A case study of acute invasive fungal sinusitis complicating central retinal artery occlusion

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Research Article

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Abstract

Acute invasive fungal sinusitis is a fungal infectious disease in which fungal hyphae invade the nasal mucosa, blood vessels and nerves, causing tissue necrosis. Acute invasive fungal sinusitis is often complicated by intracranial infection, which is a critical disease with a high mortality rate. Meanwhile, ocular manifestations such as orbital cusp syndrome, cavernous sinus syndrome, and a sudden drop in visual acuity may suggest that the disease has been complicated by intracranial or intraorbital infection. Therefore, early diagnosis and early antifungal and anti-infectious treatment are essential to improve patient survival, and recognition of specific ocular signs is crucial for early diagnosis and treatment of acute invasive fungal sinusitis. In this article, we report a typical and rare case of acute invasive fungal sinusitis complicated by central retinal artery occlusion caused by Trichoderma infection. Central retinal artery occlusion is a kind of emergency and serious disease in ophthalmology, which has a rapid onset and rapid development. Failure to relieve the occlusion in time will result in permanent blindness of the patient, which will seriously affect the quality of life of the patient.Retinal artery obstruction relies heavily on imaging:Fundus Fluorescein Angiography: Demonstrates arterial and choroidal blood flow patterns to assess retinal blood flow and vascular obstruction. Patients present with very sluggish retinal arterial filling, and large areas of no perfusion;Optical Coherence Tomography : provides high-resolution images of retinal anatomy, thickness, and vitreoretinal interface in patients presenting with thickening of the inner retinal layer with edema and a highly reflective signal. Although the patient was treated by multidisciplinary diagnosis and treatment and transferred to the intensive care unit in a timely manner, he eventually died of systemic multi-organ failure due to complicated intracranial infection and sepsis. This case was discussed and analyzed from the ophthalmology point of view, and the relevant literature was reviewed in order to provide a reference for clinicians to recognize the initial symptoms of acute invasive fungal sinusitis, to provide timely antifungal and anti-infective treatment, to reduce missed diagnosis and misdiagnosis, and to avoid further deterioration of the patient's condition and death.In particular, we ophthalmologists are cautioned that retinal artery occlusion is not a purely ophthalmic disease, but is closely related to systemic diseases.

Introduction

Fungal sinusitis is divided into two categories according to the location of fungal parasites, the fungal parasites in the superficial location of the sinus mucosa is defined as non-invasive fungal sinusitis, and invasion of the sinus mucosa, soft tissues, blood vessels, and even bony tissues is called invasive fungal sinusitis. Acute invasive fungal rhinosinusitis (AIFRS) is mainly caused by Aspergillus and Trichoderma, and its etiology is complex, and most of them are closely related to the immunocompromise or defective long, such as long-term use of antibiotics, glucocorticoids, or suffering from diabetes mellitus, tumors, HIV, and other diseases, to the onset of acute, short course of the disease, the disease progresses rapidly, and complicated by the systemic multi-organ functional damage and high mortality rate as the clinical characteristics, so it is also known as the explosive Fungal sinusitis [1, 2]. In recent years, the prevalence of AIFRS has been increasing year by year, and although there are many case reports of AIFRS complicating

intracranial infections both at home and abroad, cases of Trichophyton rubrum infection leading to AIFRS complicating central retinal artery occlusion (CRAO) are relatively rare, so this article will report a case of AIFRS complicating CRAO from an ophthalmologic perspective and summarize and analyze the relevant literature.Retinal artery occlusion is not a simple eye disease, many other systemic diseases can also cause inflammation or clots to block the retinal blood vessels.

Clinical case data

Patient **, male, 45 years old, 2023-11-12 ,patient after cold exposure to the left side of the face numbness, accompanied by periodontal pain, consultation to the local oral clinic, to be oral medication (specific unknown) after periodontal pain relief, but the left side of the face numbness gradually aggravated, accompanied by skewed corners of the mouth. 2023-11-14, patient left eye vision progressive decline with difficulty in opening the eyes, accompanied by the left side of the head distension and pain. Head swelling and pain, feeling of loss of appetite, nausea, vomiting once, which was projectile vomiting, and the vomit was gastric contents. There was no incontinence or twitching of the limbs, etc. The patient was first seen in the neurosurgery outpatient clinic of the hospital on 2023-11-15, and was admitted to the neurosurgery ward of the hospital for treatment of "numbness of the left side of the face for 3 days, accompanied by a loss of vision in the left eye for 1 day", and was admitted to the neurosurgery ward of the hospital for examination and diagnosis. The patient was in a clear state of mind, with mental weakness, numbness and sensation on the left side of the face, nausea, vomiting, and one episode of projectile vomiting, which was characterized by gastric contents, accompanied by a loss of appetite. Bilateral pupils were round and unequal in size, left:right = 5:3mm, light reflex in the left eye disappeared, loss of vision in the left eye, no sense of light, stiffness and numbness of the left side of the face, left side of the face, frowning, wrinkling of the forehead, puffing cheeks, showing teeth, whistling, the angle of the mouth was right deviated, the tongue was slightly left deviated, the left side of the frontal stripe, nasolabial groove was slightly shallower, poor mental health, poor sleep and poor sleep, tiredness, and two bowel movements. Patient's past physical condition: 7 + years history of "hyperuricemia", treated with oral herbal medicine (details unknown), self-reported uric acid control is OK. Other medical history is denied.

Admitted to the hospital and actively improve the relevant examinations: (2023-11-15) Cranial CT: 1. No obvious intracranial abnormality is seen on cranial CT scan, MRI is recommended if necessary.2. Left maxillary sinus and sieve sinusitis.3. Bilateral oblique fissures are slightly thickened locally.Cranial MRI: 1. Scanning of the left optic nerve did not see obvious thickening, slightly increased signal on FLAIR image, lesions to be ranked, please combine with the clinical, optic nerve MRI is recommended for further examination. 2. left maxillary sinus, sieve sinus and pterygoid sinusitis.Cranial MRA:1. Scanning the left optic nerve did not see obvious thickening, slightly increased signal on FLAIR image, did not see obvious enhancement, lesion to be ranked, please combine with clinical, if necessary, optic nerve MRI for further examination.2. Left maxillary sinus, sieve sinus and pterygoid sinusitis (fungal sinusitis?). Electrocardiogram: sinus heart rate; 2. cardiac axis is not deviated; 3. ST segment: II, III, aVF depression > 0.05mV. After admission, neurosurgery first diagnosis: facial neuritis; be given acyclovir antiviral,

dexamethasone fosfosfomycin sodium 10mg anti-infective, triclopyr encephalin hydrolysis to improve the microcirculation as well as mannitol injection to lower the intracranial pressure; consider the vision of the left eye with no light sensation, pupil dilatation and loss of light reflex, please ophthalmologist to see if there is any difference. The left eye was considered to have No Light Perception, pupil dilatation and loss of light reflex, and was referred to ophthalmology for treatment after an emergency ophthalmology consultation, and a complete specialty examination was performed: VOD: 0.8, VOS: No Light Perception; the left side of the face was numb, with redness and swelling of the face and face, and the mouth and eyes were tilted, with a drooping of the left eyelid, and a small amount of lipid plugs at the margins of the eyelid blocked the lid gland orifice, with slightly congested conjunctiva, slightly edema of the cornea, anterior chamber (-), pupils dilated with loss of light reflex, and the anterior eye in the right eye was clear with the eye's anterior node (-) and the crystals and vitreous in the both eyes. The fundus of the left eye was edematous in the optic disc and retina, the eyeball was fixed and could not be rotated, and the fundus of the right eye was normal. Intraocular pressure: right eye 21mmHg, left eye 11mmHg; perfect ophthalmologic auxiliary examination: macular optical coherence tomography (OCT): thickening of the inner layer of the retina in the left eye, structural disorders (Fig. 1); macular morphology and structure of the right eye can be; laser fundus photography: grayish-white edema of the retina of the left eye, macula cherry red; fundus fluorescence imaging (FFA) diagnosis: CRAO in the left eye (Fig. 2); anterior segment photography: left eyelid oedema, anterior eye fundus normal fundus. Segmental photography: left eyelid ptosis, corneal edema, pupil dilation (see Fig. 3); ocular ultrasound: vitreous clouding in both eyes; ophthalmology revised first diagnosis: CRAO in the left eye. treatment: oxygen, massage of the eyeballs, anterior chamber puncture and release of fluid and mannitol injection to lower intraocular pressure were immediately administered, atropine sulphate injection was injected behind the globe to dilate the vessels and improve the blood supply, and followed by acyclovir for antiviral purposes, discontinuation of dexamethasone sodium phosphate, and the addition of Cefuroxime anti-inflammatory, compound camphorine injection nutritional nerve, improve microcirculation. Considering that the patient's condition was related to intracranial infection, lumbar puncture was performed after consulting neurology department, and intracranial pressure of 250 mmH2O was measured.(Normal values of the CSF parameters:80-180mmHg).(2023-11-16) Cerebrospinal fluid: glucose 13.26 mmol/L, adenosine deaminase 1.71 U/L, cerebrospinal fluid/urine-total protein 0.82 g/L, cerebrospinal fluid antacid staining, Gram's staining (-), cerebrospinal fluid ink staining: not found novel cryptococcosis, cerebrospinal fluid culture results: no bacterial growth and no fungal growth in 72 hours of culture; C-reactive protein: 235.14 mg/L; in the afternoon of the same day, because the patient's condition was progressively aggravated, the body temperature rose to 38.9°C, the symptoms of infection could not be controlled, and the index of inflammation was high, and the Department of Intensive Care Unit (ICU) was requested to consider central intracranial infection after an emergency consultation and was then transferred to the ICU for comprehensive treatment.

After admission to the ICU, he was examined: he was clear, mentally flaccid, slightly short of breath under maintenance nasal oxygen tube oxygenation, and his peripheral oxygen saturation was 99%. Body temperature: 37.8℃. Bedside cardiac monitoring showed: HR: 130 beats/min, R: 33 beats/min, BP:

157/115mmHg, SPO2: 99%. Physical examination: redness and swelling of the left side of the face, whitening of the skin around the left side of the nose, elevated skin temperature accompanied by hypesthesia of the left side of the face, no light sensation in the left eye, the ptosis of the left eye completely covering the cornea, the eyeballs could not be rotated in all directions, the conjunctiva was congested, the pupil of the left eye was dilated, with a diameter of about 5 mm, the light reflex disappeared, and the cornea was slightly edematous (Fig. 4). Breath sounds of both lungs were slightly coarse, rales and wet rales were not heard in both lungs, heart rate was 130 beats/minute, heart rhythm was synchronized, abdomen was soft, abdominal breathing existed, gastrointestinal type and peristaltic wave were not seen, abdomen had no compression, rebound pain and muscle tension, there was no edema in both lower limbs, physiological signs existed, neck was soft, and pathologic signs were not elicited. Ancillary tests: noninvasive cardiac function measurements ET 34%,SV 28cm3,SVI 16ml/m2, CO 2.8L/min, CI 1.6L/min/m2, SVV 63%. ECG: 1. sinus tachycardia; 2. electrical axis not deviated. The patient's left perinasal skin was whitish, and skin temperature was elevated with left-sided facial hyperalgesia. He requested an emergency consultation with the department of otorhinolaryngology, and nasal endoscopy was performed, which showed that the mucosa of the left nasal cavity was black in color, and a large number of dry crusts, white hyphae, and necrotic-like tissues were seen adhering to the mucosa, suggestive of AIFRS (Fig. 5). The first diagnosis of AIFRS was revised, and the treatment was continuous oxygenation to improve oxygenation, "Caspofungin" antifungal treatment, "Esomeprazole sodium" acid suppression and gastric protection to prevent stress ulcers, and "sodium bicarbonate" to prevent stress ulcers. "Sodium bicarbonate was given to correct acidosis and maintain the stability of the internal environment. After the above treatment, 2023-11-17 07:20 minutes, the patient appeared to be asleep, and could not call out, bedside ECG monitoring showed: HR: 127 times/min, R: 35 times/min, BP: 141/93mmHg, SPO2: 94%, considering that the patient had a consciousness disorder, emergency endotracheal intubation, and invasive ventilator-assisted ventilation, given the patient's condition progressed rapidly, and considering that the patient was combined with a bloodstream infection and central infection, please contact us for further information. In view of the rapid progress of the patient's condition, considering the combination of bloodstream infection and central infection, the whole hospital was invited to consult and discuss difficult cases to assist in diagnosis and treatment, and at the same time, combined with the patient's current condition and nasal endoscopy, there are indications for surgical treatment, and at 08:00 on 2023-11-17, accompanied by the patient's medical staff, the patient went out to the operating room for the procedure of "Nasal endoscopic left sinus open surgery + Nasal endoscopic low-temperature plasma radiofrequency ablation resection of the left middle turbinate + left inferior turbinate low-temperature plasma radiofrequency ablation resection + nasal septum resection + left nasal cavity necrotic tissue cleanup", after the operation, at 14:57, the patient returned to the ward, to maintain the invasive mechanical ventilation treatment, persistent fever, accompanied by polyuria, inflammatory indexes continue to rise compared with the previous, combined with the patient's operation can be seen in a large area of the left side of the nasal cavity necrosis of the tissue and the growth of white mycobacterial mycelia, to be considered Diagnosis: 1. sepsis, septic shock (sinusitis), 2. multi-organ dysfunction syndrome (central, circulatory, metabolic, respiratory), 3. central pituitary insufficiency and central uremic syndrome, treatment: pumping of posterior pituitary hormone for antidiuresis, anti-infective

treatment with meropenem combined with caspofungin, rehydration to expand the volume of fluid, and treatment with norepinephrine ditartrate injection combined with norepinephrine bisulfite. Norepinephrine bitartrate injection and epinephrine were pumped intravenously to strengthen the heart and raise the blood pressure, and potassium supplementation was given to maintain electrolyte stability and other symptomatic supportive treatments. After the above treatment, the patient had high fever again at 04:30 on 2023-11-18, and his temperature was measured at 42℃, accompanied by a progressive drop in blood pressure, oliguria, cold extremities, and multiple petechiae on both lower limbs. 55mmHg (norepinephrine bitartrate pumped in), SPO2: 80%. Because the patient's family abandoned resuscitation, the patient was declared dead on 2023-11-18 07:21. Diagnosis of death: 1. AIFRS; 2. central system infection? 3. sepsis Septic shock (sinusitis); 4. multiple organ dysfunction syndrome (central, circulatory, metabolic, respiratory); 5. central pituitary insufficiency and central uremia; 6. CRAO of the left eye; 7. Ophthalmic muscle paralysis of the left eye (orbital aponeurotic syndrome? Cavernous sinus syndrome?) ; 8. facial neuritis; 9. type 2 diabetes mellitus; 10. hyperuricemia

After the patient's death, the pathology section report returned: chronic inflammation of the mucosa of the left middle and upper turbinate, a small number of fungi (morphology inclined to Trichoderma) were detected in the interstitium, and some areas were necrotic, which was consistent with invasive mycosis. Special staining: fungal PAS stain (+).

Discussion

In this case, the patient had an acute onset and a short course of illness, and died after 3 days of admission without rescue, and the cause of death was septic shock and multiple organ dysfunction syndrome caused by AIFRS. The patient's condition progressed rapidly and critically after admission to the hospital, and after transfer to the ICU, although timely emergency surgery was performed to completely debride the necrotic tissues of the nasal septum and turbinate, but due to the complication of septic shock resulting in multiple organ failure, and the death of resuscitation was ineffective.AIFRS belongs to the invasive fungal rhinosinusitis. AIFRS is a form of invasive fungal sinusitis, which is characterized by intravascular inflammation of the local mucosa, thrombosis, mucosal granulation, ulcerative necrosis, and even necrosis of the bone tissue, and mycelium can be found in the mucosa or bone on pathologic sections.AIFRS is extremely rare, and is commonly seen in immunosuppressed patients with poorly controlled diabetes mellitus, and is extremely lethal, with a mortality rate of up to 50%-80% [3, 4]. The diagnosis of AIFRS has not yet been standardized and includes the following: (1) radiographic evidence of sinusitis; (2) nasal endoscopy to confirm the presence of sinusitis; (3) histopathological confirmation of invasion of fungal hyphae into the nasal mucosa, submucosal layer, blood vessels, or bone tissues; (4) pathogenic microbiology; and (5) medical history as well as clinical manifestations[2].

According to previous literature [5, 6], AIFRS in diabetes mellitus, especially in patients with ketoacidosis, is mostly caused by fungi of the phylum Spliceomycetes, which can be up to 80%, such as Rhizoctonia solani, Rhizopus rhizopus, Trichoderma reesei, and Ploughshares, etc., which is in line with the

characteristics of the disease as well as the pathology of the present case. The final pathological diagnosis of the patient's left turbinate resection in this case was Trichoderma, cerebrospinal fluid, serum and urine glucose and urine ketone indexes were significantly higher than normal values, and glycosylated hemoglobin measured 12.2%, although the patient denied a history of diabetes mellitus, the test results showed that the patient was not a short-term glucose increase, and accordingly, it was considered that the patient had type 2 diabetes mellitus. Blitzer et al [7] analysis, diabetic patients are susceptible to infection of the physiological basis of trichothecene mycoses: one is diabetic ketoacidosis environment is favorable for the survival of this type of fungi; the second is the phagocytosis of polymorphonuclear leukocytes in diabetic patients is weakened. Trichoderma often invades the vascular wall and lumen, and after invading the tissues, it first resides in the elastic lamina of the arteries or in the veins and lymphatics, inducing an inflammatory reaction and the formation of fungal emboli, leading to embolism, ischemia, and necrosis of the adjacent tissues. Mycelial invasion of blood vessels can cause progressive tissue necrosis of the nasal septum, palate, and orbital or perisinus bones.Patients with AIFRS present clinically with painless, necrotizing nasal septal ulcers (crusts), and sinusitis can lead to death with rapid orbital and intracranial invasion. The course of the disease is acute, about days to weeks, and the fungus invades the mucous membranes, submucosa, blood vessels, and bone walls of the nasal cavity and sinuses. Hematogenous spread is common. Symptoms include fever, facial pain or numbness, nasal congestion, bloody clear mucus, and rhinorrhea. It often extends to invade the orbital, intracranial, and maxillofacial regions, resulting in protruding eyes, visual disturbances, headache, altered mental status, seizures, neurologic deficits, and coma, and swelling of the soft tissues of the maxillofacial region [8].

The symptoms of the patient in this case were consistent with most of the clinical manifestations reported in the literature.The patient was initially admitted to the hospital with headache.After admission, there was a sharp decrease in vision in the left eye, left eyelid ptosis covering the pupil, loss of light reflex, paralysis of the left eye eye muscles and inability to rotate, accompanied by redness and swelling of the left side of the face and nose, decreased sensation, increased skin temperature, and ischemic changes of the skin swelling of the nasofacial region, which progressively aggravated, prior to the transfer to the ICU. Before transferring to ICU, although the patient was conscious, the patient's mental state was getting worse and worse, and the patient fell into coma again in a short time after transferring to ICU, and after successful resuscitation, emergency surgery was performed to remove the fungal infection and necrotic lesions in the nose, but the patient fell into coma again in the night of the same day, and then died after failing to be resuscitated. This is consistent with the clinical presentation of AIFRS, and septic shock due to intracranial infection may have been the primary cause of death in this patient. Previous studies have shown possible routes of spread of fungal infection into the skull: 1. direct erosion penetrating the sieve plate and the bone wall of the frontal and pterygoid sinuses into the skull; 2. intracranial spread of the fungus via the veins of the nasal cavity and sinuses into the large internal jugular vein; 3. intraorbital spread of the fungus via penetration of the bony plates of the maxillary sinus and sieve sinus into the orbit, and then via the orbital vessels or the optic foramen into the skull. Orbital complications of fungal

sinusitis mainly include anterior chamber cellulitis, orbital cellulitis, subperiosteal abscess, orbital abscess, and cavernous sinus syndrome.

Invasive fungal sinusitis with orbital complications is a life-threatening disease with a mortality rate of up to 80%. In the present case, the patient had ocular muscle paralysis in the left eye, fixation of the eyeball and ptosis of the eyelid, which was considered to be the result of fungal infection involving the cranial nerves and presenting like orbital aponeurotic syndrome or cavernous sinus syndrome. Orbital aponeurotic syndrome is a clinical syndrome resulting from a series of etiologic factors involving cranial nerves II, III, IV, V, VI, and V1. The clinical symptoms of it and cavernous sinus syndrome are mainly orbital pain, decreased vision, ocular muscle paralysis, and ptosis. Our patient had a dramatic loss of vision to No Light Perception in the left eye 1 day after admission and was finally diagnosed with CRAO in the left eye, which may be associated with an inflammatory thrombus or a fungal thrombus blocking the ophthalmic artery in the left eye. Case reports of Trichophyton rubrum infection leading to AIFRS complicating monocular CRAO are rare. Yang Yongqi et al [9] reported a case of AIFRS complicated by cavernous sinus syndrome caused by Trichophyton rubrum infection in a 22-year-old young woman with type 1 diabetes mellitus, who complained of "recurrent fever, facial swelling, and loss of visual acuity for 15 days", and her ocular symptoms included gradual loss of visual acuity in the right eye to the point where there was no sense of light, a drooping of the right eyelid, a complete fixation of the eye, and an increase in intraocular pressure in the right eye. The ophthalmologist of the hospital considered that the ocular symptoms were related to the spread of sinus fungal infection to the cavernous sinus and the complication of cavernous sinus syndrome after consultation, but no further ophthalmologic imaging examination was performed and no ophthalmologic treatment was done, so he did not find out whether the loss of vision in the right eye was related to CRAO. The patient was discharged from the hospital with improvement after aggressive antifungal treatment and surgical debridement, but the vision and ocular muscle paralysis of the right eye failed to recover. Xie Jun et al [10] reported a case of AIFRS complicated with cerebral infarction caused by Rhizopus infection. On the second day after the onset of the disease, the vision of the right eye suddenly decreased to no light sensation, accompanied by obvious swelling of the right eyelid, and then gradually appeared to be unable to open the eye, and the left eye did not have any abnormality, and the ophthalmology department of the local hospital diagnosed the right eye as CRAO, and then the patient was given a puncture of the right anterior chamber of the eye to improve the microcirculation, mannitol to lower the pressure of the skull and other symptomatic supportive treatment, but the right eye vision did not improve. After the patient was treated with symptomatic supportive therapy such as right anterior chamber puncture, microcirculation improvement, mannitol cranial pressure reduction, etc., the vision of the right eye did not improve, and the patient developed optic nerve atrophy of the left eye, and the vision was reduced to photopic sensation after three months of "nasal sinus exploration + lesion enlargement excision" and antifungal and other symptomatic treatments under general anesthesia and rhinosonasal endoscopy in an emergency clinic.

In the China Clinical Case Outcomes Database [11], a case of AIFRS mixed infection with Trichoderma and Aspergillus complicated by orbital apical syndrome was reported in a 53-year-old middle-aged female

diabetic patient, who was admitted to the hospital with a headache of 2 weeks' duration, which was aggravated by a swelling of the left side of the nose and face for 5 days. On the day of admission, the patient's ocular symptoms were left eyelid muscle weakness, accompanied by impaired eye movement and fixation of the eyeball, and the hospital diagnosed orbital aponeurotic syndrome on the basis of the involvement of the motor and abducens nerves, probably because the patient fell into a coma the next day after admission, so the case did not mention the loss of visual acuity, and did not ask ophthalmologists to consult with the patient to do relevant specialized examinations, so the patient did not find out whether the CRAO occurred or not., and finally the patient died in the ICU without resuscitation. It has also been reported in the literature [12]that orbital cellulitis secondary to paranasal sinusitis resulted in monocular CRAO, and after aggressive rescue treatment, vision was not restored, and the prognosis was extremely poor, but not life-threatening. Due to the rarity of AIFRS and its critical condition, ocular symptoms and signs are easily overlooked by non-ophthalmology clinicians. Previous reports in the literature of concurrent ocular disorders of AIFRS were mainly orbital aponeurotic syndrome and cavernous sinus syndrome, because the signs of ocular muscle paralysis, impaired ocular motility, pupil dilatation, and loss of light reflex are more easily detected and recognized and both of them are characterized by decreased visual acuity, whereas the CRAO The diagnosis of CRAO relies on fundus imaging, such as fundus color photography, autofluorescence, and FFA, but patients with ocular muscle paralysis, ptosis, coma, and those in urgent need of resuscitation are often unable to cooperate with further fundus examination; therefore, many case reports on AIFRS are prone to miss the diagnosis of CRAO, and in the reported cases with concomitant CRAO, the vision in the affected eyes was aphakia, and the vision of those who survived remained unrecoverable. .

Treatment: At present, there is no uniform expert consensus and guidelines on the treatment of AIFRS, early nasal endoscopy and do secretion or necrotic tissue culture and pathology section, find the causative fungus, timely to give systemic antifungal treatment and local infected necrotic tissue thorough debridement surgical treatment is necessary. The final pathologic diagnosis of this case was Trichophyton infections, and according to the latest global guidelines for the diagnosis and treatment of trichophyton diseases, it is recommended that: in immunocompromised patients suspected of having trichophyton, liposomal amphotericin B 5–10 mg/kg/d is preferentially recommended as first-line treatment in all systemic infections; if severe nephrotoxicity occurs, it can be reduced in due time, but there is insufficient evidence for the recommendation of a dose of less than 5 mg/kg/d. Exaconazole is moderately recommended for the first-line treatment of trichotillomania [13]. According to the recommendations of the Chinese guidelines for the treatment of severe sepsis/septic shock (2014) [14], empiric antifungal therapy is recommended for adult patients with sepsis or septic shock who are at high risk of fungal infection, with empiric anti-G- bacillus, G + cocci, and fungal therapy at the early stage of the disease and timely addition of liposomal amphotericin B 60 mg per day for anti-infective therapy based on pathologic and culture results. In this case, the patient was admitted to the hospital without finding the infected foci in the sinus area, and imaging such as CT and MRI of the cranium was atypical for the foci in the sinus area, so empirical antifungal treatment was not carried out in a timely manner and a small amount of hormone was used in the first department, which might aggravate the fungal

infection, and the fungal infection necrosis in the sinus area was only detected after the transfer to the ICU on the second day of admission at night, and an emergency consultation with the department of otorhinolaryngology and rhinolaryngology was carried out to detect the necrotic foci in the sinus area. foci, and promptly empirically added Caspofungin acetate for broad-spectrum antifungal treatment. Caspofungin inhibits the synthesis of a basic component of the cell wall of many filamentous fungi and yeasts, i.e., β(1,3)-D-glucan, thus exerting an antifungal effect, which is more effective in controlling invasive Pseudomona aeruginosa and Candida infections [15, 16], and a study [17]confirmed that for the treatment of invasive Candida infections, Caspofungin is as effective as amphotericin B. However, this case was an invasive Trichophyton mentagrophytes infection, so the patient's inflammatory indexes kept rising after admission, with persistent fever, tachycardia, and ineffective control of the infection.

CRAO is an acute ischemic disease of the retina due to obstruction of the central retinal artery and is an acute condition leading to severe impairment of the patient's visual function or even complete loss of vision. The most common cause is embolization of the retinal artery by an embolus. The nature of the obstructing emboli can be categorized as follows: thrombotic emboli, originating from the internal carotid artery or originating from the heart, account for 15.5% of cases. Calcified emboli, usually originating from heart valve disease, 10.5%. Cholesterol emboli, 74.5%; when the possible origin of the embolus cannot be confirmed by primary screening, arterial inflammatory CRAO should be considered, especially in patients with hypercoagulable states as well as giant cell arteritis [18]. In this case, the patient was admitted to the hospital with a fibrinogen of 6.176 G/L (reference value of 2–4) and a D-dimer of 4.65 mg/L (reference value of 0-0.5), and after transfer to the ICU, the D-dimer increased dramatically from 5.76 mg/L to 15.66 mg/L, and the last value was 18.27 mg/L. The above results indicated that the patient's blood was hypercoagulable, and the patient's The white blood cell count fluctuated around 19.35-22.9210^9/L (reference value 3.5–9.5), C-reactive protein 235.14 mg/L (reference value ≤ 6), and calcitoninogen fluctuated from 1.11 ng/mL to 2.59 ng/mL (reference value 0-0.05), so the formation of thrombus was probably closely related to the fungal infection and the increasing level of systemic inflammatory factors.There have also been studies that suggest that thrombophilia plays a vital role in the pathogenesis of CRAO. Thus, proper laboratory screening should be considered in the primary and secondary prevention of those episodes, with implementing appropriate therapy as needed [19].The combination of these findings suggests that this case is a case of atherosclerotic CRAO, which is currently being treated with conservative treatments such as vasodilatation and intraocular pressure lowering, as well as aggressive treatments such as thrombolysis and Nd:YAG laser. Although there are no high-quality studies demonstrating that the visual prognosis of conservative treatment is better than that of the natural course of the disease [20], it has been observed clinically that patients who present to the clinic within 4–6 hours of onset of the disease and who are treated promptly with conservative emergency care usually do not have blindness, and typically retain light-sensitive vision and beyond. Intravenous or microcatheter intraocular arterial injection of tissue-type plasminogen activator (tPA) for the treatment of acute CRAO has been controversial because of its possible efficacy and concomitant complications. Whereas the pathogenesis of CRAO is similar to that of acute stroke, thrombolytic therapy is theoretically effective for CRAO. There have been previous case reports [21, 22] that early thrombolytic

therapy is effective for CRAO, but there has been a lack of high-quality randomized controlled trials to validate this.

Previous case reports of patients with AIFRS who had been diagnosed with CRAO were treated with a conservative regimen, and like the patient in this case, the affected eye was blinded. Because similar cases of acute fungal infections are more specific, the treatment plan prioritizes systemic antifungal and anti-infection and rescue to maintain stable vital signs, and the treatment of ocular diseases such as CRAO is easy to be delayed or even ignored. If absolute contraindications such as coagulation dysfunctions are excluded, early and aggressive intravenous or intra-arterial injections of tPA may promptly release the thrombus from the blockage, and even help to alleviate the orbital aponeurotic syndrome or the cavernous sinus syndrome caused by the orbital aponeurosis. cavernous sinus syndrome leading to ocular muscle paralysis, and an aggressive treatment program is significant for the improvement of visual function in successful salvage, especially in young patients.

Conclusion

Due to the nonspecific early symptoms of AIFRS and the rapid progression of the disease, the prognosis is often poor. This case mainly suggests that clinicians, especially non-Ear, Nose and Throat physicians when susceptible people, especially diabetic patients in the presence of acute sinusitis, septal mucosal inflammation, unexplained headache, toothache, fever, cough, should be suspected of invasive fungal rhinosinusitis, and even more suggest that ophthalmologists in the first clinic or consultation with patients with the symptoms described above, combined with orbital aponeurotic syndrome or cavernous sinus syndrome manifestations of patients with vision loss, the rapid progression of the disease should be considered as a complication of CRAO. In the rapid progress of the disease should be considered when the disease is complicated by CRAO, timely otorhinolaryngology and ICU and other departments related to carry out the necessary checks, to avoid missed diagnosis and misdiagnosis, delayed condition, if the conditions permit, please neurology to assist in thrombolytic therapy, the prudent application of hormones and broad-spectrum antibiotics, so as not to lead to or exacerbate the infection of the particular strain of fungus.Especially for us ophthalmologists, although CRAO is a critical condition in ophthalmology, it is not life-threatening, and while we are actively trying to save the patient's vision, we should also be actively looking for systemic causes of CRAO, and rule out critical illnesses that can lead to life-threatening conditions due to infections and inflammation, hemorrhages, and blood clots.

Declarations

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation. Raw data packages needed for this study can be obtained by contacting the corresponding author and the first author of this paper.

Ethics statement

The data in this case report do not involve patient privacy and have been authorized with the oral consent of the patient's family, The extraction of this data did not involve interaction with human subjects or animals. Thus, there were no ethical issues involving the use of these data.

Author contributions

LX designed the study and drafted the manuscript as the first author. CM ,WD and QX carried out the literature search. YY ,ZKand ZLcontributed to data extraction and quality assessment. LX and LZ supervised the study and LX as the corresponding author. All authors contributed to the article and approved the submitted version.

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Consent to Publish declaration

The personal information in this article has been published with the consent of the patient's family and the hospital.All authors agree to the publication of this paper.

Competing Interest declaration

The authors declare that the research was conducted in the absence of any commercial or fifinancial relationships that could be construed as a potential conflflict of interest.

Data Availability declaration

All published data can be obtained from the first author or correspondent by email.

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Figures

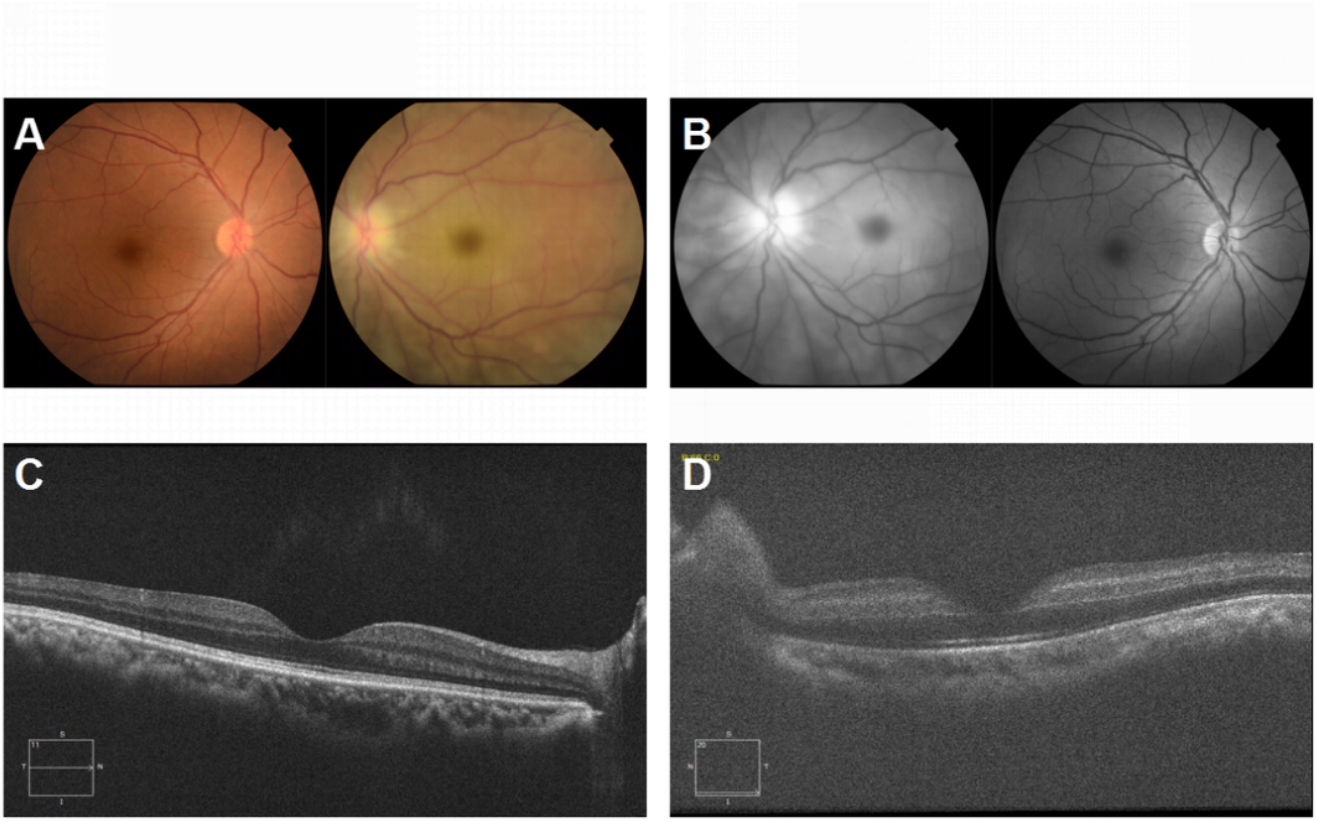

Figure 1

A: Fundus color photograph: normal fundus of the right eye, grayish edema of the retina at the posterior pole of the left eye, and cherry-red changes of the macula; B: No red light fundus photograph: normal fundus of the right eye, hyperfluorescence of the optic disc of the left eye with unclear borders, and hypofluorescent changes of the paravascular choroid of the retina; C-D: OCT photographs of the macula: C shows a normal OCT fundus of the right eye, with a morphologically structured macula that is

available, and D shows blurring of the refractive medium of the left eye, with edema of the inner layer of the retina in the macular area, an increase in the thickness, and the existence of a morphology of the central concavity of the macula.

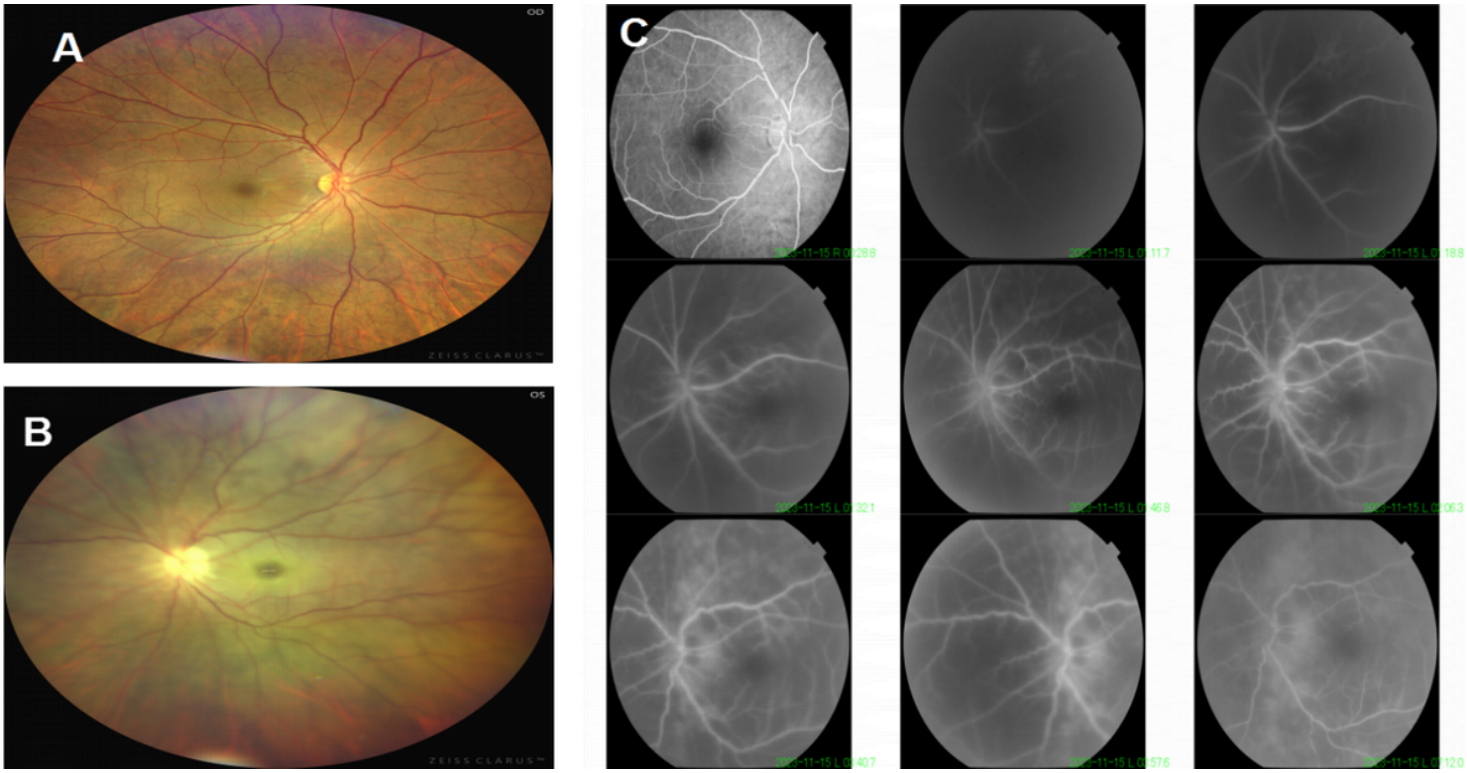

Figure 2

A-B:A wide-angle fundus color photograph, A:Normal fundus in right eye, B:the optic disc is pale, the border is blurred, the posterior retina is gray and edematous, and the macula is cherry-red, C:FFA photographs:the fluorescence filling time of the right eye is normal, there is no abnormal hyper- and hypofluorescence; the left eye is the main photographic eye, and the left eye has a prolonged brachycephalic-retinal circulation, the retinal arterioles begin to fill up in 1:11, the venules begin to fill up in late stage, and the posterior retinal artery and vena cavae show the change of the "weenie" segmentation in posterior retinal arteries and vena cava.

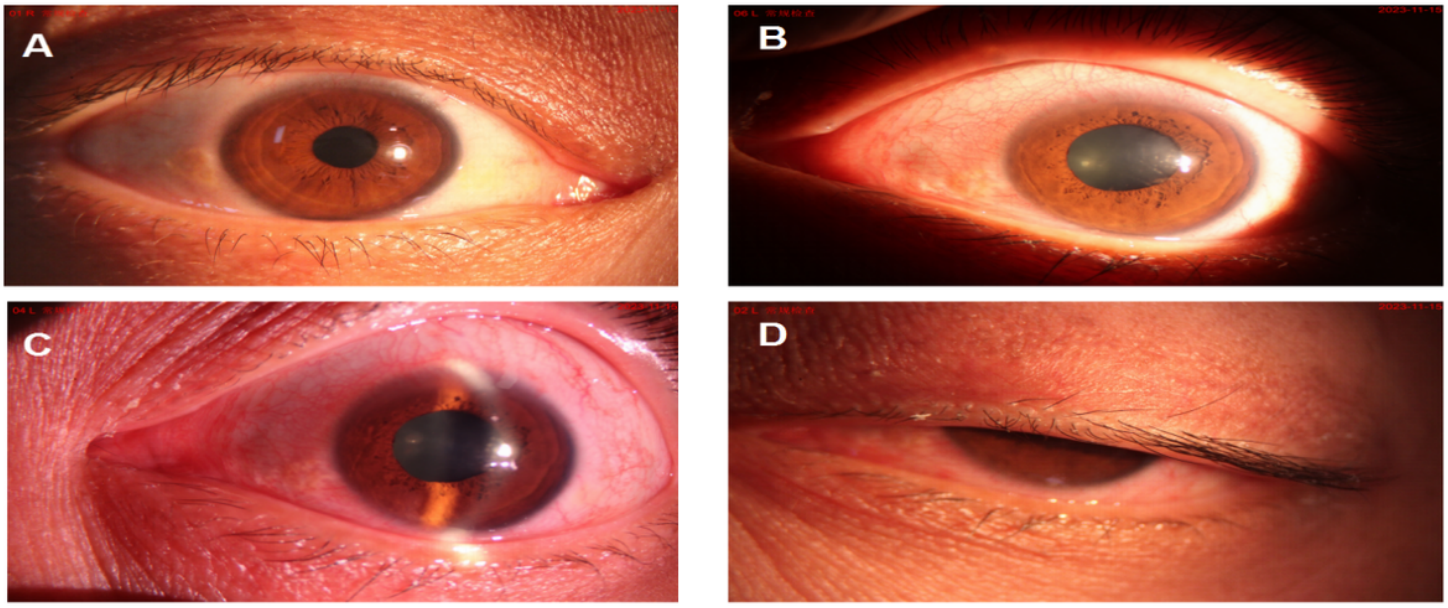

Figure 3

Anterior segment photography on the first day of admission: A: the anterior segment of the eye of the right eye (-), B-C:the conjunctiva of the left eye is congested, the pupil is dilated, the eyeball is fixed, the light reflex is lost, the crystalline lens is mildly cloudy, and the vitreous body is cloudy, D:the left eye's eyelid ptosis, which completely obscures the pupil.

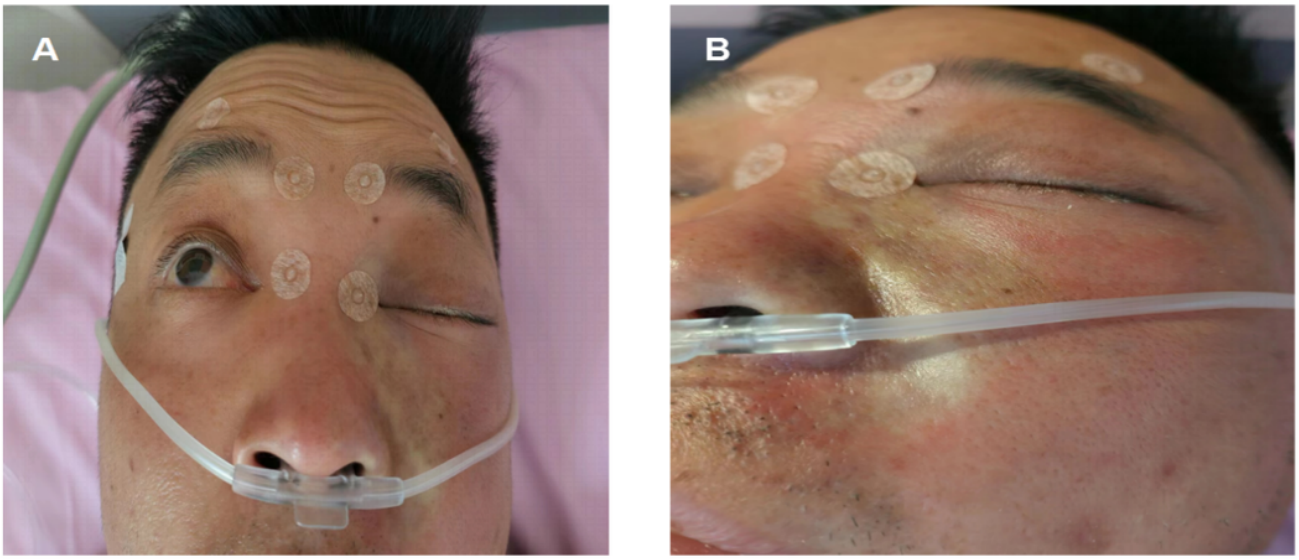

Figure 4

Nasofacial condition of the patient on the second day of admission; A: the patient with complete ptosis of the left eyelid and inability to open the eyes, B: the patient with ischemic-like changes in the skin of the

left nasofacial region, and other redness and swelling of the left side of the face.

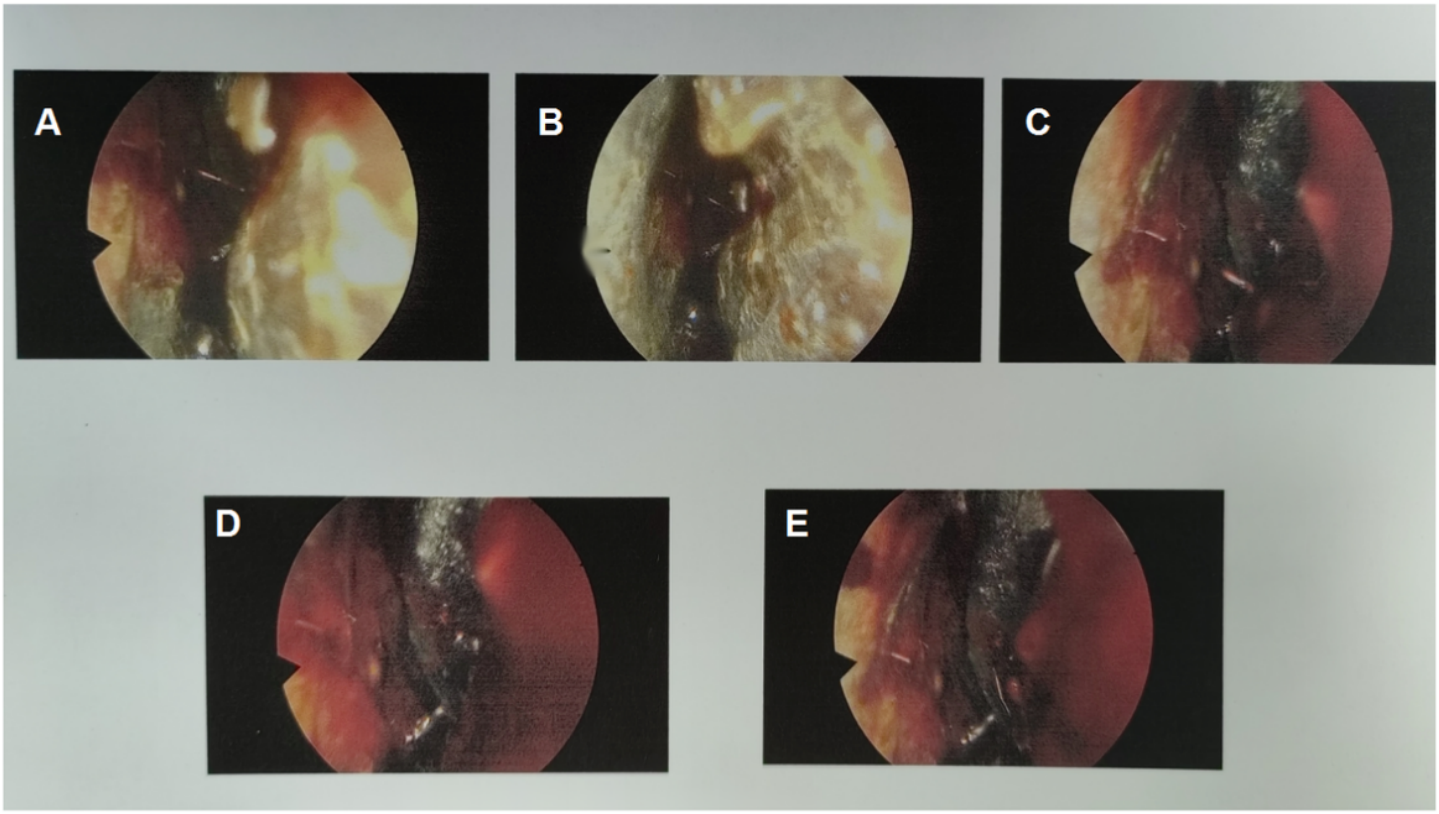

Figure 5

A-D: the left nasal mucosa was black in color and a large number of dry crusts, white hyphae and necrotic-like tissue were seen adhering to it.