

## Case Report

# Cavernous sinus syndrome in a patient with sinonasal aspergillosis undergoing concurrent chemoradiotherapy for rectal adenocarcinoma

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**Abstract:** Cavernous sinus syndrome (CSS) is a rare and complicated disease that can be contributed to by neoplasms, vascular diseases, infections, miscellaneous inflammatory disorders, and other conditions. The clinical features of CSS can result from involvement of the cranial nerve, which passes through the cavernous sinus. Ophthalmoplegia, proptosis, and trigeminal sensory loss are the most common symptoms and signs of CSS. Herein, is reported a case of a 76-year-old woman with an underlying disease of anorectal malignancy undergoing concurrent chemoradiotherapy who presented with an 8-day history of diplopia and binocular blurred vision. Left-side fungal sinusitis (aspergillosis) was identified as the cause of the CSS after careful evaluation. An antibiotic (ceftriaxone) and a systemic steroid (methylprednisolone) were prescribed, and left-side endoscopic sinus surgery was performed. The patient recovered well after treatment, exhibiting free extraocular movement. Although fungal sinusitis is a common disease, it may be fatal if the adjacent neurologic system was involved. Therefore, this article describes the clinical features of CSS caused by fungal sinusitis in detail to enable early diagnosis and treatment of the disease.

**Keywords:** Cavernous sinus syndrome, fungal sinusitis, aspergillosis

## Introduction

The cavernous sinus (CS) is a venous plexus that lies between the periosteal and dural layers of the dura mater. It is located at the central base of the skull on either side of the sella turcica. Structures passing through the CS include the internal carotid artery, its sympathetic plexus, and the abducens nerve. The oculomotor and trochlear nerves are embedded in its lateral wall, as is the ophthalmic division of the trigeminal nerve. The maxillary nerve runs through the lower border of the sinus [1-3].

CS syndrome (CSS) is characterized by signs and symptoms resulting from the compromise of the cranial nerves passing through the CS. James R. Keane defined CSS as the involvement of two or more of the third, fourth, fifth

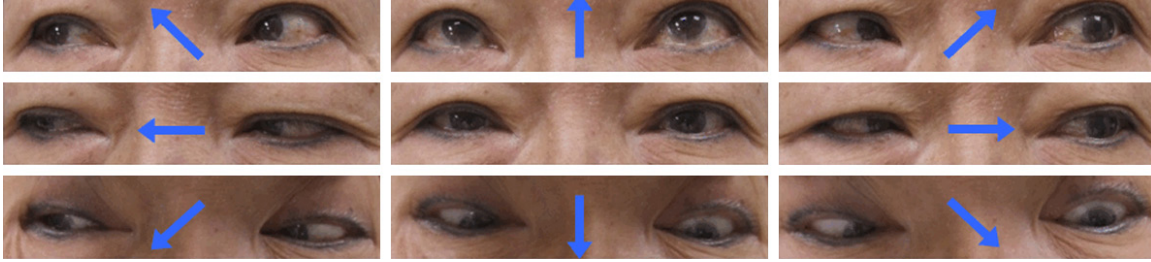
(VI/V2), or sixth cranial nerves or oculosympathetic fibers on the same side [1].

Common clinical manifestations of CSS include ophthalmoplegia, proptosis, ocular and conjunctival congestion, trigeminal sensory loss, and Horner's syndrome. Causes can be contributed to neoplasms, vascular diseases, infectious (mostly fungal infections) diseases, and miscellaneous inflammatory disorders (e.g., Tolosa-Hunt syndrome) [3, 4].

In 1938, Jefferson classified CSS into anterior, middle, and post CSS according to the involvement of the CN V.

In 1996, a classification of CSS was published by Ishikawa that emphasized the clinical and anatomical correlation of the syndrome. Ishikawa classified CSS into four categories:

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**Figure 1.** Extraocular movements in nine cardinal positions of gaze (blue arrows indicate the direction of intended movement of eyeballs); abducens palsy of the left eye.

anterior, middle, post, and whole CSS, as well as unclassified. In this Japanese study, anterior CS lesions often resulted from inflammatory etiologies, whereas middle and posterior CS lesions were caused by malignancies. However, the study found no statistically significant differences. This classification system provides hints for determining the etiology of CSS [5].

The etiological profile of CSS differs in developed and developing countries. In the Spanish city of Barcelona, a case series study reported that aspergillosis accounted for 1.25% (1 case) in an 80-case series [3]. In North India, a case series indicated that aspergillosis accounted for 10.9% (8 cases) of 73 cases [4].

CSS is rare and presents with overlapping clinical and radiological features, making its diagnosis difficult and often significantly delayed. It is vital to have a high degree of suspicion to avoid misdiagnosis of the condition as well as to initiate proper and timely treatment [2].

Herein, a case of CSS is presented that resulted in recovery through early diagnosis and timely treatment.

### Case report

A 76-year-old Taiwanese woman presented at our hospital with an 8-day history of diplopia and binocular blurred vision associated with numbness and pain of the bilateral upper face. The patient was undergoing concurrent chemoradiotherapy for stage IIIa (cT2N1aM0, American Joint Committee on Cancer S staging system, 8th edition) rectal adenocarcinoma. The regimen of concurrent radiochemotherapy (CCRT) was tegafur/uracil. The CCRT involved applying irradiation at a dose of 50 Gy

(50 Gy/25 fraction; daily Monday-Friday for 5 weeks) to the primary tumor and lymphadenopathy; irradiation at a dose of 46 Gy (46 Gy/23 fraction) to the uninvolved nodal stations; and irradiation at a dose of 25 Gy (25 Gy /25 fraction) to the whole pelvis. Moreover, she had hypertension, type 2 diabetes mellitus, peptic ulcer disease, and hepatitis B carrier.

On admission, her vital signs were as follows: temperature, 36.8°C; pulse rate, 84 beats/min; respiratory rate, 18 breaths/min; and blood pressure, 213/98 mmHg. Her level of consciousness was alert. Physical examination revealed unremarkable findings for her heart, lungs, and abdomen.

On neurological examination, she had hypoesthesia of the bilateral face (forehead, lower eyelid, prominence of the cheek, and alar part of the nose), loss of bilateral corneal reflex, and abducens palsy of the left eye (**Figure 1**).

In addition, her muscle power was normal; Kernig's sign was negative; and deep tendon reflexes were normal. Furthermore, the Babinski reflex was absent, as is typical in adults. On ophthalmic examination, her pupil size/light reflex was 3 mm/+, 3 mm/+ (OD, OS), and her visual acuity was 20/30, 20/30 (OD, OS). Her extraocular movements of the right eye were full and free, whereas her left eye was ophthalmoplegic (abducens palsy; **Figure 1**). Fundoscopy revealed that the optic discs and retinal vessels were normal, and no retinal hemorrhage or exudates were observed. Visual field examination revealed a normal visual field in both eyes.

Initial laboratory studies discovered the following abnormal findings (normal ranges in paren-

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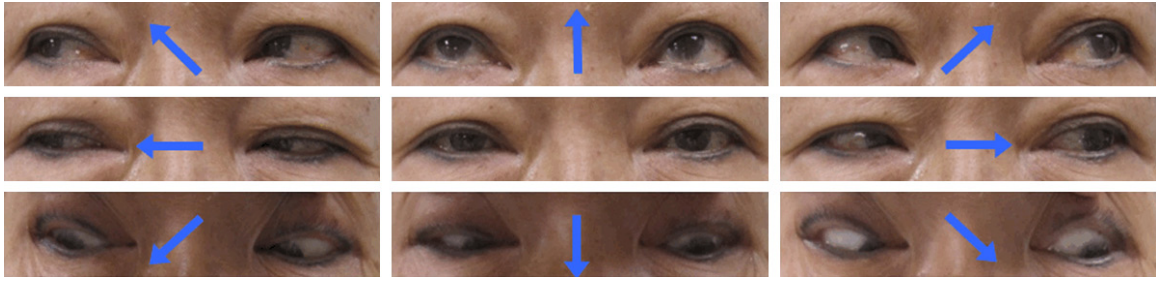


Figure 2. Improvement of the left eye; abducens palsy on postop day 3.



Figure 3. Abducens palsy of the left eye nearly completely recovered on postop day 7.

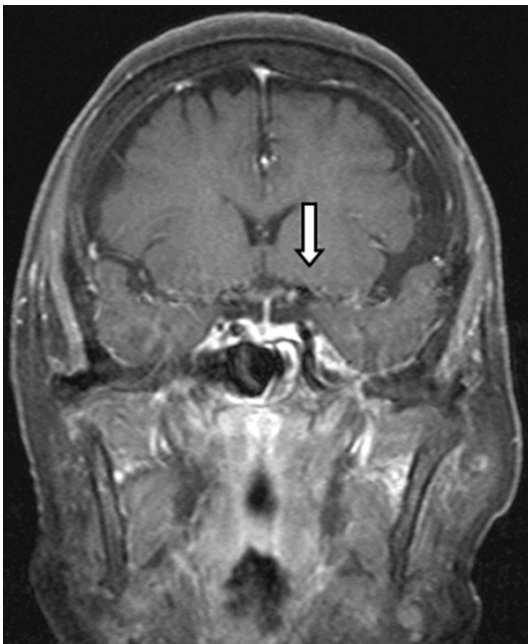
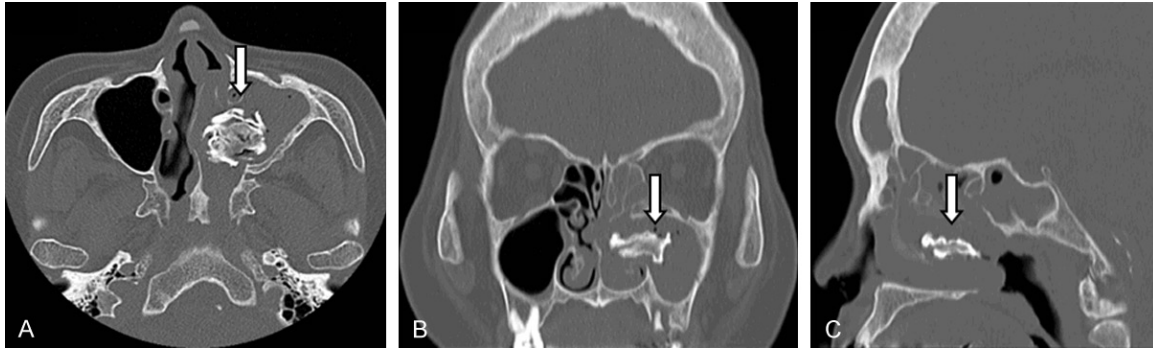


Figure 4. Imaging of the left cavernous sinus lesion; magnetic resonance imaging showing contrast enhanced lesion in the left cavernous sinus (coronal section).

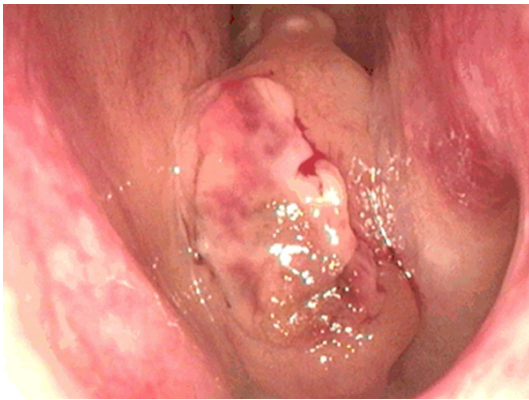
theses): hemoglobin, 10.4 g/dL (11–16 g/dL); hematocrit, 29.6% (34%–50%); fasting blood sugar, 112 mg/dL (70–99 mg/dL); serum creatinine, 1.38 mg/dL (0.4–1.2 mg/dL); D-dimer,

814 ng/mL (<654 ng/mL); N-terminal probrain natriuretic peptide, 545 pg/mL (<300 pg/mL); and erythrocyte sedimentation rate, 53 mm/h (0–12 mm/h). All other hematological and biochemical parameters were within normal limits, as were complement levels and results of assays for autoantibodies. Moreover, blood cultures showed no bacterial growth.

Brain magnetic resonance imaging (MRI) with gadolinium contrast revealed enhancement in the left cavernous sinus (CS) (Figure 4). Computed tomography (CT) imaging of the paranasal sinuses revealed opacified left frontal, ethmoid, maxillary, and sphenoid sinuses with intra-lesional hyperdensity (Figure 5). A lumbar puncture was performed, which showed a normal opening pressure. The cerebrospinal fluid (CSF) was clear and watery in appearance. Routine CSF examination revealed the following (normal ranges in parentheses): glucose, 45 mg/dL (45–75 mg/dL); protein, 46 mg/dL (10–45 mg/dL); chloride, 129 mEq/L (118–132 mEq/L); and lactic dehydrogenase, 21 IU/L (8–12 IU/L). Pandy's test was positive. Gram staining, acid-fast bacillus staining, potassium hydroxide mount, and Indian ink staining of the CSF were negative; furthermore, CSF cultures, including mycobacterial cultures, showed negative results.



**Figure 5.** Computed tomography images of fungal sinusitis; computed tomography scan showing left-side pansinusitis with central calcification in the fungus ball (A. Arrow, cross section; B. Arrow, coronal section; C. Arrow, sagittal section).



**Figure 6.** Imaging of nasal polyps; during the operation, nasal polyps were noted in the left-side ostiomeatal complex.



**Figure 7.** Imaging of the fungal ball; removing the fungal debris during operation.

Subsequently, the patient underwent surgical intervention. The time to surgical intervention following onset of diplopia and binocular blurred vision was 11 days. Functional endoscopic sinus surgery was performed under endotracheal general anesthesia. During surgery, an intranasal soil-like fungus ball was noted (**Figures 6 and 7**). The fungus ball was removed using micro-debriders (**Figure 7**), and the sinus was irrigated profusely to remove all fungal debris.

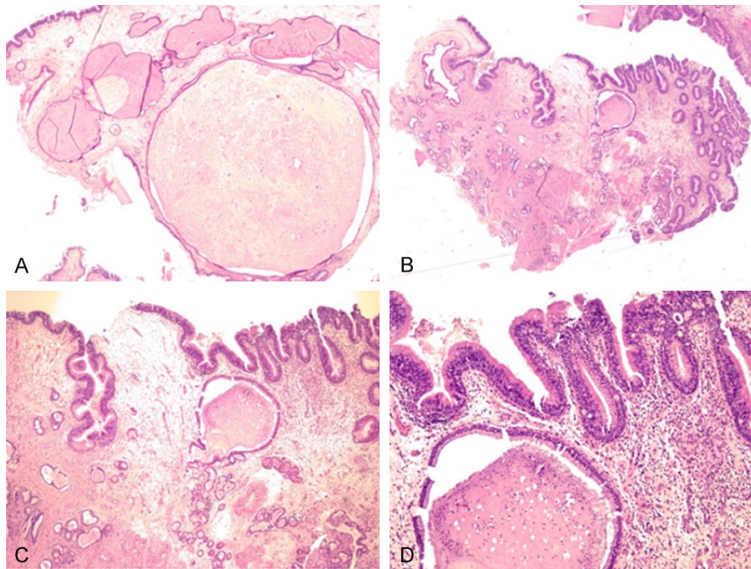
The patient's postoperative course was uneventful, and her visual disturbance was markedly improved on the first postoperative day and almost recovered in the first postoperative week (**Figures 2 and 3**). Postoperatively, histopathological sections revealed a picture of chronic paranasal sinusitis, manifested in the edematous, hyperemic, and fibrotic sinus mu-

cosa infiltrated by acute and chronic inflammatory cells, accompanied by formation of inflammatory sinonasal polyps (**Figure 8**). Many colonies of *Aspergillus* were found, which were clearly shown in PAS and GMS stains. The histopathological diagnosis was chronic rhinosinusitis with numerous colonies of *Aspergillus* (fungus ball) (**Figure 9**). Follow-up endoscopy (**Figure 10**) performed 3 months postop revealed no recurrence of a sinonasal fungus ball.

#### Discussion

CS pathology accounts for 5% of all cases of ophthalmoplegia [2]. The etiology of CSS can be divided into four categories: neoplasms, vascular diseases, Tolosa-Hunt syndrome, and infectious diseases, as well as others. Most studies have indicated that a common cause of CSS is a neoplastic lesion. Other causes of CSS

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**Figure 8.** Histological features; manifested in edematous, hyperemic, and fibrotic sinus mucosa infiltrated by acute and chronic inflammatory cells, accompanied by formation of inflammatory sinonasal polyps.

include thrombophlebitis, aspergillosis, Tolosa-Hunt syndrome, inflammatory pseudotumors, aneurysm of the internal carotid artery, carotid-cavernous fistula, and dural arteriovenous shunt [2, 3].

CSS should always be considered a differential diagnosis in patients with ophthalmoplegia. A careful approach to the evaluation of patients can lead to early recognition of serious disorders, which if left untreated, can be associated with a poor prognosis [1].

A prospective study of 73 cases by Bhatkar compared the relative utilities of the two aforementioned CSS classification schemes by Jefferson and Ishikawa. Bhatkar attempted to determine the etiology of CSS, but failed regardless of which classification system was used. No present classification system can clarify the clinicoanatomical relationship of CSS and benefits making a diagnosis [6].

In this case study, a 76-year-old woman was in an immunocompromised status. According to her medical records and patient statement, she had rectal adenocarcinoma and had received concurrent chemoradiotherapy 4 months before CSS occurred. Moreover, she had chronic diseases in the form of type II diabetes mellitus, hypertension, and hepatitis B.

After admission, CSS was diagnosed according to the clinical symptoms of binocular diplopia and upper-left facial numbness, which resulted from compromise of the left abducens nerve as well as of the first and second division of the left trigeminal nerve. Brain MRI revealed a left CS lesion. Therefore, left CSS with involvement of the left CN V1, V2, and IV was ruled in.

Following sinuscopy and sinus CT without contrast, left chronic sinusitis with fungal infection was thought to be the etiology of the CSS. Treatment involved endoscopic sinus surgery with antibiotics and steroids that could cross the brain blood barrier. After operation,

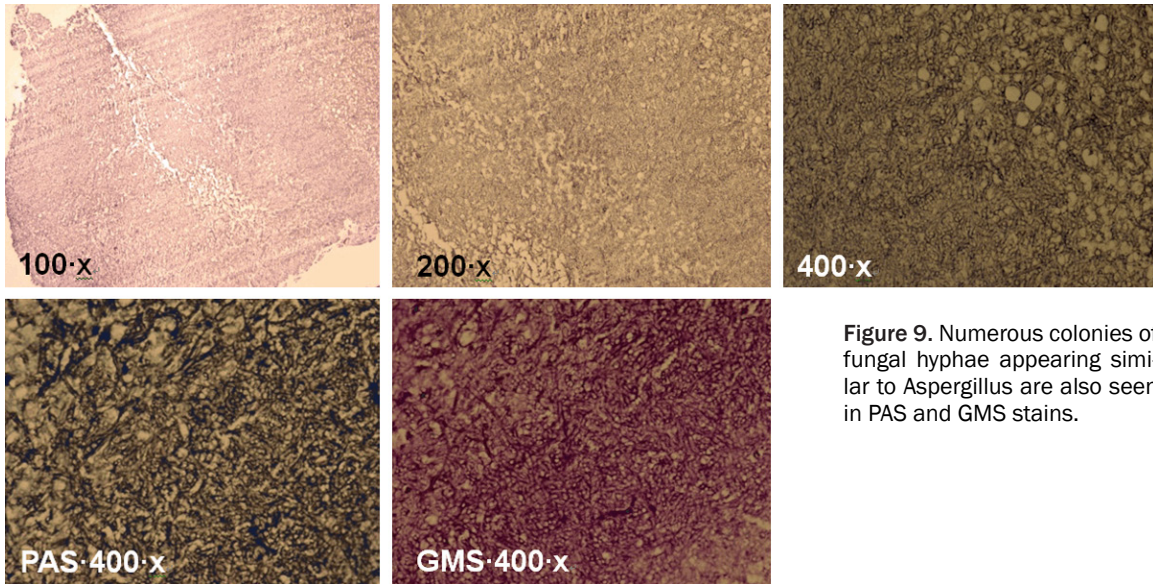
the pathology confirmed the diagnosis of sinonasal aspergillosis.

The final diagnosis of the case was CSS complicated with sinonasal aspergillosis. The patient recovered well after endoscopic sinus surgery. Left abducens palsy and upper-left face numbness rapidly improved in the first postoperative week.

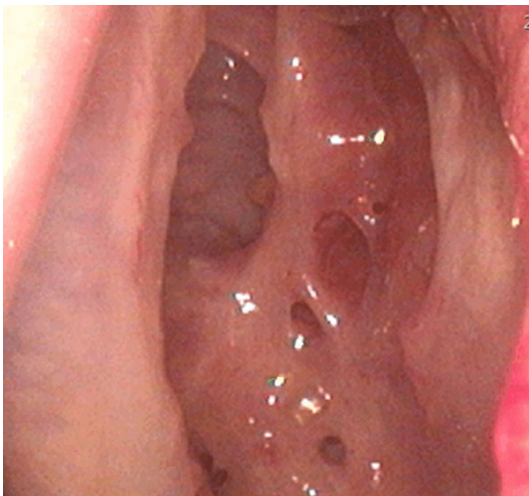
In the literature, invasive fungal sinusitis has been shown to result in severe orbital and neurological complications. In this case, allergic sinonasal aspergillosis caused the neurological complication of CSS in this immunocompromised female patient.

MRI is a useful tool for diagnosing CSS [7]. Regarding sinusitis etiology, sinus CT and sinuscopy provide more information of the disease pattern and help preparation for further surgical intervention [8]. Functional endoscopic sinus surgery is now the safest and most effective treatment for sinonasal aspergillosis [9], and a combination of antifungal agents and prophylactic antibiotics may be helpful [10]. Steroids play a controversial role in treatment [11]. In this case, the patient received endoscopic sinus surgery, steroid treatment, and prophylactic antibiotics. Considering the optimal outcome of surgery and comorbidity of

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**Figure 9.** Numerous colonies of fungal hyphae appearing similar to *Aspergillus* are also seen in PAS and GMS stains.



**Figure 10.** No recurrence of nasal polyps or fungal balls at 3 months postop.

hepatitis B with impaired liver function, antifungal therapy was not administered.

### Conclusion

The case study presented demonstrates three pertinent points. First, CSS is rare but should be considered in the differential diagnosis of ophthalmoplegia. Second, allergic sinonasal aspergillosis in an immunocompromised patient can cause severe neurological complications. Finally, early diagnosis and timely treatment are of paramount importance for a favorable prognosis.

### Disclosure of conflict of interest

None.

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