Clinical features of otogenic cerebral sinovenous thrombosis: our experience and review of literature

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May 26, 2022

Abstract

We aimed to focus on clinical features, on diagnosis of this pathology and to review the most controversial aspect of management. We reviewed 10 in patients between 1995 and 2020. All patients were treated with broad-spectrum antibiotherapy, anticoagulation in 9 patients, and surgery required in 9 patients.

Introduction:

Otogenic cerebral thrombophlebitis is a rare intracranial complication of otitis media in the modern age of antibiotics. It poses a danger that requires immediate diagnosis and urgent medical and surgical treatment. Complications are now more likely to arise from chronic ear disease or cholesteatoma rather than acute otitis media.(1) The mortality has significantly decreased but still range from 5 to 10%.(2)

This study aims to focus on clinical features, on diagnosis of this pathology and to review the most controversial aspect of management.

Patients and Methods:

We conducted a retrospective study on 10 patients with otogenic cerebral thrombophlebitis diagnosed and treated in patients admitted in the ENT Department of Farhat Hached Hospital over a period of the period of 25 years (1995 to 2020). Our series included 10 patients; they were 8men and 2 women with a sex ratio (M/F) = 4. The mean age was 35 years (11year old- 77years old). Neurologic signs (headache) were present in 5 patients and fever was noted in 3 other patients. All patients were assessed by cerebral CT scan, 3 among them benefits from a cerebral MRI also. The diagnosis was confirmed by radiographic examination in all cases. 90% of patients were anticoagulated.

Results:

A total of 10 inpatients were identified. Four patients (40%) had poorly controlled diabetes. All patients had a history of otitis, either recurrent acute or chronic otitis media. The mean delay of consultation was 27 days (extremes: from 7 days to 3 months).

The most commonly reported symptoms were headache in 5patients (50%), otalgia in all patients, otorrhea in 9 patients (90%), and fever in 3 patients (30%).

The etiology was related to an acute otitis media (AOM) in 4 cases (40%), cholesteatoma otitis media (COM) in 3 cases (30%), and necrotizing external otitis (NEO) in 3 cases (30%) (Table 1).

All patients had positive otoscopic findings, which included purulent ear discharge. Retraction pockets with cholesteatoma debris were present in 2 patients. Congested and retracted pars tensa was found in one patient

(Table 2). The decreased visual acuity was found in one case. And conductive hearing decrease was noted in one other case.

All patients were assessed by cerebral CT scan with contrast (contrast-enhanced computed tomography (CECT)) of the brain and temporal bones. The "empty delta sign" (central non-enhancing clot surrounded by enhancing dural sinus wall) which is related to the presence of thrombus which has been objectified in 7 patients (70%) (Fig1a,b). 3 patients (30%) underwent a MRI.

The thrombus was confined only to the lateral sinus in 5 patients (50%), extended to the internal jugular vein in 4 patients (40%) (fig2), and extended to the cavernous sinus in 1 patient (10%) (Fig3).

Regarding the case extension to the cavernous sinus, CT scan showed low-intensity cavernous sinus, with bulging of its lateral margins, dilatation of the ophthalmic veins, and bilateral exophthalmia more marked in the left eye.

The thrombophlebitis was on the right side in 3 cases, on the left side in 6 cases, and bilateral in 1 case. The occlusion was total in 4 cases and partial in 6 cases.

Imaging had objectified other associated signs like mastoiditis which was identified in 5 patients (50%) (fig4), swelling neck in one case, and a retropharyngeal abscess in one case (fig5).

70% of patients presented other cranial complications associated: such as frank cerebellar abscess (3 patients) and extradural empyema in two patients (20%) (fig6), and meningitis in one patient (%).

Complete blood counts showed concentration of hemoglobin < 10 g /dL in 2 (20 %) patients, leukocytosis in 7 (70 %) patients. All patients had normal plated counts. All patients had normal coagulation profiles.

Microbiologic cultures were produced from the middle ear of all patients and 3 of them had negative cultures. Among the positive cultures, Pseudomonas aeruginosa was isolated in 2 cases, Proteus mirabilis in one case, Streptococcus in one case, and streptococcus pneumonia in one case. Mycological cultures were positive in 2 cases: lichetmiae corymbiform in one case and Candida Albicans in the other case.

All patients received initially a broad-spectrum antibiotherapy, subsequently adapted according to the isolated germ. Duration of antibiotic therapy was for 15 days to 3 months (Table 3 &4).

90% of patients were anti coagulated: 6 patients were treated with subcutaneous low molecular weight heparin (enoxaparin) for an average period of 60 days, and 3 patients had intravenous unfractionated heparin for 15 days, then relayed with Sintrom (Acenocoumarol), for a mean period of 90 days.

Surgical management was completed in 5 cases. It was exclusive in 4 cases (Table 5).

All patients recovered satisfactorily; with complete resolution of their symptoms and complications except one patient who had a loss of visual acuity. The middle ear infection was controlled in 9 cases. The mortality rate was 0%. 4 patients showed recanalization, and one patient had a significant decrease of the thrombus. The average length of the follow-up was 16 months (range: 30 days to 36 months).

Discussion:

Since the advent of antibiotics, the incidence of cerebral sinovenous thrombosis has been remarkably decreased and it has rarely been reported in the few last decades(3).This rare condition has been more frequently reported in the pediatric population (3)(4), with an incidence of 0.7 per 100000 children per year (5).

A clear male predominance has been documented in most studies(2)(4)(6)(7). We also found the same predominance in our series.

The anatomic proximity of the middle ear cavity and mastoid air cells to the dural venous sinuses makes them vulnerable to thrombophlebitis secondary to infection and inflammation in the middle ear and mastoid(8). Two pathogenic mechanisms of infection spread were suggested: the direct spread of infection by erosive osteitis and retrograde thrombophlebitis (9)(10).Edema, increase in local vascular pressure, and

hyper-coagulability stateis caused by the inflammatory process. Therefore it leads to venous stasis and subsequent thrombosis (11).

Severe frontal and occipital headache, otalgia,nausea, vomiting, diplopia, loss of visual acuity, sixth nerve palsy, hemiparesis, and spiking fever, were the most common signs and symptoms found in cases of lateral sinus thrombosis before the era of antibiotics(1).Nowadays, the most commonly reported symptom was a headache. The clinical presentation was reported by Raja.K in her series "Otogenic Lateral Sinus Thrombosis : A Review of Fifteen Patients and Changing Trends in the Management ≫was made also of otorrhea, hard of hearing, and fever(2). This finding was reproduced in Bales's study and Sherer's series as well(4)(12).

Otalgia and vomiting were the commonest presenting features (63%) followed by fever (57%) and headache (43%) in Krishnan's study(11). Exophthalmos, loss of visual acuity, ophthalmoplegia, ptosis, and palpebral edema associated with headaches and fever were the major signs and symptoms of cavernous sinus thrombosis(13)(14)(15). Zanoletti and al. argues that the absence of typical clinical signs of mastoiditis does not exclude the presence of otogenic lateral sinus thromboses (16). In our series headache was present in 50% of cases and fever in 30% of cases.

The bacteriology of cerebral sinovenous thrombosishas changed with the use of antibiotics. Before the age of antibiotics, B-haemolytic streptococcus and Pneumococcus were the most cultured organisms. Pseudomonas and proteus species used to be common too(1).

The microbiological profiles are changing. Culture from the middle ear discharge characteristically yields mixed flora, including Pseudomonas, Proteus, Bacteroides, Staphylococcus, Enterobacteriaceae, and other species. It is might be frequently negative due to previous antibiotic treatment. (2)(1).In Raja's study, 6 (40%) patients had negative cultures. In patients with positive cultures, Proteus mirabilis (4 cases; 44%) and Pseudomonas aeruginosa (4 cases; 44%), followed by Enterococcus fecal (1 case; 11%) and Escherichia coli (1 case; 11%).(2). In our series, the culture was positive in 7 patients.5 one was related to a bacterial infection and 2 were related to mycologic infection which caused the external ear infection. Among the positive bacterial culture, we isolated Pseudomonas aeruginosa was isolated in 2 cases, Proteus mirabilis in one case, Streptococcus in one case, and streptococcus pneumonia in one case.

The diagnosis of cerebral thrombophlebitis is based on radiographic imaging techniques. Contrast enhancing computed tomography of the head and neck is performed to investigate intra cranial complications of otitis media, especially the cerebral sinovenous thrombosis (5), (9).

Lateral Sinus thrombosis may be diagnosed by the presence of the pathognomonic empty delta sign which consists of an empty triangle appearance created by the thrombus within the sinus surrounded by contrast-enhanced dura (9)(17)(14)(5). In our study, the lateral sinus was the most common location in our patients. It was confined in 70% of cases and spread to the jugular vein in 4 cases and the cavernous sinus in only one case.

Cavernous sinus thrombosis may be initially explored with non-contrast CT of the head which can show subtle abnormalities such as bulging of the lateral margins of the cavernous sinus, heterogeneous filling defect, and engorgement of the superior and/or inferior ophthalmic veins. In addition to the above-mentioned signs, contrast-enhanced CT/MRI, shows the presence of asymmetric filling defects, thrombosis in the superior ophthalmic vein, other venous tributaries, dural venous sinuses, and cerebral veins(18). In our case, a CT scan was able to diagnose the thrombus in the cavernous sinus by showinglow-intensity cavernous sinus, with bulging of its lateral margins, dilation of the ophthalmic veins, and bilateral exophthalmos more marked in the left eye.

CT scan can misdiagnose the thrombus pathology because of bone-related artifacts(1). Therefore, M R I / M R V is more sensitive in detecting this complication (2).

MRI/MRV is valuable to exclude other intracranial complications like adjacent subdural empyema, cerebritis, or cerebralabscess. It can also eliminate the risk ofradiation compared with CT scans, especially for

children(2). The MRI does not require contrast injection to showthe thrombuswhich seems isointense on T1-weighted images and hypointense on T2-weighted images, with increased intraluminal sign intensity onboth T1 and T2 sequences (17). The MRV remains the gold standard in diagnosing cerebral sinovenus thrombosis because it is a non-invasivetechnique;it offers the advantage of precising the patency of the central venous sinuses. Besides, itenables the distinction between a slow venous flow and an occlusive thrombus and can be performed simultaneously with cerebral MRI(17)(11). In our study, the MRI revealed the thrombus in 3 cases where the scanner was negative.

Additional intracranial complications must be investigated in the presence of cerebral sinus thrombosis. The high association of cerebral sinus thrombosis with other cranial complications is well documented (8).

In the pre-antibiotic era, concurrent complications were present in 80% of cases. The advent of antibiotics has reduced the incidence of complications to 20%. Concomitant intracranial and extracranial complications included meningitis, otitis hydrocephalus, internal jugular vein thrombosis, and intracranial abscesses(8).

Syms and al reported a series of patients who all had concurrent intracranial complications: 4 patients had a cerebral abscess and 3 patients had hydrocephalus(19). In the series of Kaplan et al, Twelve of the 13 patients suffered concurrent complications, including meningitis, cerebral abscesses, epidural abscess, and progression of the thrombus to the transverse sinus and the internal jugular vein(3).

We have objectified70% of a cranial complication associated: such as cerebellar abscess (3 patients) and extradural empyema in two patients, and meningitis in one patient.

Broad-spectrum intravenous antibiotics should be started at the earliest and must be adjusted later according to bacterial cultures. Antibiotics have led to a reduction of incidence of complications from 80% to 20%(1). The duration of the antibiotic treatment ranged from four to eight weeks(2). In our cases, we treated first with broad-spectrum antibiotics then adapted to the culture result.

The role of anticoagulation therapy in the treatment of LST is unclear. The clinician should weigh the risks and benefits of anticoagulation therapy in cases of cerebral sinovenous thrombosis. Au. JKet al reported a trend in the use of anticoagulation therapy, but lack the statistical difference(20). Anticoagulation has been advanced to offer the advantage of preventing the extension of the thrombus to distal sinuses. Thus, it might be indicated in particular cases of thrombus propagation, embolic events, and neurological changes(1)(21).LMWH in children with CSVTis recommended by The American Stroke Association, outside the neonatal period, even if there is evidence of intracranial hemorrhage(5)(22).It is preferred to other anticoagulants(17)(5), because it preventsthrombus propagation, improves recanalization rates, and preventslong-term neurological sequels. But, on the other hand, it can cause thrombocytopenia, bleeding, hemorrhagic skin necrosis, and risk of septic emboli (11).74% of patients after, showed complete recovery with complete resolution of the symptoms and recanalization after antibiotherapy associated with anticoagulation (23).

Anticoagulation was administrated in all of the patients, along with antibiotics and surgical treatment, with an excellent outcome; 9 patients recovred and only one patient had sequelae.

Surgery is an essential part of the management of this entity. It assures a better prognosis. However, controversies persist about the most appropriate surgical management (11). A cortical mastoidectomy is used successfully to treat noncholesteatoma ear disease. It confirms the diagnosis of L ST and allows the drainage of the initiating infection. A modified radical mastoidectomy is sufficient treatment for cholesteatomatous ears presenting acutely with cerebral sinus thrombosis(1). Nowadays, routine ligation of the internal jugular vein is no longer performed. It is usually reserved for unresponsive cases with persistent septicemia,lung thromboembolism, and deep neck infection(2)(9).

In our study, we realize a mastoidectomy isolated in 4 patients (40%), it was associated to an internal jugular vein ligation in one case, and to an extradural empyema evacuation in 2 patients (20%). We recommended an antro-mastoidectomy with incision of the sinus and evacuation in 2 cases (20%).

Conclusion:

Otogenic cerebral sinovenous thrombosis is a rare complication of otitic pathology. It is associated with significant morbidity and mortality. In the era of antibiotics, classic clinical signs of mastoiditis (pain, swelling, and erythema posterior to the pinna) are not always present at the presentation. A clinical presentation might be subtle, which requires clinicians to maintain a high index of suspicion of this entity. Imaging (CT, MRI) is a key component in diagnosing and managing this complication. Treatment of otogenic CSVT consists of conservative surgery, antibiotics, and anticoagulation.

List of abbreviation:

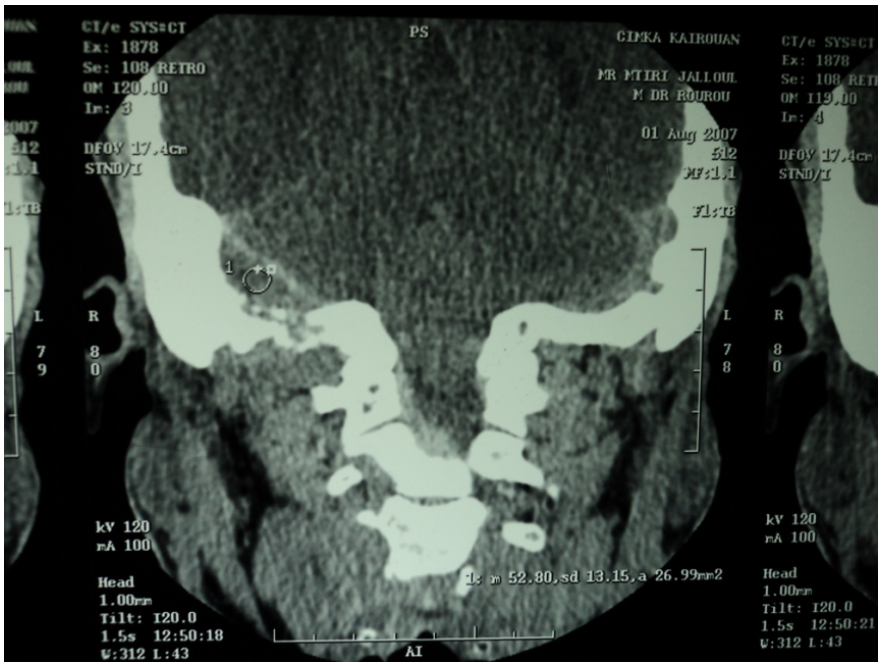
AOM: acute otitis media

COM: chronic otitis media

NEO: necrotizing external otitis

PFP: peripheral facial paralysis

IVJ: internal jugular vein



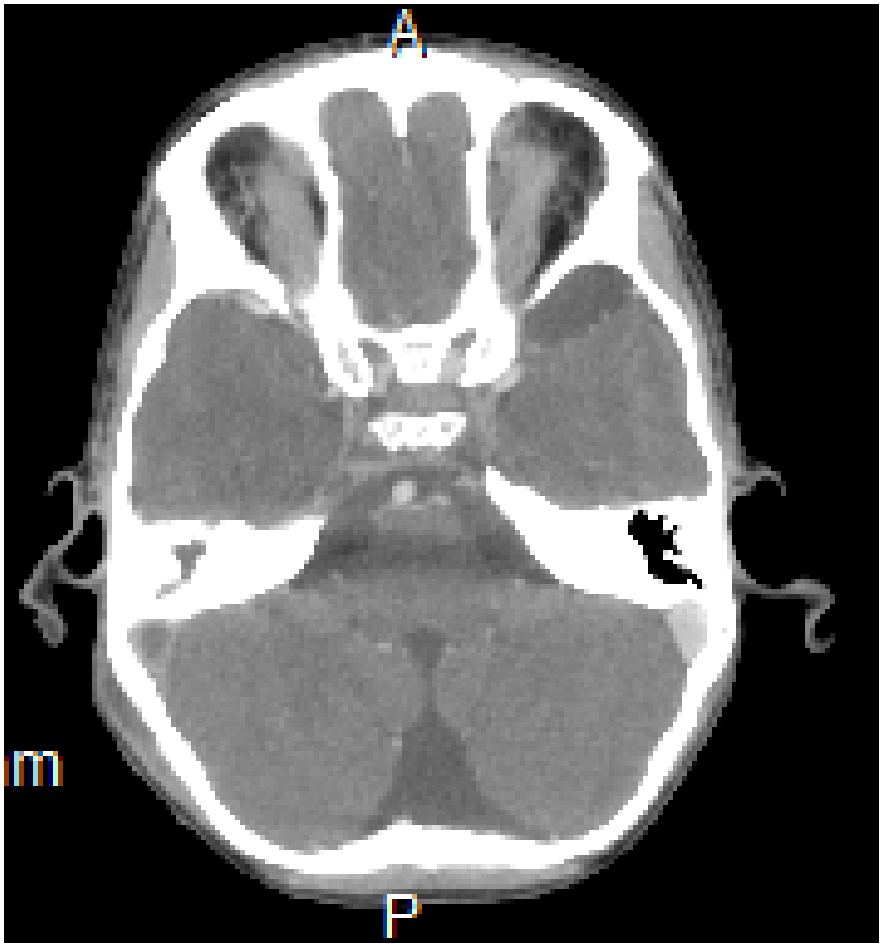


Figure 1a : lateral sinus thrombosis

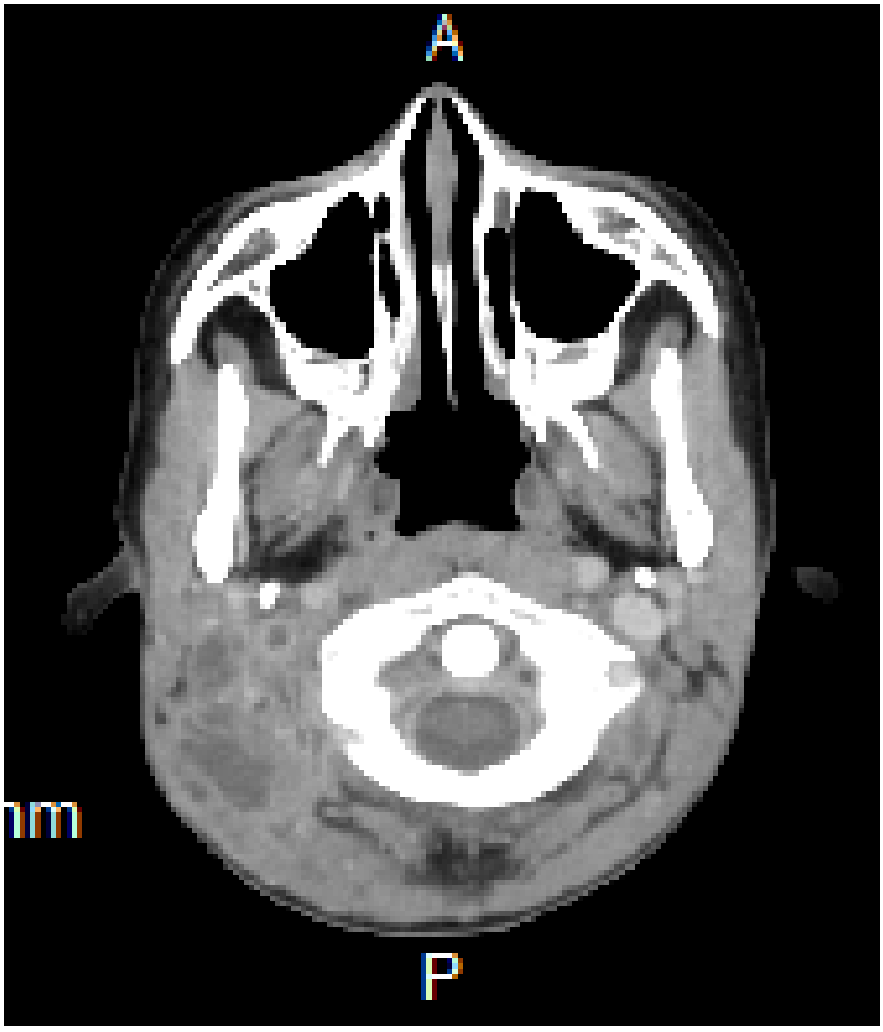


Figure2: internal jugular vein thrombosis

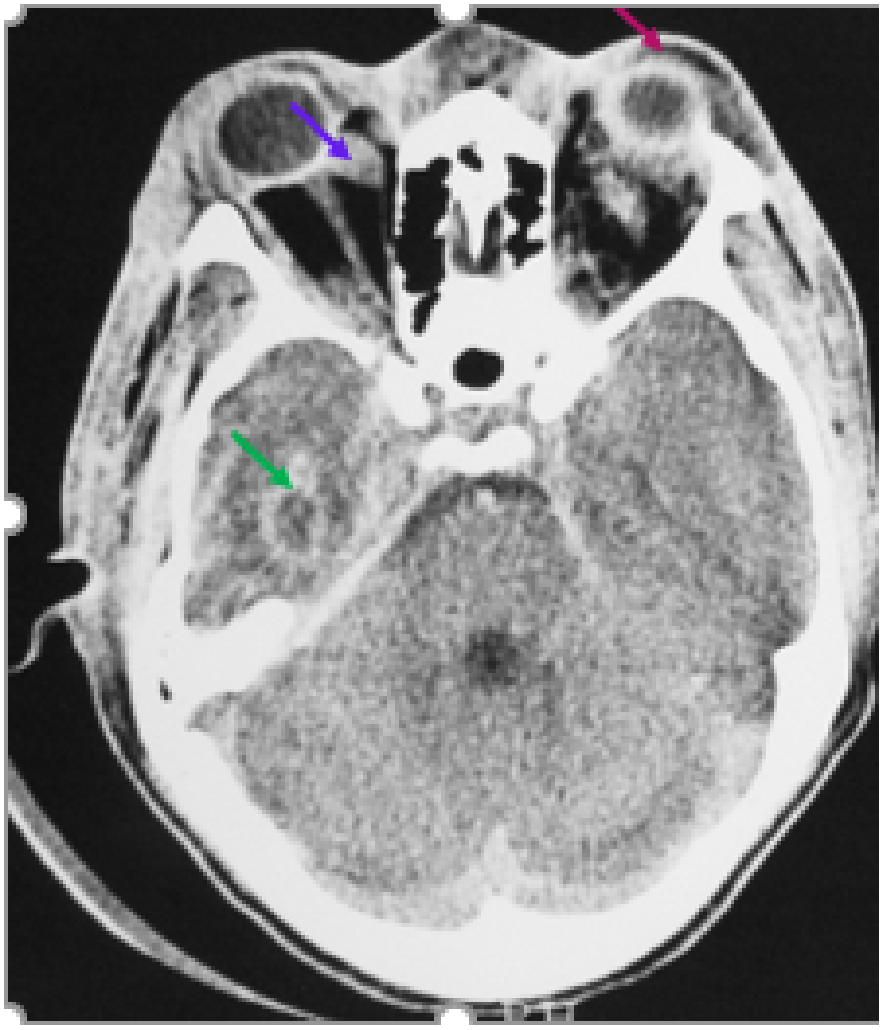
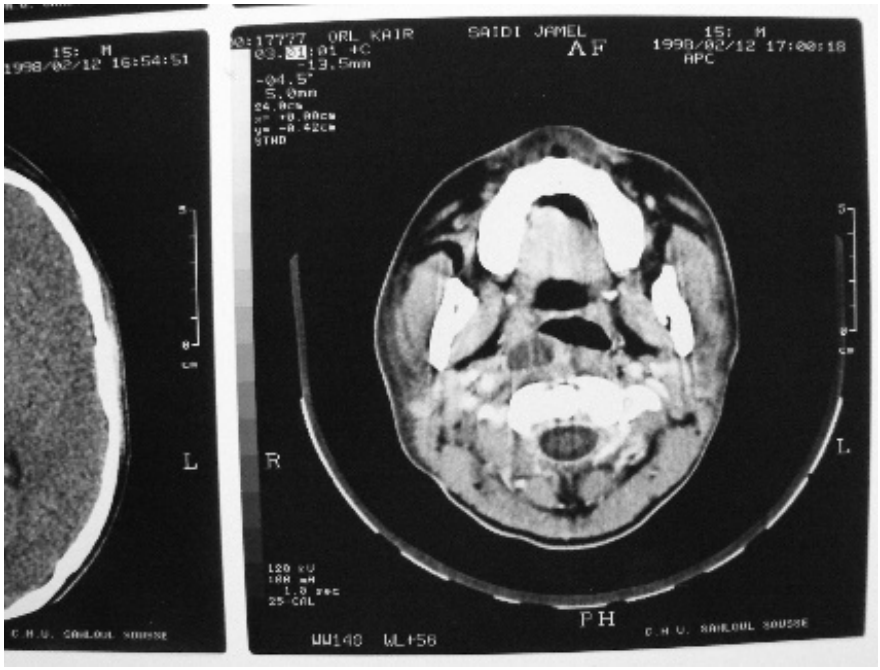
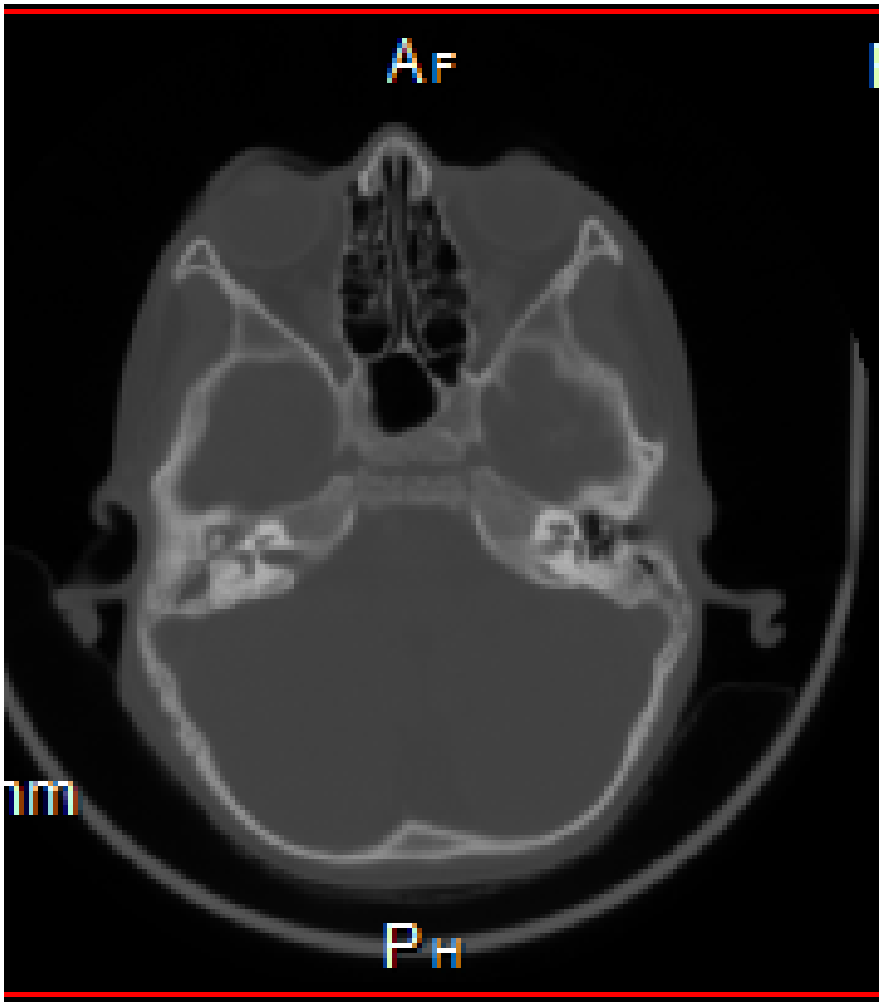


Figure3: cavernous sinus thrombosis





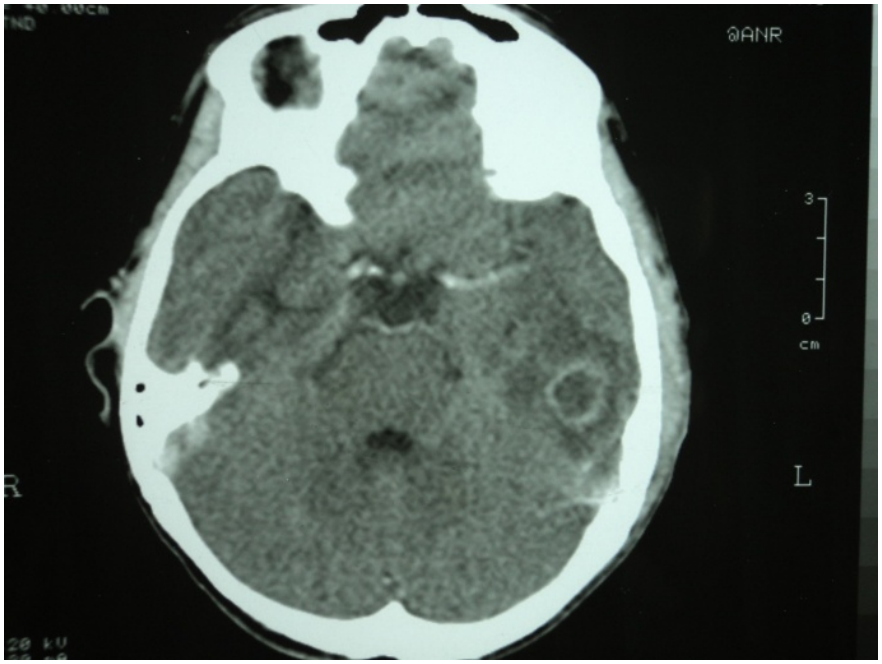


Figure5: retropharyngeal abcess

Figure4: mastoiditis Figure6: cerebral empyeme

Table 1: Table1: The aetiology was acute otitis media in 4 cases, cholesteatoma otitis media in 3 cases and necrotizing external otitis in 3 cases .

aetiologiy	Numbre of patients	Affected sinus
AOM	4	Lateral sinus: 3 cases Cavernous sinus: 1case
COM	3	Latéral sinus :3 cases
NEO	3	Sinus latéral: 3 cas

Table2: clinical examination findings

Signs	Numbre of patients
Fever	3
PFP (peripheral facial paralysis)	1
Exophtalmos with palpebral oedema	1
Torticollis	1
Cervical swelling	1
Retroauricular tenderness with swelling of the ear lobe	5
otorreha	5
Retracted tympanic membrane	1
Narrowed external auditory canal	2

Table3: repartition according to the antibiotic therapy administered and the causal pathology

Cefotaxime + fosfomycin+métronidazole	4	2 AOM 2 COM
Cefotaxime+ofloxacin	1	AOM
Cefotaxime+vancomycin+métronidazole	1	COM
Ciprofloxacin +ceftazidime	1	NEO

Table4: treatment of the necrotizing otitis externa

	Nbre of patients	Anti fungal treatment
Fungal NEO (candida)	1	Voriconazole IV then relay per os
Fungal NEO (mucorales)	1	Amphotéricin B: 1mg/kg/day IV (rupture Caspofungin)

Table5: Surgical treatment

Surgical treatment	Numbre of patients
Mastoidectomy	4
Mastoidectomy+ internal jugular vein ligation	1
Mastoidectomy+ extradural empyema evacuation	2
Antro mastoidectomy+ incision of the sinus and evacuation of the clot	2

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