Complications of Rhinosinusitis

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26.1 Introduction

Complications of sinusitis can be classified as local or systemic. Local complications are mostly due to the anatomical proximity of the sinuses to the surrounding structures. The orbit and the skull base are the most closely related structures to the paranasal sinuses as they share same bony margins. Complications generally occur when the infection spread to these areas due to anatomic proximity [1–3].

Local complications of rhinosinusitis include mucocele, pre-septal cellulitis, orbital cellulitis, subperiosteal abscess, orbital abscess, osteomyelitis, meningitis, brain abscess, subdural empyema, and thrombosis of venous sinuses [1–5]. They occur in approximately 5% of the patients who have been followed up for sinusitis [3].

Complications of rhinosinusitis can be classified as orbital, intracranial or osseous [6, 7].

26.2 Routes of Spread

Sinus infections can spread through the lamina papyracea. Ethmoidal sinuses are separated from the orbit by a thin bone layer called the lamina papyracea. Besides being thin, this lamina has congenital dehiscences and perforating vessels and nerves. Infections in ethmoidal sinuses can spread through the natural dehiscence of this layer into the orbit especially in children.

The close neighborhood of the sinuses with the orbit is another way. The base of the frontal sinus forms the roof of the orbit. The frontal sinus may have bony dehiscences that form a route for the spread of the infections. Especially in adults, infections of frontal sinuses can lead to orbital complications.

Another route of spread is anatomic dehiscences and weaknesses of surrounding bone structures. Bacterial infections can spread through these bony barriers because of sclerosis in chronic sinusitis and osteolysis in acute sinusitis.

Roots of teeth form a transition route for infections. The maxillary sinus is closely related to the roots of the first upper molar and second premolar teeth. Infections of these roots can cause isolated maxillary sinusitis [5].

Venous connections and diploic veins are another major contagion mechanism. Diploic veins (veins of Breschet) are located in frontal sinuses and infections can spread by thrombophlebitis of these structures. Also, the veins between orbit and the sinuses have no valves, so the infections of sinuses are easily spread to the structures of the orbit [7].

The infraorbital canal is located at the base of the orbit and causes the spread of maxillary sinus infections to the orbit.

Another way of spread is the extension of the infection through osteitis.

26.3 Predisposing Factors

Immunodeficiency (e.g., HIV, malignancies), diabetes mellitus, and incomplete antibiotic treatments of sinusitis are the most frequent predisposing factors for complications [5].

26.4 Complications of Sinusitis

Orbital complications such as pre-septal cellulitis, orbital cellulitis, subperiosteal abscess, and orbital abscess are the most common complications of sinusitis [5]. Meningitis,

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subdural empyema, intracerebral abscess, epidural abscess, and cavernous sinus thrombosis are intracranial complications [8]. Other complications include mucocele, pyocele, osteitis, osteoblastic osteitis [9] (Fig. 26.1a–e), and facial cellulitis. Besides that, some patients may experience hyposmia or anosmia due to the mechanical obstruction of nasal passage or inflammation of the olfactory nerve fibers.

26.4.1 Orbital Complications

The most common structure affected by sinus infections is orbit. Orbital complications arise most commonly from ethmoid sinusitis and rarely from sphenoid sinusitis [10–13]. Routes of spread that are responsible for orbital complications are dehiscent lamina papyracea, open suture lines or venous connections. Symptoms related to orbital involvement are swelling, impairment in extraocular muscle movements, and exophthalmos [14]. A direct or vascular spread of the infection may lead to periorbital or orbital cellulitis. Edema and erythema in the eyelid are the first symptoms of periorbital cellulitis. Maxillary sinusitis causes swelling in the lower eyelid and frontal sinusitis in the upper eyelid [15].

The incidence of orbital complications varies according to the literature (generally more than 20%) [5, 16, 17]. The left side is more frequently involved [16]. Since lamina pap-

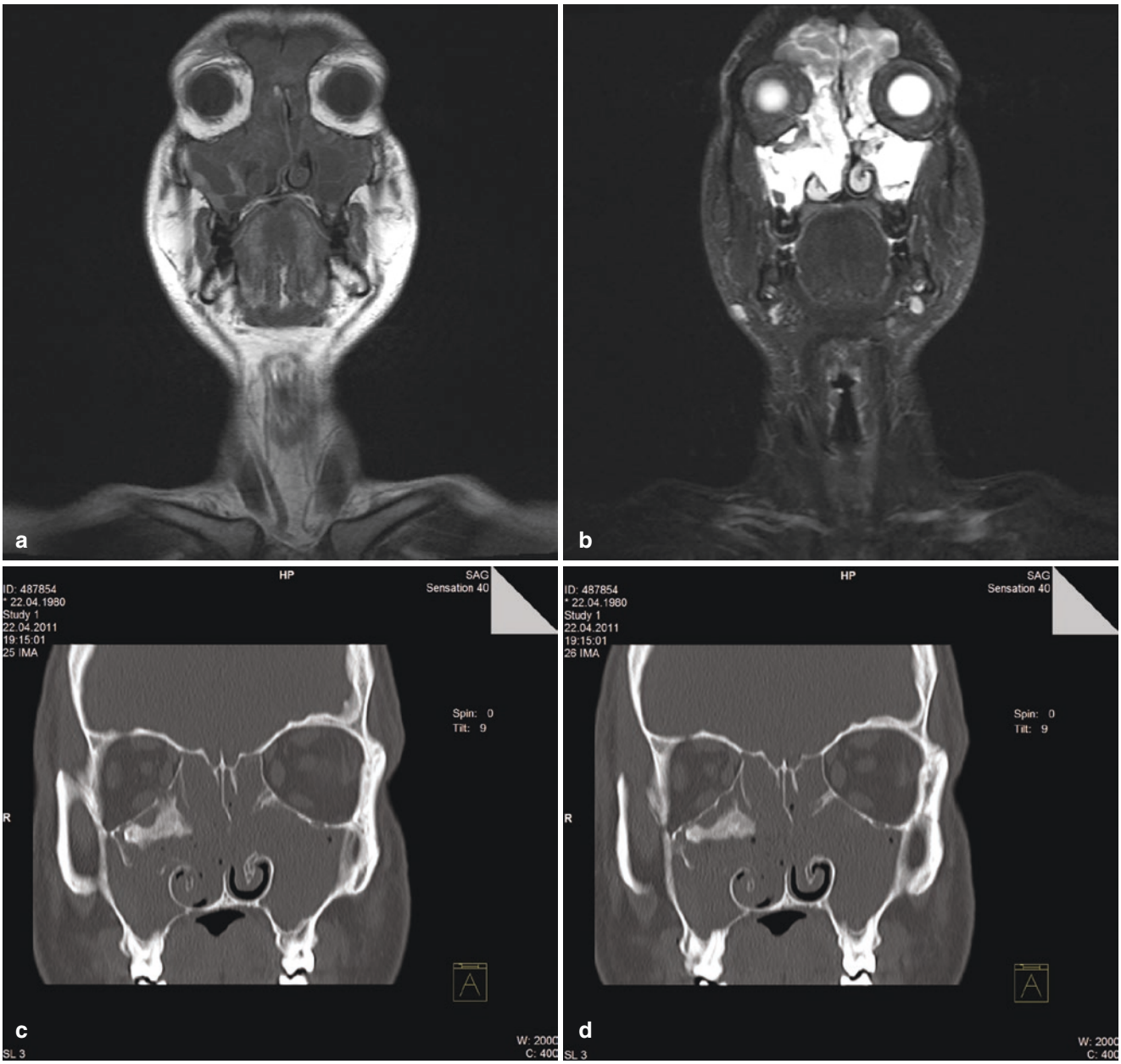

Fig. 26.1 (**a**–**e**) Osteoblastic Osteitis (Courtesy of Cagatay Oysu)

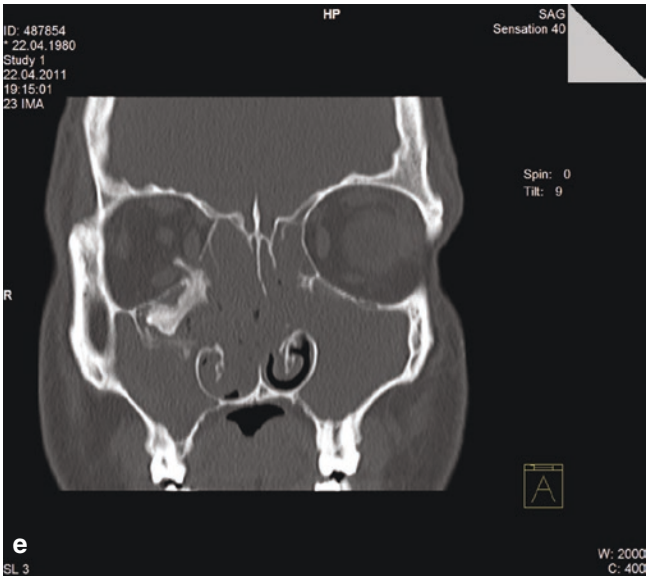

Fig. 26.1 (continued)

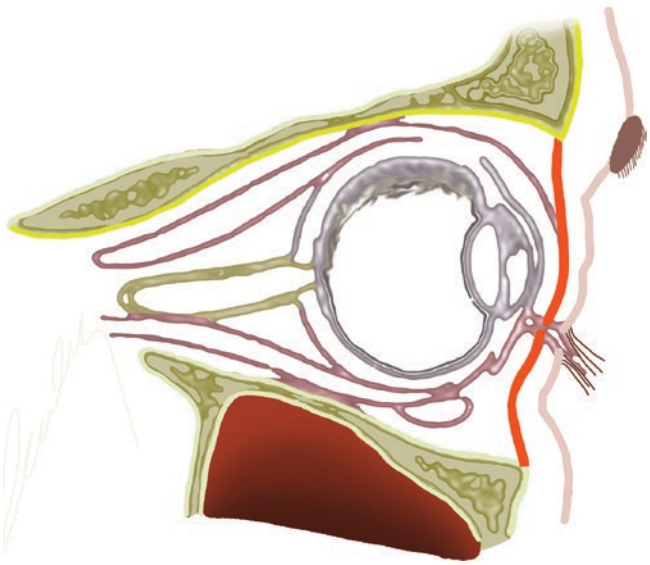

Fig. 26.2 Orbital anatomy

yracea is a thin bone layer separating the orbit from ethmoid sinuses and natural dehiscences are common, orbital complications mostly arise from ethmoid sinusitis. In younger individuals and children, ethmoidal sinusitis is the most common cause of orbital complications, whereas in adults, orbital complications mostly arise from infections in frontal sinuses. Also in adults, infections in sphenoid sinuses can spread to orbital nerve and may lead to blindness.

26.4.1.1 Pathogenesis

The roof of the orbit is surrounded by frontal sinus and the floor by maxillary sinus. The orbit is also bordered by ethmoid sinuses medially. Sometimes, orbital complications may be the first symptom of sinusitis [1].

Routes of spread to the orbit are bony dehiscence/defects (congenital/acquired), neurovascular foramens, and venous channels [5].

Lamina papyracea is a thin bone layer separating the ethmoid and maxillary sinuses from the orbit and infections can spread to the orbit by the natural dehiscences or by penetrating this bone layer (Fig. 26.2) [3].

The venous system in the orbit has no valves so the infection in the sinuses can also easily extend to orbit by the thrombophlebitis of these valveless veins [3]. Infections in the sinuses can also spread directly to the orbit by neurovascular foramens (anterior and posterior ethmoid foramina).

Orbital complications are more common in children than adults because bony septa between sinuses and orbit are thinner; also, bones have open suture lines and large vascular foramens.

Although sinus infection is responsible for 75% of cases, other causes like bacteremia, facial infections, trauma, tumors, dacryocystitis, and iatrogenic causes should be kept in mind in the differential diagnosis of the orbital complications [18].

26.4.1.2 Classification of Orbital Complications

Classification of the orbital complications helps us to decide if medical treatment is enough or surgical intervention is needed.

Orbital complications have been categorized by Chandler et al. [17] according to severity into five stages:

- Stage I: Inflammatory edema and pre-septal cellulitis
- Stage II: Orbital cellulitis
- Stage III: Subperiosteal abscess
- Stage IV: Orbital abscess
- Stage V: Cavernous sinus thrombosis

Stage I, Periorbital Cellulitis/Pre-septal Cellulitis

Orbital septum and tarsal plate play an important role in limiting the progression of the infection into the orbit [3]. Pre-septal cellulitis is the inflammation or the infection of the skin around the eye and the eyelid, located in front of the orbital septum. This complication occurs when the ethmoid vessels around the skin were obstructed by inflammation due to the sinusitis. Patients with pre-septal cellulitis have edema and erythema around the eye and eyelids but no tenderness and no proptosis/chemosis [17]. The movement of the eyeball and vision are normal. Also, these findings are used in the differential diagnosis of pre-septal and orbital cellulitis.

Stage II, Orbital Cellulitis/Post-septal Cellulitis

In contrast to pre-septal cellulitis, orbital cellulitis is the edema and inflammation of the orbital contents behind the

orbital septum without abscess formation. Main complaints are proptosis, restricted and painful eye movements, and chemosis. Examination of the vision is of great importance as the visual loss may accompany [17].

Stage III, Subperiosteal Abscess

This condition is the formation of an abscess between the periosteum and the bone. Because of the mass effect of the abscess, the orbit is generally displaced in inferolateral direction. Proptosis, chemosis, impaired eye movements, and loss of vision are constant findings of abscess [17].

Stage IV, Orbital Abscess

Orbital abscess refers to the formation of pus within the orbital content. Patients are representing complete ophthalmoplegia, severe proptosis, and loss of vision [17].

Stage V, Cavernous Sinus Thrombosis

This complication has the worst prognosis. Patients have bilateral ocular involvement. High fever, severe headache, photophobia, proptosis, bilateral ophthalmoplegia, loss of vision, and palsies of III, IV, V1, V2, and VIth cranial nerves are the signs of cavernous sinus thrombosis [19].

26.4.1.3 Periorbital Cellulitis

Periorbital cellulitis is the most common complication of sinusitis and defined as the inflammation of the tissues in front of the orbital septum [20–22]. The representing symptoms generally include orbital pain, fever, periorbital edema, and erythema [23]. A soft tissue swelling around the orbit and mucosal thickening in sinuses was seen on CT scans [6]. Oral antibiotics are generally enough for the treatment of this complication, but clinicians should be alert about spreading beyond the orbital septum and take the necessary precautions [22].

If alerting symptoms such as proptosis, ophthalmoplegia or visual abnormalities in a patient with known sinusitis occur, an urgent CT scan is essential to evaluate orbital tissue for the differential diagnosis of orbital or periorbital cellulitis and abscess. Urgent surgical indications are the presence of an abscess on CT scan or progression of orbital complaints despite intravenous antibiotics. Visual acuity should be checked periodically in these patients. If the patient was afebrile during 48 h and ophthalmological symptoms are improving, antibiotic therapy can be continued orally [6, 22].

26.4.1.4 Orbital Cellulitis

Orbital cellulitis represents an "inflammation and cellulitis of the orbital contents with varying degrees of proptosis, chemosis, limitation of extraocular movement, and/or visual loss that depend on the severity of the process." Orbital involvement causes diffuse edema and bacterial infiltration of the adipose tissue, but no abscess (Fig. 26.3) [3].

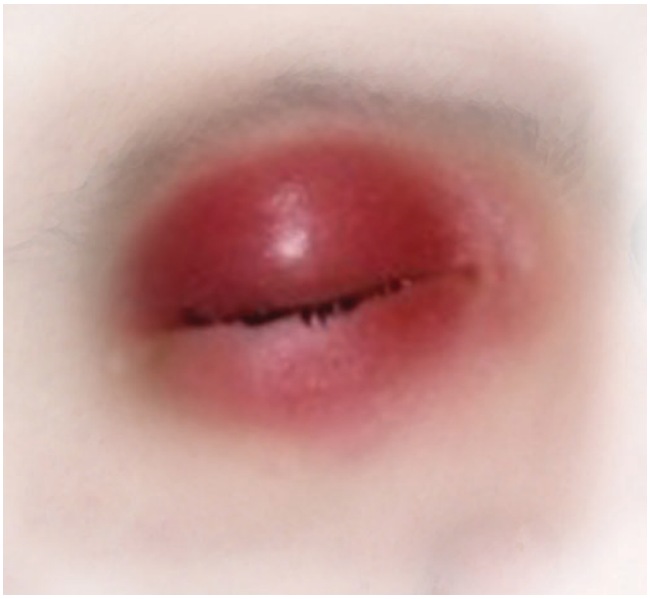

Fig. 26.3 Orbital cellulitis

26.4.1.5 Subperiosteal or Orbital Abscess

A subperiosteal abscess is a collection of pus within periosteum of the ethmoid, frontal, or maxillary bone. Edema, erythema, restriction of the eye movements, chemosis, and proptosis are the major symptoms. There may be a displacement in the globe due to the abscess (globe can be displaced laterally due to ethmoid sinusitis or inferiorly due to frontal sinusitis). Visual acuity or conjunctival examinations are generally normal in early stages [3]. Then, ophthalmoplegia occurs due to the paralysis of extraocular muscles followed by visual loss if not intervened. In many studies, the frequency of orbital abscess in pediatric patients was reported as 8.3 and 9% [24, 25].

Orbital abscess is the formation of an abscess within the orbital content. Patients have severe chemosis, proptosis, and complete ophthalmoplegia (paralysis of cranial nerves II, III, IV, V, and VI). Loss of vision may be due to the occlusion of the central retinal artery. Other causes responsible for the visual loss may be corneal ulceration, optic neuritis or panophthalmitis. In patients with ophthalmoplegia, edema of the medial rectus muscle in CT scans which causes lateralization of the orbit was detected. This situation requires urgent intervention, and if not treated properly can lead to permanent blindness. Visual acuity should be controlled periodically by an ophthalmologist from the moment of diagnosis.

Differential diagnosis of a periorbital and orbital abscess is made by a CT scan. Obliteration of the optic nerve and the details of extraocular muscles and on CT scan is indicative of orbital abscess development. Sometimes, even air can be detected in orbit due to anaerobic bacteria. Also, in some patients, sepsis can spread intracranially into the orbit [6,

26]. Indications of orbital exploration include the presence of an abscess in orbit on CT scan or progression of clinical findings in spite of intravenous antibiotic treatment that covers aerobic and anaerobic pathogens after 24–48 h.

26.4.1.6 Cavernous Sinus Thrombosis (CST)

Cavernous sinus thrombosis (CST) constitutes 9% of intracranial complications and occurs when the infection spread outside the orbit [27–31]. The spread of the infection is due to the valveless veins between the cavernous sinus and the orbit and generally occurs in ethmoidal or sphenoidal sinusitis. CST is a rare life-threatening complication and can lead to permanent blindness. The mortality rate is approximately 20% [27–29]. Patients have bilateral ocular involvement. High fever (fever spikes because of septic emboli), prostration, severe retro-ocular headache, photophobia, proptosis, chemosis, bilateral complete ophthalmoplegia, loss of vision, and palsies of III, IV, V1, V2, and VIth cranial nerves are the major signs [6, 15]. If not treated, CTS progresses rapidly and leads to meningitis, toxicity, and sepsis [22].

Definitive diagnosis is made by high-resolution CT scan [32], which shows low enhancement compared to normal [33]. The use of anticoagulants is controversial [15] but if the patient has no sign of intracerebral hemorrhage, clinicians generally tend to use them [6, 34, 35].

Microbiology

The most frequently isolated microorganisms in orbital cellulitis and abscess are *Haemophilus influenza*, *Streptococcus pneumoniae*, *S. aureus*, and anaerobic bacteria (*Prevotella, Porphyromonas, Fusobacterium*, and *Peptostreptococcus* spp.) [(1, 3, 36)]. The pathogens isolated in CST are *S. aureus* (50–70%), *Streptococcus* spp. (20%), and gram-negative anaerobic bacilli (pigmented *Prevotella*, *Porphyromonas* spp., and *Fusobacterium* spp.) [37–39].

Treatment

The outcome of medical treatment largely depends on the stage and persistence of the orbital involvement. Chandler I to III is primarily treated with antibiotics. However, if the loss of vision develops, additional surgery can be needed. Ophthalmology consultation and close monitoring of vision are essential if orbital involvement is suspected. Chandler IV and V are directly treated with urgent surgical intervention in addition to intravenous antibiotics. In the case of cavernous sinus thrombosis, another treatment agent is anticoagulants, but this is controversial since intracranial hemorrhage may occur.

Patients with class I complications (pre-septal cellulitis) can be treated with oral antibiotics; symptomatic treatment of sinusitis should also be added. Amoxicillin-clavulanate and cefuroxime axetil are first-choice antibiotics. Patients should be followed closely for the progression of the clinical findings. If the involvement of orbital content (classes II to V) is suspected, parenteral treatment should be initiated immediately. Ceftriaxone/cefotaxime combined with metronidazole/clindamycin should be preferred for parenteral therapy [3].

Patients with class II complications should be treated more aggressively. Ophthalmology consultation is essential if orbital involvement is suspected. Since disease progression can be rapid, imaging methods and treatment plan should be done as quickly as possible [3]. Antimicrobial agents such as penicillin-clavulanic acid, carbapenems, and cefoxitin that are effective to aerobic and anaerobic bacteria including methicillin-sensitive *S. aureus* should be started. Also, metronidazole can be added as a combination. In patients suspected of methicillin-resistant S. aureus, vancomycin should be administered [3].

Patients with class V complications (CST) should be treated with wide-spectrum antimicrobials. The use of anticoagulants or corticosteroids are still controversial [40] but indicated if the patient has no sign of intracerebral hemorrhage [6, 35]. Urokinase which has fibrinolytic activity may help dissolve the cloth. Despite proper treatment, CST still remains as a life-threatening complication and can lead to permanent blindness. Nowadays, early diagnosis and aggressive treatment strategies increase survival rates to 70–75% [39–41].

26.4.2 Intracranial Complications

Although the exact incidence of intracranial complications in sinusitis is unknown, it has been reported as 4% in various studies [2]. They are still the second most common complication of acute sinusitis despite the widespread use of antibiotics [2]. On the other hand, it has been reported that paranasal sinusitis and dental infections are the origin of one to two-thirds of brain abscesses [1, 42]. Despite their decreasing frequency, intracranial complications are still potentially life-threatening situations and should always be kept in mind in patients with sinusitis [3].

Intracranial complications generally occur as a result of ethmoidal or frontal sinusitis. Infections can spread to endocranial structures by two routes, most commonly by diploic veins or rarely by eroding the sinus bones [30].

Non-specific symptoms such as high fever, nausea/vomiting, mental state problems, meningeal irritation signs, and frontal or retro-orbital headache are the main clinical findings [29]. A patient with intracranial abscess can be completely asymptomatic or may show focal neurological findings such as mild affective or behavioral changes, altered consciousness, and imbalance due to increased intracranial pressure [6, 14].

Cerebritis is the first stage of all intracranial complications. Then, an abscess formation occurs due to the encapsulation of necrosis in brain tissue. Most common iso-

lated bacteria from patients with intracranial complications are anaerobic or mixed aerobic-anaerobic microorganisms. For an accurate diagnosis, generally, a CT scan is enough; MRI is indicated if sinus thrombosis is suspected [30]. If there is a clinical suspect of meningitis, lumbar puncture is indicated after exclusion of intracranial abscess [6].

Intracranial complications of sinusitis include epidural and subdural empyema, sagittal sinus and cortical vein thrombosis, brain abscess, meningitis, facial osteomyelitis, and mucocele [3].

26.4.2.1 Pathogenesis

Intracranial extension of sinus infections can be due to retrograde thrombophlebitis, hematogenous spread, or direct bone erosion.

Bone erosion occurs as a result of osteitis (i.e., posterior wall of the frontal sinus in frontal sinusitis). Blood vessel coursing along the dura mater facilitates the bacterial penetration and a granulation tissue develops due to the inflammatory reaction of the dura resulting subdural empyema [3, 43].

The second route for the spread is the diploic veins between paranasal sinuses and intracranial venous structures [44]. This path is usually seen in acute sinusitis or acute exacerbations of chronic sinusitis. The absence of valves in these veins allows thrombosis progressing to venous sinuses, subdural and cerebral veins (retrograde thrombophlebitis).

The third route of spread is the hematogenous way which is important in the development mechanism of intraparenchymal brain abscess [3].

Routes for the spread of infections from sinuses to intracranial structures [5]:

1. Venous spread; septic thrombophlebitis in venous structures of paranasal sinuses passes through valveless Breschet veins in the frontal bone and leads retrograde thrombophlebitis of meningeal veins [45].
2. Arterial spread; this way is the extension of the infection by direct arterial embolization.
3. Bony erosion; this route is due to the bone erosion separating paranasal sinuses and intracranial structures by osteitis.

Extension of the infection via immature arachnoid is another route of spread mentioned in the literature especially in infants. In a study, this route was reported as responsible for 75% of the subdural empyema cases. On the contrary, arachnoid acts as a barrier to prevent the spread of infection to intracranial structures in adults [46].

A common complication is extensive cortical thrombophlebitis [46]. Edema, hyperemia, and small infarct areas occur in the brain parenchyma [47]. Bilateral cerebral edema and hemorrhagic infarction can also be triggered by septic thrombosis of dural sinuses [46, 47]. This table leads to various findings such as focal neurological deficits, seizures, and increased intracranial pressure [3].

The exact mechanism of brain infection during the course of intracranial spread is still unknown. A necrotic focus may cause venous obstruction and leads to the growth of anaerobic bacteria [48]. Then the infection spreads to cerebral vessels and results in cerebritis. After that, the liquefied necrosis encapsulated inside is composed of three layers (granulation tissue layer, collagen layer, and glial cell shell). Abscess formation takes 2–3 weeks to complete. Cortical abscesses are settled more superficially and more vascular than the white matter abscesses. White matter abscesses can easily rupture to ventricle because of deep location and thin capsule.

Subdural empyema may be located at four sites (frontal lobe, occipital lobe or posterior fossa tentorium) [43, 44, 46, 47].

Microbiology

Anaerobes such as *Prevotella* spp. and *Porphyromonas* spp., *Fusobacterium* spp., and *Peptostreptococcus* spp. are recovered from over two-thirds of patients with brain abscesses [42]. Microaerophilic microorganisms like streptococci are generally isolated from patients with brain abscess due to the spread of maxillary sinusitis originated from dental infections [44]. From the aerobe organisms commonly *S. aureus*, rarely *H. influenzae* is isolated [3].

26.4.2.2 Predisposing Factors

Predisposing factors for intracranial complications are diabetes mellitus and chronic renal failure [48, 49].

26.4.2.3 Management

A patient suspected of having cerebritis should be urgently treated with antibiotics in order to prevent abscess formation [50]. Urgent surgical intervention is indicated if brain abscess has been developed. After drainage, the patient should receive antibiotic treatment for 4–8 weeks. If symptoms of intracranial increased pressure occur, additional treatment modalities are needed such as mannitol, hyperventilation or dexamethasone [3].

For proper antibiotic treatment, microbiological diagnosis is of great importance. Material intake for culture can be done by CT-guided needle aspiration or during surgical drainage. Treatment response can be traced with CT-scans. Although surgical drainage is still the gold standard management of brain abscess, follow-up with long-term high-dose antibiotics may be a treatment choice in selected patients [51].

The use of steroids in the treatment of brain abscess is controversial. Corticosteroids are generally used for reducing cerebral edema, but it is shown that they increase necrosis and therefore inhibit the maturation process of the abscess. Additionally, steroids also reduce the penetration of the anti-

biotics to the tissue. According to these data, the efficacy of steroids in the course of treatment is still unknown, so dosage and time of starting are varying in different studies [3]. If started, steroid therapy should be of short duration.

When an intracranial complication is suspected, an empirical antimicrobial therapy should immediately be started covering most commonly isolated microorganisms. Penicillins which penetrate well to the abscess are used to cover non-beta lactamase producing, gram-positive aerobes and anaerobes. Carbapenems are used for beta-lactamase producing bacteria. Third generation cephalosporins are commonly administered for aerobic gram-negative organisms, and metronidazole and chloramphenicol, which both penetrate intracranially, provided coverage against anaerobes [52, 53]. For *Pseudomonas aeruginosa*, ceftazidime or cefepime can be preferred [54]. Vancomycin is used in cases of methicillin-resistant *S. aureus*.

The gold standard treatment modality for intracranial complications is surgical drainage combined with a long course of antibiotics. Delays in surgical interventions can lead to morbidity and increase mortality [50]. Related sinus infections or periodontal/dental lesions leading to complication should also be treated concomitantly if the patient's general condition is permissible [3].

26.4.3 Osseous Complications

Another complication of sinus infections is the osteitis of the surrounding bone tissue leading involvement of the brain and nervous system. Studies demonstrate that mucosal infection can cross the membrane and induce an inflammatory response in the underlying bone. Infection in any sinus can cause osteitis but the most common localization is frontal sinus [15]. Typically, maxillary osteitis is common in infants [6, 33].

In some patients, frontal sinusitis leads to vascular necrosis of the frontal bone; osteitis occurs in the anterior and posterior table of the frontal sinus. Involvement of the anterior wall clinically presents as a "pulpy" mass under the skin of the frontal region called "Pott's puffy tumor." Osteitis of the posterior wall leads to meningitis, peridural abscess or brain abscess [15]. Gallagher reported in his review of 125 patients with complicated sinusitis that osteitis was seen in 9% of cases. The sinus walls were found to be affected in 32% of the patients in another study [54]. In a study made by Lang in 2001, it was reported that subdural empyema was seen in 10 patients with frontal sinusitis, of which 4 had Pott's puffy tumor and 1 had a periorbital abscess [55, 56].

A combination of an intravenous broad-spectrum antibiotic administration, surgical drainage, and debridement of necrotic bone are the main treatment options [6, 15].

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