

Management of acute invasive fungal rhinosinusitis with orbit-cranio-facial involved—— our experience with 8 cases

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Abstract

Key points: ? Diagnosis of AIFRS should be alert in the immunocompromised patient presenting with new-onset, rapidly progressive sinusitis with facial-cranio-orbital spread. ? Extended debridement should be considered on a case-by-case basis. ? Antifungal agent contributed greatly to the outcome of AIFRS. ? Prognosis mostly up to the balance of underlying disease and fungal invasion, more emphasizes should be focused on comprehensive treatment. ? AIFRS with facial-cranio-orbital involved often had a disastrous end.

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1 Introduction

Acute invasive fungal rhinosinusitis (AIFRS) are rare events which generally occurs in immunocompromised patients, management of such disease means great challenge to ENT doctor because of its dangerous outbreak and poor general condition, with mortality up to 50-80%[1,2].

The concept of invasive fungal infection refers to the invading of fungal hyphae to epithelial tissue, bone, with potential neural and vascular invasion. It generally classified into chronic invasive fungal rhinosinusitis (CIFRS) and acute invasive fungal rhinosinusitis (AIFRS). CIFRS is an indolent infection with a slow destructive process while AIFRS is defined by a time course of less than 4 weeks' duration, with predominant vascular invasion and fast spread which need an urgent management.

In this paper, by analyzing the clinical features, management and follow-up of 8 AIFRS patients with orbit-cranio-facial invasion, we aimed to share clinicians with our experience on how to manage such a disease and discuss the main factors which predict the survival outcomes.

2 Materials and methods

2.1 Study design and patients.

This is a retrospective analysis, including 8 cases of "acute invasive fungal sinusitis with cranio-facial-orbit involved" who admitted to our hospital from Feb.2016 to Oct.2022. There were 4 males and 4 females, with an average age of 59.8 ± 13.1 years. The lesions originated from nasosinus, with a rapid spread to orbit, skull base, face and/or palate. A definitive diagnosis based on histopathological examination (6 cases), or microbiological detection (1 case), or gross sign of mucor growth (1 case).

2.2 Clinical data of the participants

All Patients' data including age/sex, main symptoms, underlying diseases, sites of infection, causative fungus, CT/MR findings, individualized therapeutic schedule, following-up and the prognosis were listed in table1-3, Fig1-2, supplementary Fig1-4. Tissue sample for histopathological examination were collected during operation, swab sample for microbiological detection was taken from nose's or eye's secretions. Lesion scopes were mostly based on CT/MR findings. retrospective analyzed the treatment and prognosis of these cases, we shared our experience on management of AIFRS patients with cranio-facial-orbit involved.

2.3 Ethical consideration

This study was approved by ethical committee of our hospital that exempted it from requiring individual patient consent. All procedures performed in studies were in line with declaration for ethical consideration.

Results

3.1 Typical clinic features aided to a rapid diagnosis

All 8 patients had severe immunocompromised disease, i.e. poorly controlled diabetes, malignant hematological diseases, cancer (advanced stage) undergoing chemotherapy afflicted with granulocytopenia, renal insufficiency. The primary and main symptoms were severe headache, progressive eye disorder, facial pain. Because of severe underlying disease, 7/8 patients firstly admitted to corresponding department, after multi-disciplinary treatment (MDT) consultation, they were transferred to ENT department (table 1). Radiological features: computed tomography (CT) and magnetic resonance imaging (MRI) were used preoperatively to determine the extent of fungal invasion, all patients showed extra-sinus dissemination: orbit and orbital apex(5/8), cavernous sinus(2/8), face(3/8), palate(2/8). 6/8 patients had unilateral involvement and 2 patients with bilateral involvement. CT often showed heterogeneous opacity with or without bone erosion. MR usually showed a relative hypointense signal in T2W1 compared with bacterial inflammation, and an uneven enhancement in enhanced T1-weighted image. The main radiological findings with CT/MRI and endoscopic findings were summarized in Fig1-2 and supplementary Fig1-4 respectively. Based on an immunosuppressive history, rapid spread of orbit-cranial-face invasion, and radiological features, all cases were suspicion as AFIRS at first glance. Among them, 6 cases were pathologically confirmed after operation, 1 case was microbiological confirmed as Rhizopus and the other one evidenced by gross sign of mucor growth.

3.2 Detailed therapeutic strategies were made case by case.

In principle, surgical debridement and antifungal agents remained the two cornerstones of AIFRS treatment, and what's more, it should be performed as soon as possible when diagnosis preliminary made. However, because of severe underlying disease for these patients, detailed therapeutic schedule were made case by case. In this group of 8 cases, 6 patients underwent endoscopic debridement with endoscopic surgery (ESS), most under general anesthesia except one, removal of necrotic tissue as much as possible according to CT/MR. However, for some region, such as orbital apex, cavernous sinus, it was difficult to be completely debrided, detailed information was listed in table3. The other two (6# and 8#) were contraindication to an operation because of poor general condition under chemotherapy and a rapid disastrous spread. All patients were given sensitive antifungal drugs when AIFRS diagnosis made. voriconazole 200mg Q12h for Aspergillus, amphotericin B or amphotericin B liposome and/or posaconazole for mucor was the first choice. Dose and duration were scheduled case by case (detailed in table2). All patients were given broad-spectrum antibiotics and symptomatic supportive treatment during hospitalization.

Follow up and recovery

Those patients were followed up for 10 days to 58 months, except 2# and 7# cured, 4# still under control with oral Posaconazole intake, the remaining 5 patients died. Duration from the patient's diagnosis to death ranged from 10d to 50m (10d, 1m, 2m, 2.5m and 50m respectively), mainly died of multiple organ failure (MOF) and uncontrolled infection (detailed in table2).

4 Discussion

For patients with typical clinical features, diagnosis of AIFRS should be alert

AIFRS is characterized by a rapid spread to adjacent orbits, cavernous sinus, face, which need an urgent management, early diagnosis is very important. To immunocompromised patients with severe underlying diseases, such as AIDS, poorly controlled diabetic, haematological malignancies undergoing chemotherapy or transplantation, if they were afflicted by headache, eye pain, impaired vision, nasal obstruction, and the symptom worsening rapidly, we should be highly alert the diagnosis of AIFRS. Though lack specificity, some features of CT and MR Imaging may help us to make such a diagnosis. For example, CT findings showed unevenly increased density of soft tissues within involved nasal cavity and sinus, spreading to adjacent area with bone erosion. On MRI image, the lesion may show equal or low signal on T1WI, while relative high on T2WI, but compared with acute suppurative inflammation, the signal of T2WI in AIFRS still showed lower. Infection usually invaded to adjacent area with unclear boundaries, predominant orbit and cavernous sinus. Usually the lesion may uneven enhanced after enhancement. However, it's worth mentioning that if MR enhancement is not obvious, it means tissue infarction with a necrotizing pathological reaction, and the prognosis may even worse [3]. For highly suspected patients, smear or fluorescent staining of secretions from eyes or nasal should be taken as soon as possible to obtain a quick microbial evidence. In line with literature, in most cases, intraoperative frozen section could offer us a rapid diagnosis [4,5].

Surgical debridement: the more, the better?

Principally, surgical debridement should be carried out as soon as possible and as much as possible. However, because of generally poor condition for such a group, operation should be considered on a case-by-case basis. For example, case 6 and case 8, after assessment, they were contraindicated for surgery because of poor general condition. The extents of debridement were mainly based on CT/MR, however, it was not always an intellectual decision to force a complete debridement. For example, management on the area of orbital apex and cavernous sinus were extremely difficult. Risk and benefit should be carefully balanced. Antifungal treatment seemed equal important. For example, case2, we only performed a complete debridement of sphenoid sinus while left the orbital apex and the cavernous sinus in place. Voriconazole was taken orally for 4 months after the operation and the patient was cured during 58 months follow-up. The same result displayed in case7. While for case3, though we gave the patient a thoroughly debridement including enucleation of orbital contents. However, due to the patient's advanced age (74 years old), poor diabetes mellitus, severe granulocytopenia and Mucor invasion, he still died of multiple infections 1m after operation. According to literature, survival rate seemed not improved by an aggressive debridement such as orbital contents enucleation, maxillectomy [1,6]. The outcomes of our group supported such a conclusion.

Antifungal agent was important to AIFRS patients

As to our experience, once suspicion of AIFRS was raised according to clinical manifestation, antifungal treatment should be initiated as soon as possible, usually Voriconazole for Aspergillus and amphotericin B for Mucor. In recent years, FDA has approved isavuconazole, which was effective against Aspergillus and some Mucor, and it was water-soluble, with less impact on renal function and hepatic function than amphotericin B [7,8].

Antifungal treatment was equal or even more important than surgical debridement, as we learned inflammation could not be fundamentally solved by operation. If the patients could not tolerate anti-fungal treatment, mainly because of hepatic and renal dysfunction, their prognosis were usually poor, such as case3 and case5, though they underwent an extensive debridement, still died after 1 and 2.5 months after diagnosis. On the contrary, for case1,2, 4,7, though only administered a part debridement, the results were not so bad after

antifungal treatment. There were also reports which showed some survival AIFRS cases were managed only by medical treatment [9].

As for the duration of antifungal treatment, although it was clear that patients suffered with invasive fungal infection need a long time of antifungal therapy, however, up to now, there was no consensus on the optimal duration. We suggested a range of 6-12 months if the patient could be tolerated with the drug. However, most of them died within several months. We also have a group of 6 patients with CIFRS (not provided in the data), who maintained oral antifungal drugs for 6-14m after operation, and had a good prognosis.

Prognosis mostly up to underlying disease, we should focus more emphasizes on comprehensive treatment.

Prognosis of AIFRS is extremely poor. It's mortality rate was high up to 50-80% [1]. Now with the rapid development of endoscopic technology, more thorough debridement was possible, and more effective antifungal drugs could be available, however, compared with 20 years ago, the mortality rate did not decreased significantly [10]. Why? The end of AIFRS largely depends on the struggle between the body's immunity and fungal invasion, for those patients with severe neutropenia, poorly controlled DM, immunosuppressive therapy and insufficient hepatic and renal function, if they infected with fungi, especial highly invasive *Mucor*, a disastrous end was almost inevitable, such as case 3,5,6,8 in our group, so we should focus more emphasizes on comprehensive treatment.

5 Conclusion

In a word, clinical suspicion of AIFRS should be alert in the immunocompromised patient presenting with new-onset, rapidly progressive sinusitis with facial-cranio-orbital spread. A multidisciplinary approach consisting of antifungal therapy, surgical debridement, immunodeficiency reversal, and supportive treatment were essential to improve the control. We need more focus on comprehensive assessment, an extended debridement such as maxillectomy and orbital exenteration should be considered on a case-by-case basis. The outcome of AIFRS with facial-cranio-orbital involved was usually fatal which mainly defined by the underlying disease.

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Conflict of interest

The authors declare no conflicts of interest.

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