



OTOGENIC INTRACRANIAL COMPLICATIONS

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Abstract. Central nervous system (CNS) infections present significant mortality and morbidity, being life threatening diseases which can easily develop into challenges for physicians, despite the advances of modern medicine, in respect to development of antibiotics and modern surgical techniques [16]. Since the advent of magnetic resonance imaging (MRI), the mortality has dropped significantly. We present the cases of two patients with intracranial complications of mastoiditis and respectively an infection of the paranasal sinuses. A patient of 33 years-old has been addressed with suspected meningitis after surgery for chronic suppurative otomastoiditis. The MRI showed the presence of an abscess of 2.5 cm in the right temporal lobe with perilesional edema and thrombosis in the right transverse sinus, accompanied by oto-mastoids inflammatory infectious changes which required surgical drainage and then parenteral antibiotic therapy for one month. Our second case was a 15 year-old patient without an eloquent medical history who was addressed by a neurosurgery service, with the diagnosis of acute encephalitis secondary to an acute pansinusitis. After admissions into our service his clinical and neurological status rapidly deteriorated and an emergency brain MRI showed an extended subdural collection on the right side of the brain (frontal, parietal and temporal lobe) and interhemispheric collection carrying out a mass effect on the ventricular system and intrasinusal collections in the maxillary, right frontal and anterior ethmoidal sinuses. He was transferred into a neurosurgical service where surgery was performed in association with pre and postsurgical antibiotic therapy. The patient had a slow but favorable recovery. We emphasize the need of an early and appropriate diagnosis using imaging techniques in order to improve the management of intracranial complications of ear and sinus infections.

Keywords: brain abscess, mastoiditis, subdural empyema, transverse sinus thrombosis, pansinusitis

INTRODUCTION

Brain abscess, subdural empyema and septic intracranial thrombophlebitis are serious, life-threatening emergencies, more common in developing countries. The introduction of cross sectional imaging has granted access to an earlier diagnosis, which consequently led to a decrease in both morbidity and mortality. The use of computed tomography (CT) and MRI scan has determined a decrease in mortality among patients with CNS infections. Therefore, MRI has become the first-choice

imaging investigation employed in the evaluation of suspected CNS infection [16].

We present the cases of two patients with intracranial complications of mastoiditis and respectively an infection of the paranasal sinuses.

CASE REPORT

Case 1

A 33 year-old male, diagnosed with right chronic otomastoiditis three years ago. Three days before admission the patient underwent surgical evacuation of the pus and cerebrospinal fluid (CSF) cutaneous fistula filling flap, followed by persistent fever and headache and he was addressed to our hospital

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with suspected meningitis. Physical examination showed no significant clinical signs except abundant purulent secretions in the surgical wound. The laboratory panel demonstrated leukocytosis (20 000/mm³) with neutrophilia (79%), hyperfibrinogenemia (800mg/dl) and slightly elevated liver enzymes. The lumbar puncture showed a CSF with 20 elements and normal biochemistry. Despite of broad spectrum antibiotic therapy (Meropenem, Teicoplanin and Levofloxacin) after two weeks the fibrinogen levels remained high (838mg/dl) and headache persisted. The brain MRI showed the presence of an encapsulated collection of about 2.5 cm in the right temporal lobe associated with perilesional edema and right transverse sinus thrombosis as well as right oto-mastoids changes. Neurosurgical evaluation established the need for a surgical intervention. One month after the intervention, the patient returned to our clinic for reevaluation. The MRI as well as the lab tests were normal and antibiotic treatment was stopped after a total duration of six weeks.

Case 2

A 15-year-old male, without any eloquent medical history, was addressed to our hospital by a neurosurgery hospital with the diagnosis of acute encephalitis, secondary to acute pansinusitis. The onset of his illness, three days before admission consisted in: severe headache, dizziness, fever, vomiting, unilateral weakness on the left side followed by altered mental state and cranial nerve signs. An initial cranial CT scan was made in the neurosurgical service (without intravenous administration of iodinated contrast medium) which revealed acute pansinusitis, increased cerebral oedema with displacement of the median line to the left. The cranial CT scan also showed the presence of a minimal subdural fluid accumulation located on the right side of the brain. In our department the patient rapidly deteriorated presenting severe headache, anisocoria, hemiparesis on the left side of his body, altered mental status with Glasgow Coma Scale (GCS) =10 points and stiff neck. The brain MRI showed an extended subdural collection on the right side of the brain (frontal, parietal and temporal lobe) and interhemispheric collection carrying out a mass effect on the ventricular system and intrasinus collections in the maxillary, right frontal and anterior ethmoidal sinuses. He was transferred to a neurosurgical service where surgery was performed in association with pre and post-surgical antibiotic therapy (Meropenem, Linezolid and Chloramphenicol). The culture aspirate revealed anaerobic bacteria such as *Fusobacterium varium*, *Fusobacterium mortiferum*, *Propionibacterium propionicum*. Two weeks after surgery a second

brain MRI showed empyema in the right cerebral hemisphere and transverse sinus thrombophlebitis, right sigmoid sinus thrombophlebitis and posterosuperior sagittal sinus thrombophlebitis. This MRI also showed disabling character intraparenchymatous changes without intraparenchymatous abscesses, right acute mastoiditis and chronic pansinusitis (figure 1-6). One month after the intervention the patient returned to our clinic for reevaluation still having left hemiparesis, dysarthria and seizures. He continued antibiotic therapy for 3 months associated with anticonvulsant therapy with a good recovery.

DISCUSSIONS

Brain abscess is a focal intraparenchymal infection, which forms when organisms are inoculated into the brain parenchyma, usually from a site distant to the CNS [1,2]. Subdural empyema is an intracranial focal collection of purulent material located between the dura mater and the arachnoid mater [3,4]. Suppurative intracranial thrombophlebitis may be caused by infections of the paranasal sinuses, middle ear and mastoid, which can spread to the brain sinuses by contiguity along emissary veins and lead to thrombosis of the brain sinuses by increasing blood viscosity (or inducing a hypercoagulation state) [3,5,6].

The main modes of dissemination of the sinuses and mastoid infection into the brain parenchyma are: following penetrating head injuries, hematogenic and via direct extension along classic pathways. The direct route of intracranial extension via emissary veins is more commonly associated with CNS infections due to sinusitis and otomastoiditis [1,2,3]. Intracranial extension of infection by the venous route is common in paranasal sinusitis. Frontal and ethmoidal sinusitis are the most common causes of subdural empyema due to extension through emissary veins [4]. Infections of paranasal sinuses, middle ear and mastoid often involve the cavernous sinus, the lateral (transverse) sinus, the superior sagittal sinus. The location of an abscess may depend on the location of the primary infection [1,2,4,5].

The pathologic changes involve venous thrombosis and suppuration. Venous thrombosis determines intracranial hypertension and parenchyma ischemia ranging from small petechiae to an intracerebral hemorrhage. Intracranial hypertension is the consequence of brain edema due to an important vasogenic component. Local suppuration may produce venous necrosis and hemorrhage or it may produce intracranial suppurative processes (brain abscesses, subdural empyema) or septic metastasis involving other organs [5,6].

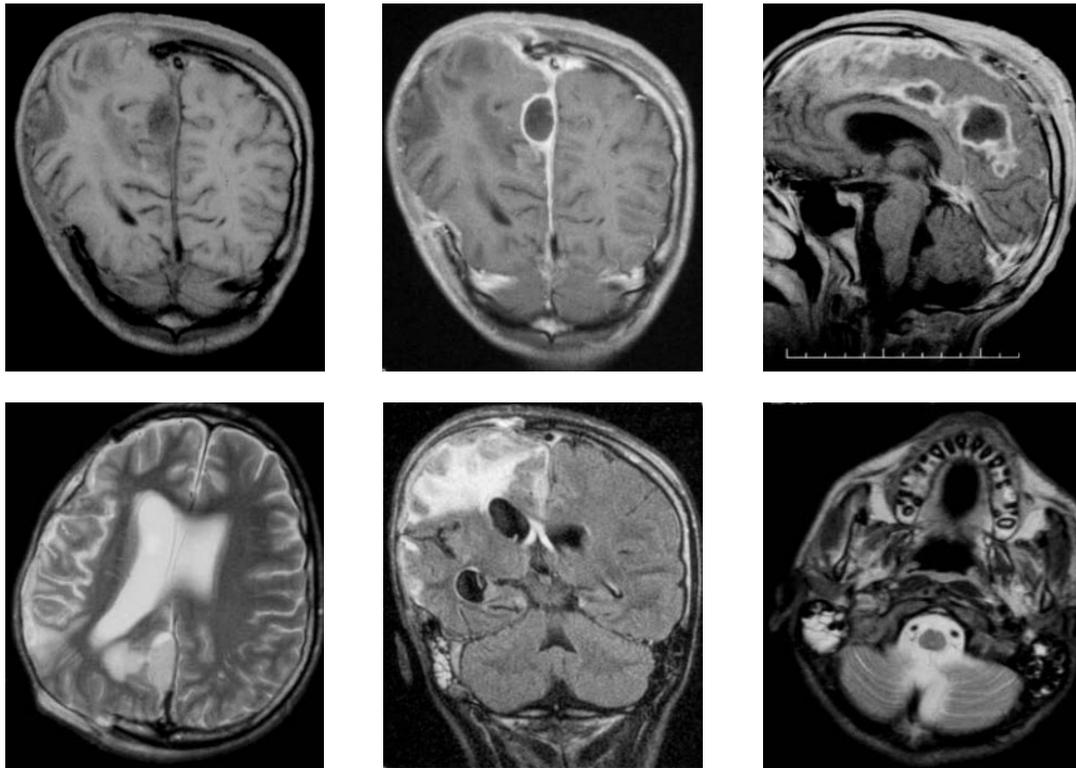


Figure 1-6. MRI evaluation shows lense shaped images, hyperintense to CSF and hypointense to cerebral parenchyma in T1 weighted images (fig.1), with ring enhancement related to presence of inflammation (fig.2,3) and hypersignal on T2 weighted images (fig. 5), with extra-nevrxial topography in the parieto-occipital and fronto-parietal regions, suggestive for abscesses. FLAIR and T2 weighted images (fig. 4, 5) show important cerebral edema in the right fronto-parieto-temporal area with secondary cerebral displacement. Bilateral inflammatory reaction in the mastoidian cells can also be observed, affecting mostly the right side (fig. 6).

In CNS infections due to contiguous spread there are specific organisms associated with certain predisposing conditions. Most CNS infections are produced by pyogenic bacteria and they are often mixed infections. *Streptococcus* species (aerobic and anaerobic) are the organisms most frequently isolated from brain abscesses and subdural empyema due to otomastoiditis and paranasal sinusitis. *Staphylococcus aureus* is also frequently isolated.

Other organisms include *Bacteroides spp*, *Enterobacteriaceae*, *Pseudomonas*, *Fusobacterium*, *Prevotella*, *Peptostreptococcus* and *Propionibacterium* [1,2,3,7,8].

CNS infections present with a wide spectrum of **clinical manifestations** depending on the localization of the pathologic process (thromboses, abscess, empyema), the degree of intracranial hypertension and parenchyma damages. The clinical findings are nonspecific and include an altered mental state, headache, fever, seizure, vomiting, unilateral weakness or hemiparesis, and cranial nerve signs [3,4,5,7,9].

Headache is the most common presenting symptom of CNS infections. Also focal neurological deficit (50%) may correlate with the local region of

infection. The classic triad of headache, fever, and focal neurological deficit is rarely seen. Seizure and mental status changes are common. Nausea, vomiting, or stiff neck may be reported with increased cerebral edema due to the mass lesion [1,2,7,10].

Abscesses secondary to otitis media are usually located in the temporal lobe or cerebellum. A temporal lobe abscess may present with ipsilateral headache, aphasia, upper homonymous quadrantanopsia. Abscesses of the cerebellum often produce nystagmus, ataxia, dysmetria [3].

Infection spread from the paranasal sinuses most commonly presents in the frontal and subfrontal brain and the clinical presentation includes: headache, deterioration in mental function, hemiparesis with unilateral motor signs and motor speech disorder. Frontal and ethmoidal sinusitis are the most common causes of subdural empyema due to extension through emissary veins [3,5].

As reported in our second case, subdural empyema has the tendency to spread rapidly in the subdural space and tends to behave like an expanding mass lesion with associated increased intracranial pressure and cerebral intraparenchymal penetration. So clinical findings vary from fever,

headache, vomiting, signs of meningeal irritation to focal neurological signs which progress rapidly, seizures, aphasia, signs of increased intracranial pressure with herniation of the brain [4].

Cavernous sinus thrombosis (CST) may occur as a late complication of an infection of paranasal sinuses, especially the ethmoidal and sphenoidal sinuses. The most common findings of CST include headache and cranial nerve signs. Although physical examination can reveal typical findings for CST such as: periorbital edema, chemosis due to occlusion of the ophthalmic veins, cranial nerve dysfunctions (VI, III, IV and V), exophthalmia and ophthalmoplegia due to increased retrobulbar pressure, decrease of visual acuity and sluggish pupillary reflexes due to increased intraocular pressure [6].

Infections of the middle ear and mastoid may involve the lateral (transverse) sinuses.

Lateral sinus thrombosis affects cranial nerves III, IV, VI and V, and the venous route of CSF re-absorption, so clinical findings consist of: ophthalmoplegia, altered ocular reflexes, signs of intracranial hypertension, sensitivity disturbance over the upper face, and if the thrombosis extends to the jugular vein, the patient may develop jugular foramen syndrome with involvement of cranial nerves IX, X, XI and XII [3,5].

Laboratory tests are not specific in establishing a diagnosis of CNS infections, but they are valuable in the evaluation of the patients' condition. **Lumbar puncture** is contraindicated in patients with suspected or proven brain abscess and subdural empyema because it may result in herniation of the brain. This procedure could be justified in patients with brain abscess in the absence of increased intracranial pressure and with manifestations of meningitis [1,2,7]. In septic intracranial thrombophlebitis, lumbar puncture may reveal lymphocytic pleocytosis and mild elevation of proteins or evidence of subarachnoid blood but cerebrospinal fluid is usually sterile [2,4]. **Microbiological investigations** of the abscess and subdural collection content are some of the most important factors for the management of brain abscess. These consist of culture aspirates of abscess for aerobic, anaerobic, acid fast and fungi, Gram stains, acid fast stain, special stains for fungi [1,7,8]. We noted that in our first case the surgical intervention for chronic mastoiditis has not been followed by aspirate culture, which made difficult the choice for antibiotic. When the etiology of an abscess is undetermined the antibiotic treatment should be continued covering all potential resistant bacteria that might be involved, therefore the cost of the treatment substantially increases. Electroencephalography (EEG) is usually abnormal and occasionally reveals a focus of high voltage with slow activity [3].

Early and improved diagnostic imaging techniques allow the discovery of brain abscess, subdural empyema and suppurative intracranial thrombosis at a much earlier stage [7,8,11].

The **neuroimaging studies** are compulsory for the diagnosis (usually both CT and MRI being necessary). The imagistic appearance of both brain abscesses and of the subdural empyema is not pathognomonic. The preferred initial examination of the patient in whom CNS infection is suspected is MRI with and without gadolinium enhancement. Similar diagnostic results can be expected from cranial CT scans with the intravenous administration of iodinated contrast medium. Both imaging techniques help detect the mass effect of the abscess; however, findings in MRI with a diffusion protocol are more specific in differentiating cerebral tumor, stroke, and abscess [9,11]. CT is generally sufficient to make the preliminary diagnosis, which mandates neurosurgical consultation and admission to the hospital. However, MRI is increasingly being used for further evaluation. MRI is more sensitive in detecting early cerebritis [1,2]. Once the diagnosis is clear, immediate neurosurgical consultation is mandatory.

Cerebral abscesses occur usually at the junction of white-gray matter, secondary to bacterial meningitides, trauma, hematogenous septic dissemination or adjacent infectious processes – otitis, mastoiditis, dental infection or paranasal sinusitis [12].

Initially the cerebral lesion consists in a localized inflammatory process, with small necrotic regions, which occurs 4-5 days after the onset of local cerebritis. At this stage, CT scan may reveal a hypodense aspect with ill defined limits due to the local alteration of permeability of the blood-brain barrier, while MRI investigation reveals hypointense aspect on T1-weighted images and hyperintense aspect on T2-weighted images. After 6-8 days, the necrotic central lesions become confluent and are surrounded by inflammatory cells – neutrophils, macrophages and fibroblasts - with synthesis of collagen and reticulin fibres and formation of a peripheral capsule [13]. Blood vessels adjacent to the lesion proliferate, presenting increased permeability due to inflammatory conditions. The lesion appears round-oval on the CT scan, presenting a moderate-attenuating peripheral capsule, with enhancement after contrast medium administration, associated with important adjacent edema with proportional mass effect on the ventricular system and surrounding structures. The center of the lesion appears iso/hypointense on T1-weighted slices and hyperintense on T2-weighted scans on the MRI scans, while the wall is hypointense on both T1-weighted and T2-weighted images. The associated edema presents an increased signal on

T2-weighted sequences and appears hypointense on T1-weighted images. In order to appreciate the extent of the lesion, the active infection areas and possible associated vascular pathology (thrombotic processes), T1-weighted gadolinium enhanced acquisitions are required. In advanced stages, the abscess may be also multilocular, with possible detection of secondary satellite lesions.

Localization of abscess in the epidural space requires differential diagnosis with epidural chronic hematoma. CT scan reveals the presence of a hypodense lenticular image with rim enhancement and cerebral adjacent edema. MRI exam shows an iso/hypointense image on T1-weighted scans and a hyperintense aspect on T2-weighted images.

Both CT and MRI examinations can locate the lesion with accuracy; both can appreciate the mass effect and possible complications and also may additionally characterize the blood flow and blood volume in the interest area.

MRI examination is preferred if suspicion of a cerebral tumor or stroke is raised – diffusion-weighted sequences and MRI spectroscopy can contribute to the differentiation between tumoral and inflammatory processes. Diffusion-weighted echo planar imaging showing a high signal, correlated with a reduced apparent diffusion coefficient can lead to establishing a positive cerebral abscess diagnosis. MRI spectroscopy identifies the spectral profiles of the specific metabolite peaks - lactate and amino-acids can be seen in patients with cerebral abscesses, regardless of the time of spectroscopy, while acetate and pyruvate disappear after 1 week of combined treatment [14].

An additional positive argument for cerebral abscess is represented by the dynamic evaluation – an appropriate therapeutic approach is followed by diminution of abscess dimensions and surrounding edema and resolution of the rim enhancement.

Plain radiographs of the paranasal sinuses can also be useful, indicating a possible etiology for cerebral abscess if inflammatory aspects are detected.

The diagnosis of **cerebral venous thrombosis (CVT)** is typically made on the basis of imaging studies consisting of CT scan and MRI.

CT scan is often the first imaging study obtained and it may be normal in the first 48-72 hours or it may show only the indirect signs of cerebral venous thrombosis such as brain edema, hemorrhages and infarcts. CT scan also can rule out other conditions such as neoplasm and can evaluate coexistent lesions such as subdural empyema or can evidence the underlying conditions such as sinusitis and mastoiditis.

Many neurologists now consider that the procedure of choice for diagnosing cerebral venous thrombosis is the combination of MRI to visualize

the thrombosed vessel and magnetic resonance venography to detect the nonvisualization of the same vessel. The MR appearance of a thrombosed cerebral vein is dependent on the age of the (isolated cortical venous thrombosis desktop) clot. Usually, the thrombotic material appears isointense in T1 and hypointense in T2 during the first 5 days, subsequently it becomes hyperintense in both sequences until 1 month [5].

The **interdisciplinary management** (surgeon and infectious diseases specialist) reduces the period of time when, after surgery, the patients undergo a large spectrum of combinations of antibiotics to no more than 72 hours. Thus, it allows an earlier onset of the targeted antibacterial treatment. After the germ is identified, the antibiotic treatment respects the principles of de-escalation. In our second patient the interdisciplinary management allowed the identification of the germs responsible and therefore de-escalation of the antibiotic treatment.

Selection of appropriate antimicrobials with adequate CNS penetration and coverage of typical anaerobic and aerobic organisms is critical in controlling infection and preventing complications. Empiric antibiotic therapy must be early, and it should cover all likely pathogens in the context of the clinical setting. It should have broad spectrum coverage for gram-positive including *Staphylococcus spp*, gram-negative and anaerobic organisms and it should be capable to achieve high levels in the CSF. For CNS infections (brain abscess) due to direct extension from the mastoid, middle ear, sinuses and teeth, an ideal empiric antibiotic therapy can be performed with Penicillin G + metronidazole + third-generation cephalosporin [1,2,3,4]. If MRSA staphylococci are suspected, a glycopeptide like vancomycin should be used. If a specific microorganism is isolated from an abscess or subdural collection, the antibiotic therapy can be adjusted after the result of susceptibility testing.

Duration of antibiotic treatment is unclear and is dictated by clinical response. Traditionally 6-8 weeks of intravenous antibiotics have been used for brain abscess followed by oral antibiotics for another 4-8 weeks to prevent relapse.

Corticosteroids can be used for the treatment of perilesional edema and reducing intracranial pressure. In brain abscess they can retard the encapsulation process, reduce antibiotic penetration into abscess, increase the risk of ventricular rupture and may decrease the contrast enhancement of the abscess capsule in the early stages of infection. In cavernous sinus thrombosis corticosteroids may reduce inflammation and edema and they are definitely indicated to prevent adrenal crisis when pituitary insufficiency occurs [4,6,10]. The anticoagulation therapy with heparin should be consid-

ered when there are thrombotic complications of CNS infections [5,6]. Anticonvulsants for seizures prophylaxis are recommended since seizures are frequent complications of brain abscess [10]. The source of infection should be treated to prevent recurrence of the CNS infections.

A combined medical and surgical approach is used for most brain abscesses to eradicate the invasive organism. Small abscesses and lesions in the cerebritis stage respond well to medical therapy alone [8,15]. Surgical options include craniotomy, stereotactic aspiration, neuroendoscopic drainage depending on the location, size, number of sites, and other characteristics of the abscess and subdural collection as well as the patient's clinical status. The specific choice of surgical technique is less important than the basic principle of removing the pathogen. Immediate neurosurgical drainage of the subdural empyema can be necessary. The primary surgical option is craniotomy, which allows wide exposure, adequate exploration, and better evacuation of the purulent collection than other procedures. It may be essential in the posterior fossa subdural empyema [3,4].

Interval CT scans (3 months) are recommended for inpatients and outpatients to follow up for complications and resolution of abscess [1, 17], as there is a risk of abscess re-accumulation or failure to resolve in some cases requiring re-aspiration [2, 17].

Antibiotic treatments have improved the prognosis of patients with CNS infections. Mortality rates have decreased from 40-50% to less than 5%. Morbidity in survivors is generally due to residual neurological defects, increased incidence of seizures due to scar tissue foci, or neuropsychiatric changes [8].

CONCLUSIONS

Central nervous system (CNS) infections present significant mortality and morbidity, being life threatening diseases which can easily develop into challenges for physicians, despite the advances of modern medicine, in respect to development of antibiotics and modern surgical techniques [16]. We emphasize the need of an early and appropriate diagnosis using imaging techniques, usually both CT and MRI being necessary. The preferred initial examination of the patient in whom CNS infection is suspected is MRI with and without gadolinium enhancement. The interdisciplinary management (surgeon and infectious diseases specialist) reduces the period of time when, after surgery, the patients undergo a large spectrum of combinations of antibiotics. A combined medical

and surgical approach is used for most brain abscesses to eradicate the invasive organism whereas immediate neurosurgical drainage of the subdural empyema can be necessary.

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