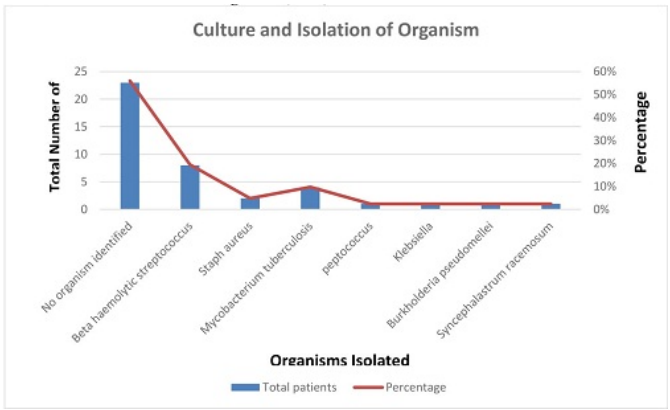

Figure 8 Culture and isolation of organism (n=41)

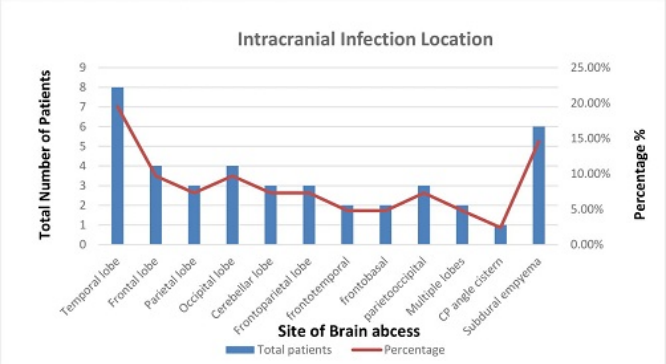

Figure 7 Intracranial Infection locations (n=41)

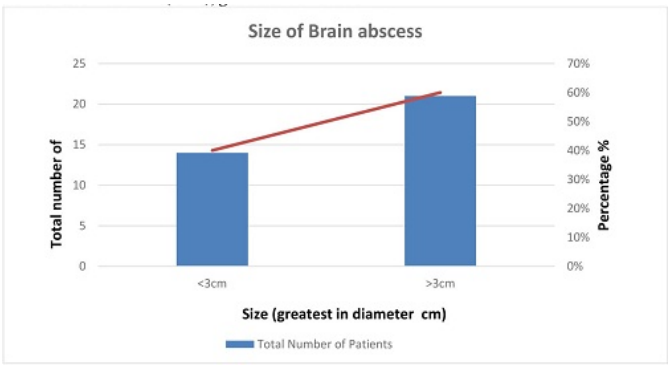

Figure 9 Size of brain abscess (n=35), greatest diameter in cm

Table 2

Study authors	Most common presentation	The most common site of abscess location	Abscess multiplicity	No organism isolated	Types of organism
Tanon ,et al[15]	Fever 79% Headache 59% Neurological deficits66% Seizure27%	Frontal=30.7% Parietal =26.7%	Single 75% Multiple25%	57%	Staphylococci (predominant)
Chowdhur y, et al [16]	An acute abscess(113) Headache=89.3 Fever67.5 Vomiting 38 Focal deficit31 Seizure22.6 A chronic abscess(49) Fever=51.7% Headache=100%	Frontal 30.2% Temporal 22.8%	Single 77.7% Multiple 36%	89.50%	Streptococcus (predominant)
Kural, et al[17]	Headache65% N/V 31% Confusion/Dro wsy=10% Neuro deficit=8% Seizures=6%	Frontal 29%	Single 27% Multiple8% Subdural empyema 65%	56%	Staphylococcus sp. (Predominant)
Kothari, et al[18]		Frontal 23.77% Temporal 20.83	Solitary 79.03% Multiple 20.97		
Our study	Headache=78% Fever=53.6% Vomiting=29.2% Confusion/dro wsiness=24.3% Neurodeficit=19.5% Seizure=19.5%	Temporal=19.5% Frontal=9.7%	Solitary=51.2% Multiple=29. 2%(Out of 33)	56%	Streptococcus sp.(Predominant)

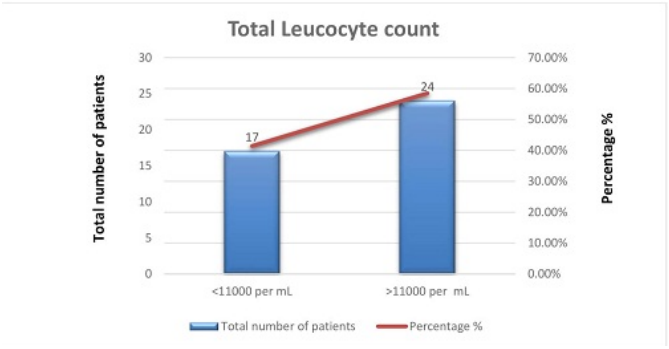

Figure 10 Total leucocyte count (n=41)

Figure 11 Mortality and morbidity (n=41)

Table III

Study authors	Total patients studied	Pyogenic abscess	Tubercular abscess	Fungal abscess	Tumor-associated with abscess
Chowdhury ,et al[16]	162	88.19%	14(8.64%)	3(aspergillus)	3(1.85%)metastasis
				0.018	
Kural, et al[17]	52	86.95%	nil	13%	nil
Kothari, et al [18]	715	39%	60%	1%	
Our study	41	85.36%	9.70%	2.40%	2.4%(High-grade glioma)

Table IV

Study authors	Mortality
Chowdhury, et al[16]	13.58%
Kural, et al[17]	1.92%
Zhang C, et al[1])	20%
Our study	12.1%

aspiration about the duration of antibiotic use, length of hospital stay, the overall cost of treatment and most importantly, recurrence. [7] Endoscopic approaches are being used for deep-seated abscesses. [13]. However, endoscopic or stereotactic methods will have difficulty in-wall sampling when the capsule is dense or strong, crucial for histopathological examinations.

Resection using craniotomy is usually the preferred technique for large, multiple abscesses causing mass effect or superficial lesions located in non-eloquent brain regions. [12,14]. Stereotactic aspiration is reserved for deep-seated abscesses or those located within or adjacent to eloquent regions.[1,10,13] We conducted a retrospective review of the intracranial infections treated in our Neurosurgery department over the past three years. We focused on patients with brain abscess and subdural empyema who underwent surgical intervention. Surgical techniques and postoperative outcomes, in particular, are presented and discussed.

Methods

Our study is a retrospective study conducted in the Neurosurgery department which is part of tertiary care institution located in the northern part of Kerala. Out of 46 patients diagnosed with Brain abscess, we selected 41 patients as five patients were not fulfilling our criteria for the study. We collected data of patient's information from department records and operation registers between 2017(Jan) to 2020(May). We considered different variables in our studies like age, sex, radiological distribution of intracranial infection, clinical characteristics, total leucocyte count, etc. Depending upon the pathology and may it be an acute or chronic presentation and GCS on admission radiological imaging CT scan and/or MRI had chosen. If there is an emergency CT scan with or without contrast, suffice to go for surgical intervention. The decision of the surgical interventions was made according to the size and locations of the abscess. All patients were undergoing craniotomy, except patients who had cerebellar infection underwent craniectomy. Three patients undergo decompressive craniectomy for low GCS and significant Mass effect. The critical aspect of our surgical technique was the drainage of abscess with complete or partial excision of the abscess capsule. In subdural empyema, a craniotomy was contemplated, and drainage of infective material was done and drained kept for 24-48 hrs postoperatively. Abscess and infective material were sent for gram stain, AFB stain, and geneXpart for Mycobacterium tuberculosis, smear for fungus, and culture to identify sensitive antibiotics. We also analyzed how many patients were symptoms free and how many were clinically improved. We considered at least two increase in GCS score considered clinically improved and most important is the motor score of GCS. The study is a descriptive longitudinal study based on a literature review.

Results

We summarized the different variable characteristics in tabular form below. In our case series out of 41 patients, 33 patients had brain abscess, and eight patients had subdural empyema. Study shows there was male predominant constituting 30 patients, and 11 were female patients. The majority of intracranial infections were among the third decade to the fifth decade of the patient group. Predisposing factors or probable source of infection could not find in the case of 18 patients. However, total probable source identified as follows, the previous craniotomy in 5 patients and history of sinusitis, Chronic suppurative otitis media(CSOM) with mastoiditis, heart disease every four patients. The tubercular abscess was diagnosed in 4 cases which constitute 9.7%. One fungal abscess (2.4%) with rare aetiological agent Syncephaslastrum racemosum was found. High-grade glioma associated with abscess found in one case (2.4%). In our study most common clinical presentations were headache 32(78%), fever (53.6%), nausea/vomiting 12 (29.2%), confusion/drowsiness 10 (24.3%), neurological deficits in 8 (19.5%) and seizures was in 8 (19.5) cases. However, the clinical triad of brain abscesses like fever, headache, and neurological deficits only in 8 cases constitute 19.5% only. The most common form of brain abscesses was solitary in 21 patients, and the most common lobe involved was temporal lobe. Size of the Brain abscess (n=35) with greatest diameter, >3cm in 21 (60%) patients and <3cm in 14 (40%) cases. Total leucocyte count in 24 cases is raised (>11000/ml), constituting 58.5%. There was a recurrence of an abscess within 1

month and undergo re-do surgery in 4 cases and mortality registered within one month were 3 (7.31%) cases. Overall symptoms free were 26 (63.4%) and clinically improved were 10 (24.39%) patients. All patients were undergone contrast CT scan postoperatively do not show residual abscess, and some cases 6 (14.6%) partial capsule remnant because of eloquent proximity. The average hospital stays for our patients were 7 to 45 days.

Discussion

The first reference to brain abscess is attributed to Hippocrates, who in 460 BC while reporting a febrile patient with purulent otorrhoea and delirium, postulated that intracranial infection was the primary focus and the ear involvement secondary with the ear canal draining the intracranial suppuration. [20]

Brain abscess is defined as a focal intracranial infection initiated as an area of Cerebritis and evolves into a collection of pus surrounded by a vascularized capsule. Subdural empyema is also a pyogenic infection but is located between the dura and arachnoid maters. It is an uncommon condition, representing 15%-20% of confined intracranial infections. [4]. The most common cause is a previous neurosurgical procedure. previous skull trauma and meningitis may also be responsible for subdural empyema. [4,21]

Thirty-three (80%) of the patients had an intracerebral abscess. In contrast, the remaining eight patients had subdural empyema secondary to previous craniotomy, implanted material like V-P shunt tube, G- patch, surgical site infection etc. We reviewed the different brain abscess studies across the Globe. Chowdhury F.H et al., studied 162 brain abscesses from multiple hospitals in Dhaka, Bangladesh and Kural C, et al., from turkey reported out of 52 patients Male: Female ratio was 3.37:1 and 2.68:1 respectively. [16,17] Moreover, our study shows 3.66:1. We found solitary brain abscess, which constitutes 51.2% and multiple brain abscesses accounted for 29.2% and subdural empyema 19.5%. Berlit et al. study of 67 patients found solitary brain abscess in 70% and 30% multiple abscesses [22]. Our study shows that the Majority abscess located in the temporal lobe constitutes 24.2% out of a total of 33 brain abscess. However, most studies show frontal lobe predominant, which we have shown in Table II. Predisposing factors or probable sources were not identified in 18 (46.3%) cases. Four cases each (9.7%) had a history of Chronic suppurative otitis media (CSOM) with mastoiditis, heart diseases, and sinusitis. Patients with the previous craniotomy were in 6 cases (14.6%) and in one patient (2.4%) with brain abscess had a history of recurrent lung infection. Worth to be mentioned that, 46 years male, diagnosed with an abscess situated in cerebellopontine angle and presented with features of obstructive hydrocephalus and cerebellar signs. The abscess was drained via retrosigmoid suboccipital craniectomy and partial excision of capsule done. So message from this type of rare presentation that Cerebellopontine angle abscess can occur as a primary source of infection and Brain abscess should be considered as a differential when rapidly evolving neurology is present. [23]. The working diagnosis should be revisited and revised when the clinical picture alters. [23] A high index of suspicion, timely diagnostic support by CT scan, surgical intervention and vigorous antimicrobial therapy are crucial for better outcome. [23]

Berlit et al. show the underlying conditions of hematogenous brain abscesses (49%) included lung infections (23.88%), heart disease (5.97%), sepsis (14.92%), and other foci (4.47%). [22] The most common organism isolated from a brain abscess was Staphylococcus aureus in the pre-antibiotic era. [24] Streptococcus spp. have replaced Staphylococcus spp. as the most common organisms. [25]. The mode of entry of organisms could be by contiguous spread, hematogenous dissemination, or following trauma. [26] The common predisposing factors of a brain abscess are CSOM, congenital cyanotic heart disease, and paranasal sinusitis. [27–30]. Brain abscesses were singular in 77.7% of the subjects.

Moreover, multiple in 22.3%, a result similar to that reported by Landrieu et al. [31]. The frontal lobe was the most common abscess location in the patients, followed by the temporal and occipital regions. However, in a study carried out by Cavusoglu et al., [32], the temporoparietal region was the most commonly affected location. In our study, the most common site of abscess involved was temporal lobe, and we have shown different other studies in Table II. Tonon E et al.,[15] found the mean dimension of the lesions from 42 patients 33.93±13.68(mm) which is more similar to our study, where we got >3cm in most significant dimension constitute 60% of brain abscess. Abscesses of unknown cause(cryptogenic) accounted for 54.94% of the subjects, higher than the values reported for other series. [28,31,33].In the largest series of brain abscesses from developing countries, middle ear infection has been reported to be the most common source of intracranial suppuration. [34]. We also reviewed literature of pediatric case series study conducted in 47 patients by Malik S et al. [35], Otogenic source (34%) was the commonest predisposing factor, followed by scalp and face infection (21.3%) and congenital cyanotic heart disease (12.8%). [35] In our study, the most common clinical manifestation was Headache (78%) and fever (53.6%). We also have shown multiple studies of brain abscess literature and compared them to the clinical manifestation of our study in Table II.

Our study shows the most common isolated organism found to be Streptococcus groups. We found a pyogenic abscess in 85.36%, fungal abscess in 2.4%, and tumor with abscess was 2.4%. Worth noting in our study there was only 9.7% tubercular abscess compared to the rest part of India where the tubercular abscess was the predominant cause of Brain abscess. [18] .We also encountered rare bacterial abscess caused by Burkholderia pseudomallai, and the patient was too suffering from Melioidosis with uncontrolled Diabetes mellitus. Literature shows that brain abscess due to B.pseudomallai is very much rare.[36,37] According to a study conducted by Kothari M, et al.,[18] found to be 60% of cases were tubercular abscess out of a total of 715 patients admitted for brain abscess. Contrary to the study by Menon S et al.,[38] found only 5.4% of Mycobacterium tuberculosis in AFB stain from 57 pus samples of brain abscess collected. M. tuberculosis is a rare cause of brain abscess; however, this organism should be considered in patients with disseminated Tuberculosis or in individuals from areas where Tuberculosis is endemic. [39]. We considered following three criteria of confirmation of Tubercular Brain abscess described by Whitner et al., [40] in 1978; 1. Macroscopic evidence from true abscess formation within the brain substance, characterized by cavity formation with central pus 2. Sufficient histological description to assure that the inflammatory reaction in the abscess wall was composed predominantly of vascular granulation tissue containing epithelioid cells and 3. Proof of Tuberculosis origin by either a positive culture of the pus for M. tuberculosis or demonstration of acid-fast organisms in the pus or abscess wall. If there is a strong suspicion of Tubercular Brain abscess and the above criteria did not come out to be conclusive then we conduct the GeneXpart testing method. In our study, we confirmed 2 cases

of Tubercular Brain abscess through isolating bacteria under microscopy and rest 3 cases diagnosed through GeneXpart. The advantage of GeneXpart is the early detection of etiology and the status of resistance to rifampicin can be known.[41]

From the review of literature, conventional MRI imaging in 100% of the pyogenic and 90.9% of the tubercular abscesses, the outer margin of the wall was either smooth or lobulated in contrast to the fungal lesions, which had a crenated wall in half of the abscesses. All the fungal abscesses showed intracavitary projections directed centrally from the wall without any contrast enhancement in these projections. These projections were not seen in the other types and seemed to be a distinguishing feature of a fungal cause on conventional MR imaging. [42] In the study, Ashdown et al.,[42] described 4 cases of fungal abscesses in patients who were immunocompromised; these abscesses had an irregular T2 hypointense rim that showed post-contrast enhancement. From the study Luthra G, et al., [42] Pyogenic and tubercular abscesses may be differentiated by their unique metabolite pattern with recognition of amino acids, acetate, and succinate in pyogenic abscesses and lipid peak in tubercular abscesses. A ring-enhancing T2 hetero intense lesion with irregular walls and irregular projections into the cavity with low ADC and no contrast enhancement of these projections carry a high probability of being a fungal abscess[42]. We had reported a brain abscess with an extremely rare fungal abscess caused by Synecephalstrum racemosum is a type of subspecies under family Syncephalastraceae and order Mucorales. [43] Usually, this type of Mucormycosis seen in skin, intra-abdominal locations as reported. [44] Fungal infections of the central nervous system (CNS) are rare and are invariably secondary to primary focus elsewhere, usually in the lung or intestine. [45] Except for people with longstanding diabetes, these are most frequently encountered in immunocompromised patients such as those with acquired immunodeficiency syndrome (AIDS) or after organ transplantation.[45,46] The first report of a case of brain abscess in conjunction with Ulcerative colitis and Septic pulmonary embolism was done by Yamauchi T et al., [47]. It is believed that patients with UC have compromised immunity and exhibit activation of the blood coagulation system. [47] Our ulcerative colitis patient was on Azathioprine for his treatment, and there was a history of recurrent fever, headache, and evaluation, the temporal lobe was involved with abscess. His abscess was drained, and the patient was managed with Amphotericin B, followed by an oral Itraconazole for 4 weeks. Due to the lack of inflammatory response, neuroradiological findings are often nonspecific and are frequently mistaken for tuberculous meningitis, pyogenic abscess, or brain tumor.[45,46]

The most-reported tumor coexisting with abscesses are glioblastomas, but meningioma, astrocytoma, and metastases have also been reported. [48–52] We had one case brain abscess associated with high-grade glioma.

A subdural empyema can be misdiagnosed as a subdural hematoma or fluid collection [53]. Contrast-enhanced radiological examinations are necessary for the differential diagnosis of subdural empyema. Previous neurosurgical procedures and trauma should also be included in the patient's medical history for an accurate diagnosis.[4,5,51] Moreover, subdural empyemas are a causal factor in the pathogenesis of cerebral venous thrombosis in adults.[54] Therefore, these lesions should be treated urgently to avoid cortical vein thrombosis or cerebral infarction.

In our series, 8 out of 41 patients had subdural empyema and underwent surgical treatment via craniotomy. Two patients died and one patient discharged with a tracheostomy to a local hospital for nursing care. . Those patients who had associated pathology like CSOM/mastoiditis were sent to the ENT department for further management after Brain abscess managed. CSF diversion procedures for post meningitic hydrocephalus should be performed timely to prevent long-term neurological and cognitive decline.

Mortality in our study was found to be 12.1% and we have shown a comparative study in table IV, from different kinds of literature. However, in pediatric series, mortality was 44.7%. [35] Mortality from a Brain abscess has recently decreased from about 50% to 20%, mostly due to the introduction of CT scanning that resulted in earlier diagnosis and accurate localization. [7]

Conclusion

Central nervous system infections continue to be a severe and life-threatening medical condition despite newer antimicrobial chemotherapy. The most critical factors influencing mortality from an intracranial abscess are age and GCS of the patient at the time of admission. The treatment of brain abscess requires a multidisciplinary approach, including neuroradiological evaluation, surgical intervention, use of antibiotics, and eradication of primary infected foci. Broad-spectrum coverage of antibiotics, including third/fourth-generation cephalosporin, metronidazole, and vancomycin, based on predisposing factors, can be administered until the pus culture report is available. Carbapenems can be used in place of the combination of cephalosporin, and sometimes penicillin can be added. Probably the majority of the patients got few dosages of empirical antibiotic prophylaxis before surgical drainage. As a result, the most culture found to be negative. Worth note that we got a very less number (<10%), tubercular abscess patient, because of better socio-economic conditions, health care access and Kerala, has the highest portion of literate persons in the population among the Indian states. Prevention, including awareness programs and good hygienic practices, are of paramount importance to alleviate the load of intracranial infections.

Abbreviation

CT-Computed Tomography
MRI-Magnetic Rasonance Imaging
CSOM-Chronic Suppurative Otitis Media
GCS-Glassgow Coma Scale
CHD-Chronic Heart Disease
M:F-Male:Female
F+E-Frontal+Ethmoid
N/V-Nausea/Vomiting

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Conflict of interest

The authors declared that this project was done independently without any conflict of interest.

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