Sinonasal Orbital Apex Syndrome

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Rhinosinusitis (RS) is an inflammatory disease of the nose and paranasal sinuses with a clinical picture of anterior or posterior nasal discharge, congestion, olfactory dysfunction, and facial pain or pressure. It must be confirmed with endoscopic or radiological signs of inflammation. By its duration, it is classified into acute (i.e., duration <4 weeks), subacute (4–12 weeks), and chronic RS (>12 weeks). Moreover, RS can be named according to the inflamed paranasal sinus, e.g., sphenoiditis in sphenoid sinus inflammation. RS significantly affects the patient's quality of life due to the significant impact on personal development, sleep hygiene, mental health, physical condition, self-perception, and family relationships.

Keywords: sphenoid sinusitis ; skull base ; ocular infections ; sphenopalatine neuralgia

1. Introduction

Acute rhinosinusitis (RS) commonly arises as a viral infection, which may present as a brief episode or prolonged disease due to an impaired mucociliary clearance caused by viruses. Impaired mucociliary clearance predisposes a mucosa to a bacterial or fungal superinfection [1][2]. Acute bacterial RS is most commonly caused by *Streptococcus pneumoniae*, *Haemophilus influenzae* type B, *Moraxella catarrhalis*, *Staphylococcus aureus*, and some anaerobic bacteria [3]. *Aspergillus* spp. are the most common causative agents of the fungal ball, a chronic RS, and the most common type of fungal RS—other fungi, e.g., *Mucor* spp. and *Rhizopus* spp. rarely cause fungal RS but typically present a type of acute fulminant invasive fungal RS called mucormycosis [4]. Less often, an invasive fungal RS can be caused by *Candida* spp., *Alternaria* spp., *Scadesporium* spp., and *Fusarium* spp. [5].

2. The Clinical Picture of Fungal Rhinosinusitis

The sphenoid sinus is rarely involved in invasive fungal rhinosinusitis. Nonetheless, the acute, chronic, or acute fulminant form that can develop present a higher morbidity and mortality rate compared to other paranasal sinuses due to the proximity of vital neurovascular structures to the sphenoid sinus (internal carotid artery, cavernous sinus with contents, pituitary gland, optic nerve) [6].

Asymptomatic clinical picture and long-term indolent disease are more typical for non-invasive than invasive fungal RS. Among more or less troublesome symptoms could also be a bad smell in the saprophytic fungal infection, facial pain, post-nasal drip and cacosmia in the fungal ball, and proptosis in the allergic FR. There could be a slower progressive appearance of bloody nasal discharge, unilateral nasal obstruction, cacosmia, eye proptosis and sinonasal tumour-like lesion in the chronic invasive fungal RS. Conversely, the acute and subacute invasive fungal RS are clinically rich. They start as a short prodrome followed by rhinorrhea, nasal congestion, facial pain or pressure, and fever in the acute invasive fungal RS [7][8]. Fungal sphenoid sinusitis is usually asymptomatic in the early stages, delaying the diagnosis [9]. An unspecific or even florid clinical picture can support the possibility of fungal infection.

3. Orbital Complications of Sinonasal Disease

The spread of the infection to the orbit is uncommon in acute RS but occurs more frequently than the intracranial spread. Children and immunocompromised adults are more commonly affected. The predisposing factor is most commonly a dehiscence in the *lamina papyracea* in the posterior ethmoid, maxillary or frontal sinus due to an acquired bony erosion. A fungal orbital infection could also result from a venous spread [3][6][10]. The cases of orbital cellulitis and abscess occur mainly in the retrobulbar compartment of the orbit [11], e.g., in the orbital apex.

Orbital apex refers to the most posterior part of the orbit. Numerous neurovascular structures communicate with it through the superior orbital fissure and the optic canal. Disorders of orbital apex comprise three syndromes depending on the lesion's location: orbital apex syndrome, superior orbital fissure syndrome (Rochon-Duvigneaud syndrome) and

cavernous sinus thrombosis (CST) [12]. Orbital apex syndrome encompasses CN II, III, IV, V_1 and VI impairment due to inflammatory damage or direct compression [13]. Superior orbital fissure syndrome is caused by a lesion immediately anterior to the orbital apex. Its clinical presentation resembles the orbital apex syndrome. However, it lacks the CN II impairment. Cavernous sinus thrombosis presents with cheek and lower eyelid hypesthesia (both caused by damage to the CN V_2) apart from the OAS signs. In addition, cavernous sinus thrombosis can be accompanied by Horner syndrome [11]. The latter evolves if the pericarotid sympathetic plexus is damaged anywhere along the course of the internal carotid artery, including its cavernous segment. It typically comprises ipsilateral upper eyelid ptosis, myosis and sometimes facial anhidrosis due to the damage in the sympathetic pathway. Pupillary responses are normal [14][15]. Another possible cause of diplopia is the myositis of extraocular muscles [11].

The patient had eroded and dehiscent bony walls of the right sphenoid sinus, eroded and expanded Vidian canal and dehiscent posterior wall of the pterygopalatine fossa. The lateral recess of the sphenoid sinus was filled with swollen mucosa and mucus. The pterygopalatine fossa was inflamed, expanded and widely communicated with the orbital apex via an inferior orbital fissure and with the lateral recess of the sphenoid sinus via dehiscence through the posterior wall. Most observed changes can result from a fungal ball evolving into invasive fungal RS causing orbital apex syndrome, pterygopalatine fossa infection and Horner syndrome [16].

4. Risk Factors and Pathogenesis of Invasive Fungal Rhinosinusitis

There were no obvious identified risk factors for the development of invasive fungal RS as the patient did not have immunodeficiency or disease such as diabetes mellitus [17] or haematological malignancy [18]. These findings are consistent with the previously reported cases of invasive rhino-orbital-cerebral aspergillosis and invasive oronasal aspergillosis in immunocompetent patients [9][19][20][21].

According to the literature, a patient's high age cannot be identified as the only risk factor contributing to the development of chronic RS. However, presbynasalis, which consists of collagen and nasal mucosa atrophy, a decrease in mucociliary transport, mucus production, the loss of vessel patency, and especially immunosenescence in older patients are considered a significant determinant in the development of RS [5][22].

The patient had no classic environmental or occupational fungi exposure (e.g., working or living in a moist environment, exposure to construction or excavation sites) according to the epidemiological enquiry performed by the infectious disease specialist. However, the patient's residence was not examined, which could reveal the link between domestic mould exposure and invasive aspergillosis as already described elsewhere [23]. Nevertheless, it has been stated that fungi are almost ubiquitous in the paranasal sinuses. After inhaling the spores, their pathogenicity depends more on the patient's state than the fungi [7][24]. If the fungi had passed the epithelium, the infection could be considered invasive and vice versa. Therefore, even extensive growth of the fungi could be only saprophytic colonization or fungal ball on one side of the spectrum or a fatal invasion of the central nervous system in invasive fungal RS on the other side of the spectrum [6]. Namely, the fungal ball can progress to acute invasive fungal RS [21] or to micro-invasive form, which was recently termed intermediate invasive fungal RS [16].

5. Microbiology and Histopathology Analyses

Microbiological analyses from the transnasally collected specimen are considered in diagnosing acute RS when the treatment fails [3][25][26][27]. The efficacy of pus specimen cultivation in acute RS varies between 33% and 66% [3][25][26]. Moreover, the rate of positive results for fungal cultivation is only 33% due to microinvasion of vascular tissues, which results in negative results [5][9][26]. Histopathological analyses can be negative in the presence of sparse fungal forms, which is typical in chronic invasive fungal RS [28]. In addition, microbiological and histopathological analyses yield depends upon properly sampling the infected tissue. Therefore, negative fungal cultures and histopathology results do not rule out the presence of fungal infection [8][28]. When the infection invades the skull base and presents as atypical skull-base osteomyelitis, obtaining the specimen to perform analyses may be even more challenging. It is paramount to put a multidisciplinary team effort into managing these cases [10][29][30].

In the presented case, a microbe was not identified microbiologically or histopathologically after two surgeries. Moreover, systemic markers of fungal infection (galactomannan, beta-D-glucan) were negative. Nevertheless, the fungus was observed macroscopically intraoperatively as a fungal ball in the sphenoid sinus. Due to the clinical and radiological characteristics of orbital apex syndrome, Horner syndrome, and pterygopalatine fossa infection, the patient's diagnosis was an acute invasive fungal sinusitis treated empirically. PCR of tissue samples obtained during the first surgery at the regional secondary otorhinolaryngology service could confirm the presence of fungi as already described elsewhere [28][30]

but were unfortunately not performed. It is possible that microbiological and histopathological analyses obtained during the second surgery were negative due to the previous initiation of antimicrobial therapy and other already described reasons related to microbiology and histopathology analyses [3][5][9][25][26]. Moreover, tissue sampling was more challenging than the first surgery, when the fungal ball was observed macroscopically. Since the patient's condition improved after the second surgery, no debridement and second sampling were performed, as in other studies [28].

6. Surgical Treatment and Postoperative Management

Complications of RS need to be treated aggressively, either conservatively and/or surgically. The decision for surgical treatment depends on the clinical picture and radiological findings. Nevertheless, appropriate broad-spectrum intravenous antibiotics must be initiated to cover staphylococci, streptococci, and anaerobes. Eventually, culture and laboratory test results should guide the definite therapy [10].

Surgical intervention can be performed via a transnasal endoscopic approach for medially located lesions, e.g., medial to the sagittal mid-pupillary line. A transorbital approach (e.g., via blepharoplasty or lateral decompression incision) should be utilized for laterally located lesions. Other transorbital approaches for the medially located disease include the Lynch–Howarth or transcaruncular incision, the transconjunctival approach, and a combined external and transnasal endoscopic approach. The endoscopic technique can be used transorbital as well [10]. Nowadays, in a sinonasal orbital or orbital apex complication, the transnasal endoscopic approach presents a standard treatment since it enables the causal treatment of orbital disease (i.e., paranasal sinus drainage in endoscopic sinus surgery) [31].

A transnasal endoscopic unilateral sphenoethmoidectomy, pterygopalatine fossa dissection, medial orbital wall and orbital apex decompression were performed efficiently. The indication for the surgery was clear since there were no symptoms resolution days after the first surgery, and the different potential pathologies caused the patient's clinical picture.

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