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Case Report

Rhinocerebral Mucormycosis Complicated with Cavernous Sinus Thrombosis and Collet-Sicard Syndrome: A Case Report

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Abstract

Rhinocerebral mucormycosis is an invasive fungal infection of the paranasal sinuses, orbits, and cranium, caused by saprophytic fungi of the order Mucorales. This infection spreads locally and rapidly in susceptible individuals due to the angio-invasive nature of the fungi. Infection spreading into the base of the skull can cause lesions of the jugular foramen and hypoglossal canal, leading to Collet-Sicard syndrome.

We report a 57-year-old woman who presented with fever, headache, vomiting for four days and acute loss of vision in the right eye on a background of long-standing diabetes. She had chemosis and proptosis of the right eye with blindness and complete ophthalmoplegia. There was facial sensory loss in the distribution of the ophthalmic and maxillary divisions of the trigeminal nerve. Non-contrast computerised tomography scan of the head showed right maxillary, sphenoid, and ethmoid sinus inflammation, with cavities filled with heterogeneous material. Subsequently, she developed right lower four cranial nerve palsies suggestive of Collet-Sicard syndrome. To our knowledge, this is the first reported case of Collet-Sicard syndrome due to mucormycosis in the global literature.

Keywords: Collet-Sicard syndrome, rhinocerebral mucormycosis, type 2 diabetes

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Introduction

Mucormycosis, previously known as zygomycosis, is caused by fungi in the order Mucorales [1]. Rhizopus oryzae is the causative agent in most patients [2]. It is an opportunistic infection affecting patients with diabetes, especially those with ketoacidosis, neutropenia, elevated levels of free iron (end-stage renal failure and frequent blood transfusions) or immunosuppressive therapy [2,3]. However, 4-19% of patients with mucormycosis have no obvious risk factors and are immunocompetent [4]. It is highly invasive and relentlessly progressive, resulting in high morbidity and mortality [2].

Mucormycosis can present as six clinical variants: rhinocerebral, pulmonary, cutaneous, gastrointestinal, disseminated and miscellaneous. Among these, rhinocerebral mucormycosis, which affects the sinuses and the central nervous system, is the most common [2,3]. The fungal spores are thought to enter the human body through inhalation, via disrupted skin and mucosal barriers, ingestion, and via iatrogenic routes [5]. Presentation is vague, with features suggestive of sinusitis, headache, and facial pain or numbness.

Infected tissues initially appear normal but become erythematous and finally form a necrotic eschar [2]. Septic cavernous sinus thrombosis is a rare complication seen in this era of super-strength antimicrobials. Infections of the paranasal sinuses or any structures draining into the cavernous sinus may lead to cavernous sinus thrombosis unless treated urgently. The cavernous sinus drains into the internal jugular vein, spreading the infection and potentially triggering thrombophlebitis that may lead to Collet-Sicard syndrome. Collet-Sicard syndrome is the unilateral palsies of the lower four cranial nerves, which is caused by lesions of both jugular foramen and hypoglossal canal [6]. The most common causes for Collet-Sicard syndrome are tumour metastasis of the skull base, vascular disorders and trauma. [6]

We report a case of rhinocerebral mucormycosis complicated with cavernous sinus thrombosis and Collet-Sicard syndrome in a patient with uncontrolled diabetes.

Case presentation

A 57-year-old woman with a history of diabetes was admitted to the Teaching Hospital, Anuradhapura, with fever, worsening headache, vomiting for four days and acute loss of vision in the right eye. During the two weeks before admission, she had been feeling generally unwell with loss of appetite, right-sided fascial pain, and a frontal headache (Figure-1). She had had type 2 diabetes for 15 years, and her glycaemic control had generally been poor. She was a housewife and a lifelong non-smoker.

On examination, she was febrile with a temperature of 102°F, drowsy but easily rousable and had features of meningism. There was proptosis and chemosis of her right eye (Figure 2), visual acuity was 0/6, and the pupil was non-reactive to light. It was associated with complete painful ophthalmoplegia, compatible with paralysis of the right cranial nerves III, IV, and VI (Figure 2). Right facial hemisensory loss was noted in the distribution of the ophthalmic and maxillary divisions of the trigeminal nerve, with absent corneal reflex. Four hours later, she developed lateral rectus palsy of the left eye, indicating a possible cavernous sinus thrombosis. Her hard palate was erythematous, and it progressively became necrotic (Figure 3).

Laboratory investigations showed leucocytes of 19,800 x 109/L with granulocytic predominance, C-reactive protein 253 mg/L, random blood sugar 573 mg/dL, and serum creatinine 194 µmol/L. Her cerebrospinal fluid (CSF) was clear, with normal opening pressure, white cell count of 75/mm^3 (lymphocytes 85%) and red cell count of 2/mm^3. CSF glucose was 136 mg/dL, and proteins were 41 mg/dL. Non-contrast computed tomography of the head showed right maxillary sinus (figure 4b, 4c) and sphenoid and ethmoid sinus inflammation, with cavities filled with heterogeneous material (figure 4a). No evidence of high-density thrombus in the cavernous sinus was noted to confirm the clinical suspicion of cavernous sinus thrombosis

Intravenous ceftriaxone, flucloxacillin and liposomal amphotericin B were commenced in the medical ward empirically to cover bacterial and fungal sinusitis. Anticoagulation was not initiated due to impending surgical intervention and unacceptable risk of bleeding. Rhinoendoscopy showed the right middle turbinate and septal necrosis compatible with bilateral acute fulminant fungal sinusitis. Urgent bilateral sphenoethmoidectomy and middle meatal antrostomy were performed. Postoperatively, the patient was transferred to the intensive care unit under the shared care of medical, ENT and critical care teams. She remained unwell, but was haemodynamically stable, and no organ support was required postoperatively. On postoperative day one, she developed chemosis of the left eye and complete ophthalmoplegia suggestive of cavernous sinus thrombosis. Later, she was noted to have soft tissue swelling in the neck. Subsequent ultrasonography examination confirmed that the swelling was due to thrombosis of the right internal jugular vein. Clinical examination, on postoperative day one, revealed right-sided palatal palsy with deviation of the uvula to the left, hoarseness of voice, loss of gag reflex, weak right sternocleidomastoid and deviation of her tongue to the right on protrusion, indicative of cranial nerve IX, X, XI and XII paralyses. Soon after, she developed acute shortness of breath, tachycardia and widespread ST and T segment changes followed by sudden cardiorespiratory arrest refractory to resuscitation. Histopathologic examination of the debrided surgical tissue revealed a mixed inflammatory infiltrate with granulomatous inflammation. Fungal elements demonstrated characteristic features of mucormycosis, including broad, ribbon-like, paucisep-tate and non-septate hyphae with irregular branching at approximately 90° angles. Evidence of angioinvasion was present, with fungal hyphae invading vessel walls. These morphological features were consistent with fungi of the order Mucorales.

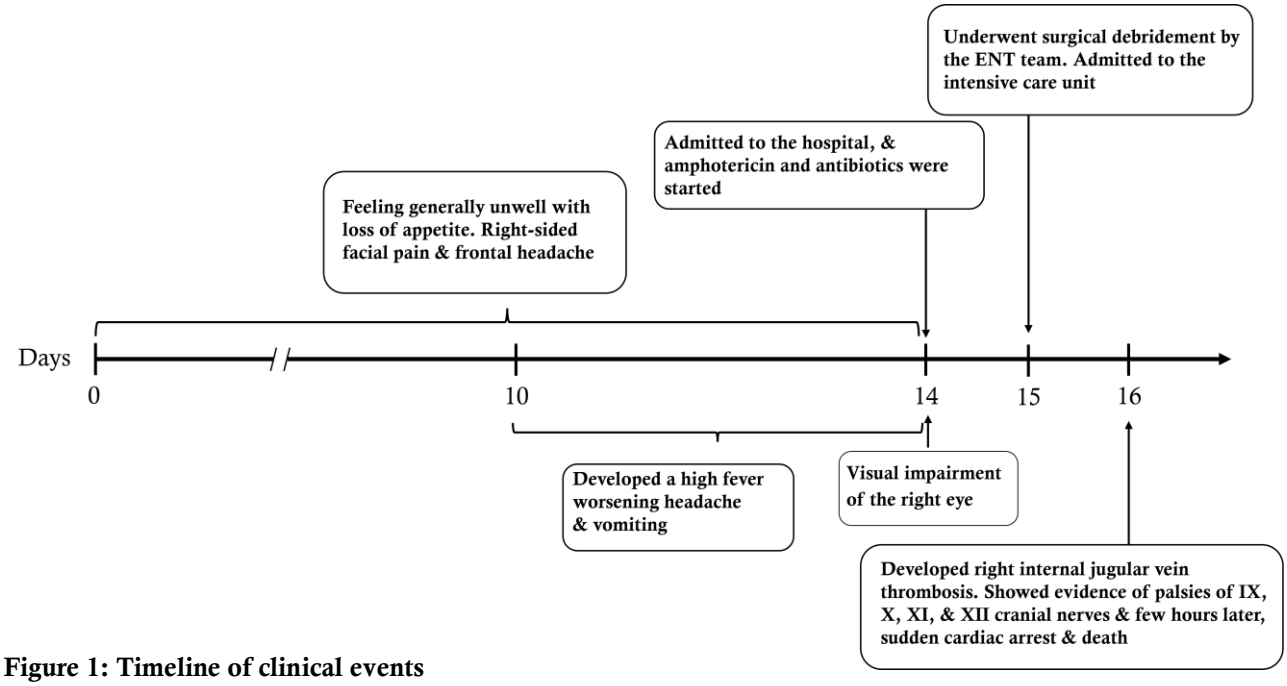

Figure 1: Timeline of clinical events

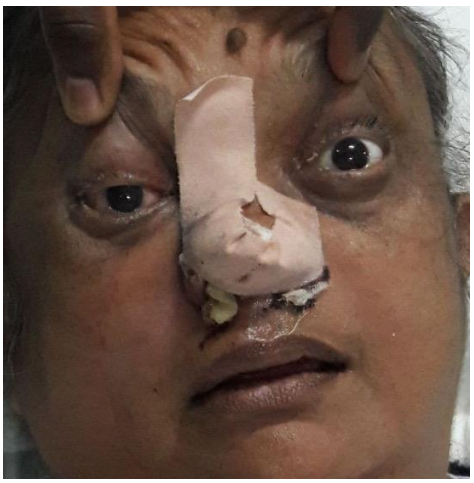

Figure 2: Proptosis and chemosis of her right eye, associated with complete painful ophthalmoplegia compatible with paralysis of right cranial nerves III, IV and VI

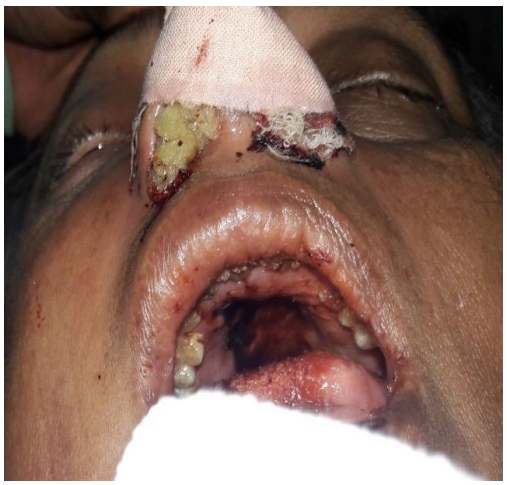

Figure 3: Erythematous and necrotic hard palate

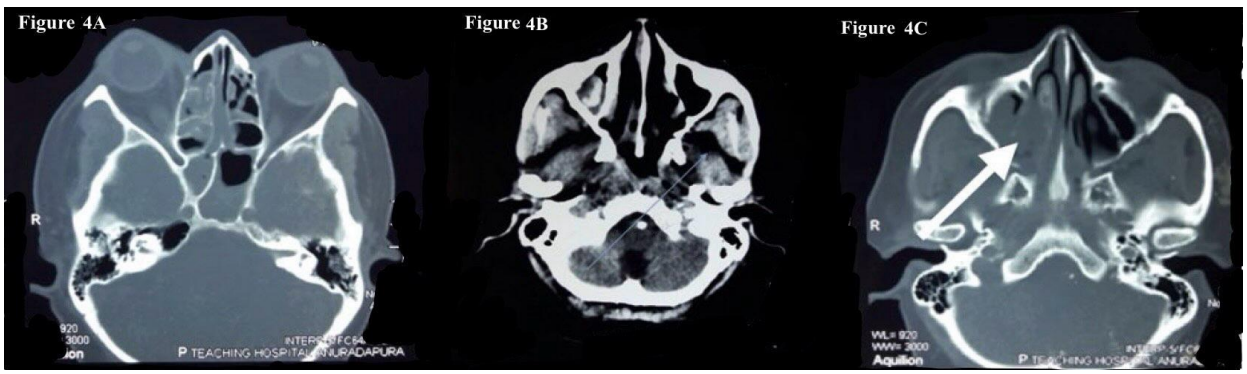

Figure 4: Non-contrast computed tomography of the head in the axial plane demonstrates orbital and sinonasal involvement. **(4A)** Axial section showing proptosis of the right eye with associated inflammatory changes in adjacent paranasal sinuses. **(4B, 4C)** Sequential axial sections demonstrating opacification of the right maxillary,

sphenoid, and ethmoid sinuses with heterogeneous material consistent with inflammatory debris and mucosal thickening

Discussion

This case highlights the critical importance of reporting rare and complex presentations of invasive fungal infections such as rhinocerebral mucormycosis. Although mucormycosis is a well-recognised opportunistic infection in immunocompromised individuals, its progression to involve the jugular venous system and result in sequential lower cranial nerve palsies is exceptionally rare. To our knowledge, this is the first documented instance of Collet-Sicard syndrome secondary to mucormycosis, underscoring the need for prompt multidisciplinary interventions.

Our patient presented with right-sided sinus mucormycosis and the symptom triad of chemosis, proptosis and painful ophthalmoplegia suggestive of cavernous sinus thrombosis. The presence of contralateral lateral rectus palsy and subsequent complete ophthalmoplegia was diagnostic of cavernous sinus thrombosis [7]. Infection spreads to the contralateral side via the intercostal sinuses. Palatal palsy, a weak sternocleidomastoid, and hypoglossal paralysis can be explained by thrombophlebitis spreading to the sigmoid-jugular vein junction, leading to Collet-Sicard syndrome [8]. Frederic Collet and Jean Sicard first described the clinical findings of simultaneous, unilateral paralysis of the lower four cranial nerves [9, 10]. The jugular foramen, containing the cranial nerves IX, X, XI and the jugular bulb and the hypoglossal canal, containing the hypoglossal nerve, lie adjacent to each other [11]. In jugular bulb thrombosis, the thrombus compresses the above structures, leading to this distinct neurological syndrome.

Distant metastasis, local invasion, trauma and vascular lesions are known to cause Collet-Sicard syndrome. Only four patients had internal jugular vein thrombosis in a series of 51 cases published between 1915 and 2012, and none were due to mucormycosis [6]. Additionally, sepsis and septic thrombophlebitis are seen when the cause of Collet-Sicard Syndrome is infectious. Collet-Sicard syndrome is predominantly a clinical diagnosis. Magnetic resonance venogram (MRV) is the imaging of choice to confirm the diagnosis. It will demonstrate the absence of venous flow in the thrombosed internal jugular vein. At the acute setting, Doppler ultrasound is usually the investigation of choice. It will reveal a dilated and non-compressible vein associated with a clot. Contrast-enhanced CT will show a low-density thrombus in the internal jugular vein and venodilatation proximal to the clot. The other primary differential diagnosis was nasopharyngeal cancer or metastatic cancer. However, the presence of fungal hyphae in debrieded surgical material confirmed the diagnosis of invasive fungal infection. Further, there was no evidence of malignancy in the CT scan.

The definitive diagnosis of the causative agent is based on histopathological evidence or positive culture from the affected site. The mainstay of treatment is surgical debridement of necrotic tissue and antifungal therapy. Liposomal amphotericin B is the drug of choice [1, 2, 3]. Novel triazole, isavuconazole, was licensed in 2015 as an alternative to Liposomal amphotericin B in the treatment of mucormycosis [12]

Our patient is the first reported case of rhinocerebral mucormycosis causing both cavernous and internal jugular vein thrombosis and subsequently leading to Collet-Sicard syndrome. Unfortunately, the unacceptable post-surgical bleeding risk in our patient precluded the use of anticoagulants and led to clot propagation. The sudden severe deterioration and resistant cardio-respiratory arrest following the jugular venous thrombosis could most possibly be due to a pulmonary embolism caused by the dislodged blood clot from the jugular venous system. However, it could not be confirmed as consent for a pathological post-mortem was not granted by the family.

Poorly controlled diabetes would have been the most likely reason for a more acute presentation and an aggressive clinical course in this patient, which underscores the need for strict glycaemic control in all those with diabetes, as fungi causing this deadly infection are ubiquitous.

Conclusion

This case underscores the aggressive and life-threatening nature of rhinocerebral mucormycosis and highlights a previously unreported complication, the Collet-Sicard syndrome. The case demonstrates the critical importance of maintaining a high index of suspicion for invasive fungal infections in patients with poorly controlled diabetes who present with sinusitis-like symptoms and cranial neuropathies. Early recognition, prompt initiation of antifungal therapy, and aggressive surgical debridement remain the cornerstones of management. This case expands current understanding of the potential extent of vascular involvement in mucormycosis and emphasises the need for early diagnosis and comprehensive management to improve patient outcomes.

Consent: The patient's daughter gave written consent for publication.

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