Introduction

Non-invasive fungal sinusitis, unlike bacterial sinusitis, is relatively rare and occurs primarily in the elderly female population for reasons not clearly understood. Fungal balls tend to involve a single unilateral sinus; the maxillary sinus is the most common, followed by the sphenoid sinus. Aspergillus species is the most common fungal pathogen of paranasal sinusitis. Hora classified aspergillus sinus infection into invasive and noninvasive forms by the presence or absence of mucosa invasion. The presenting symptoms of noninvasive forms are usually indolent and vague; yet, the complications and risks are severe and may be life-threatening when fungal balls occur in the sphenoid sinus because of the anatomical location. Delayed treatment may lead to complications with catastrophic results, such as cavernous sinus thrombophlebitis or a carotid stroke. Before antimicrobial agents became available, the mortality rate of cavernous sinus thrombosis was near 100%. Even in the antibiotic era, mortality remains high (up to 20–30%) with severe neurological morbidity in about one-third of cases. We report a case of sphenoid fungal balls in an immunocompromised patient, complicated by cavernous sinus thrombophlebitis and carotid artery stenosis. In spite of reasonable diagnosis and therapy, the patient’s general condition deteriorated and she eventually died. The clinical presentation, diagnosis, and treatment strategy are discussed.

Case report

An 80-year-old woman with a history of poorly-controlled diabetes mellitus (DM) and hypertension (HTN) was sent to the emergency department of our hospital due to right eyelid ptosis lasting four days. She had suffered from left arm weakness for many years and this symptom had recently worsened. Physical examination showed a body temperature of 36.8°C and blood pressure of 160/95 mmHg. Ptosis of the right eyelid was noted, with normal light reflex, extraocular movement, and isocoria of pupils. The patient experienced no specific nasal symptoms and no facial palsy or meningeal signs were observed. The muscle power of the left arm was obviously decreased. The patient’s hematological and biological data were as follows: white blood cell count, 9500/mm³; neutrophil-seg, 76.4%; hemoglobin, 12.9 g/dl; glucose, 250 mg/dl; HbA1c, 10.1%; normal liver and renal function. A non-contrasted computed tomography (CT) scan was initially done and revealed expansive lesions with mixed hyperdensity and isodensity occupying the sphenoid sinus and eroding its posterior wall, which suggested sphenoidal fungus ball or tumor (Figure 1A). Magnetic resonance imaging (MRI) with enhancement revealed the following: (1) an expansive lesion of the sphenoid sinus with strong mucoperiosteal enhancement was noted, infected sinusitis with fungal ball or bacteria with thick pus was considered; (2) T1-weighted sequences with contrast showed only mild heterogeneous enhancement and widening of...
the bilateral cavernous sinus regions, bilateral cavernous sinus thrombophlebitis was suspected (Figure 1B); (3) moderate to severe stenosis of the cavernous carotid artery was considered after reviewing magnetic resonance angiography (MRA, Figure 1C); (4) Diffusion weighted image (DWI) for the evaluation of acute brain hemodynamic infarction showed tiny high signal lesions over the right frontal lobe and right centrum semiovale (Figure 1D).

A sphenoid sinusitis was confirmed, complicated by a cavernous thrombophlebitis, a third cranial nerve palsy, and minor stroke or transient ischemic attack. Intravenous antibiotic treatment was administered (cefazolin, 1 gm four times a day). A neurologist and neurosurgeon were asked to consult prior to emergency surgery and suggested the right eyelid ptosis was due to cavernous third cranial nerve involvement and the left arm weakness to median nerve neuropathy. During the surgical procedure, the bilateral sphenoid natural orifices were enlarged to a common opening by partial removal of the posterior septal part with back-bite cutting forceps. Many clay-like materials filled the sphenoid sinus with minimal pus underneath (Figure 2A). Cultures were performed and the sphenoid sinus was irrigated with large amounts of saline at the end of operation. It was noted that the posterior wall of the sphenoid sinus was eroded and the pulsatile dura exposed (Figure 2B). The sphenoid was packed loosely with absorbable gelfoam.

After surgery, the ptosis gradually improved. The patient was discharged six days later in stable condition. Oral antibiotic treatment in the form of augmentin and drugs for DM and HTN were prescribed; the patient was educated in the nasal irrigation procedure to continue with care at home. The pathology report revealed the clay-like material was composed of fungal hyphi and there was no fungus or necrosis noted in the inflammatory soft tissue. Fungal and pus cultures found the presence of an aspergillus species and coagulase-negative staphylococcus. Unfortunately, the patient suffered from a sudden onset of unconsciousness, left-side extremities hemiparalysis, and slurred speech following dinner one day after discharge. Acute ischemic infarction involving the right internal carotid artery territory was confirmed by radiography (Figures 3A,B). The patient was transferred to the intensive care unit for aggressive treatment with intravenous antibiotics and anticoagulant drugs and died six days after readmission.

Discussion

Fungal ball infection of the sinuses progresses slowly and can have nonspecific symptoms, unless superinfected by bacteria. Bony remodeling, either osteosclerosis
Lethal sphenoid fungal sinusitis

or erosion, is frequently present. Solitary sphenoid fungal ball is rare and easily missed by the patient and physician until radiological examination is performed; it tends to be a disease of the elderly with female preponderance and close attention should be paid when it occurs in an immunocompromised patient. The sphenoid sinus is in close proximity to the skull base; neurovascular structures involved include the dura mater, pituitary gland, superior orbital fissure, carotid artery, cavernous sinus, and optic chiasma. Infection of the sphenoid sinus may lead to intracranial complications by direct invasion of the wall, hematogenous spread, or extension through a pre-existing or acquired bony dehiscence. Many important neurovascular structures are contained in the cavernous sinus, including the internal carotid arteries and the third, fourth, fifth, and sixth cranial nerves. Both cavernous sinuses are located at the skull base superior-lateral to the sphenoid sinus and drain the anterior portion of the face, including the nose, orbit, tonsils, and oral cavity, into the superior and inferior petrosal sinuses which ultimately empty into the internal jugular veins. Sinusitis, particularly involving the sphenoid and ethmoid sinuses, is currently the most common primary source of infection potentially leading to cavernous thrombosis. Thrombophlebitis of the cavernous sinus may affect all contained neurovascular structures. There are many manifestations of cavernous sinus thrombosis including fever, chills, nausea, vomiting, and a change in consciousness. Eyelid edema and proptosis may indicate venous obstruction. Paresis, diplopia, limitation of extraocular muscles, or paresis of the upper two-thirds of the face suggest cranial nerve involvement. Our patient suffered from right eyelid ptosis without fever, chills, headache, or meningeal signs, suggesting isolated oculomotor nerve involvement.

Before CT or MRI became available, cavernous sinus thrombosis was diagnosed by its clinical features. Price et al. proposed five clinical criteria for the diagnosis of cavernous sinus thrombosis (Table 1). Nowadays, enhanced MRI offers the best tool for diagnosis. Abnormal findings may appear as enlargements and expansions of the cavernous sinus with lateral wall flattening or convexity, rather than the normal concavity. Direct suggestive signs of thrombi may appear as multiple irregular or single large filling defects within the enhanced cavernous sinus. Indirect suggestive signs may appear as concomitant venous obstruction and include: dilation of the superior opthalmic vein, exophthalmos, soft tissue edema, and thrombi visualized in the veins and sinuses adjacent to the cavernous sinus.

In our patient, CT and MRI confirmed sphenoid inflammatory disease with bilateral cavernous
thrombophlebitis. The gold standard of treatment for cavernous sinus thrombosis is eradication of the inflammatory source with a high dose of intravenous antibiotic. The duration of antibiotic therapy is not standardized, but 3 to 4 weeks is consistent with the management of suppurative phlebitis and seems to be a reasonable projection, especially if the signs of inflammation, toxic effects, and fever cease during that period. We prescribed an oral antibiotic to the patient after being discharged in stable condition.

Sphenoid fungal balls have a low rate of operative morbidity, even when exposed to structures adjacent to the sinuses, and should be effectively managed by transnasal endoscopic sphenoidotomy. At first presentation, our patient did not have fever or other toxic signs. The universal corner- stone of treatment for noninvasive aspergillus sinusitis is surgical removal of the fungal balls. Systemic antifungal drugs are not necessary once the possibility of invasive fungal infection is excluded. In our patient, after exposure of her sphenoid sinus and removal of the fungal balls, the intact mucosa and good-appearance of the dura did not present as typical invasive aspergillus. Both the radiologist and pathologist consultation favored noninvasive fungal infection with bony erosion, instead of invasion. We excluded systemic antifungal drugs due to their potential side effects. Close observation of her admission course also supported our decision. However, the outcome forced us to reconsider this controversial issue. The older female was an immunocompromised patient with poor DM and HTN control; the fungus balls may have been potentially invasive. When a fungus ball is found, it is nearly impossible to prove if fungal invasion has occurred, unless there are vast biopsies of brain tissue. Yet, this case was suggestive of invasive disease which pathology specimens can easily miss. High dosage antifungal treatment might be considered for aggressive therapy and continued therapy after surgery.

Although moderate to severe stenosis of the cavernous carotid artery was identified by MRA, no other neurogenic defects were noted clinically. An intravenous antibiotic was administered during admission. After the operation, the patient felt well and the ptosis gradually improved. The patient was closely observed during her admission course and there were no clinical signs of stoke. Anticoagulant was not prescribed at the time as the inflammatory source was drained out and there was a high risk of postoperative bleeding. A neurologist consultation suggested follow-up at the outpatient department for her right
cavernous carotid artery stenosis. Acute carotid artery stroke following the eradication of noninvasive sphenoid aspergillus is rare; although, it has been associated with invasive pathogens. Wong et al. reviewed the images from four healthy children with internal carotid artery narrowing and sphenoid bacteria sinusitis to delineate whether cavernous carotid artery stenosis should be considered in patients with sphenoid sinus infection. Perez Bareto et al. reported four cases of carotid artery stroke with less severe sphenoid sinus disease and found the internal carotid artery lies immediately adjacent to the sphenoid sinus and the two structures are separated by a piece of thin bone or only by mucosa (bone absent in some cases). Retained sinus fluid containing inflammatory materials and cytokines (e.g. interleukin-1) may come into direct contact with perivascular structures and contribute to the spasm or obstruction of the internal carotid artery. However, no consensus has been reached for the role of anticoagulants in septic emboli of cavernous thrombosis. Arguments against the use of anticoagulants include the higher risk of systemic and/or intracranial bleeding and that the thrombus provides a protective role by preventing emigration of septic emboli. Others argue that early administration of heparin may prevent the spread of thrombosis to other venous sinuses and reduce mortality and morbidity. Levine et al. recommended that if activated partial thromboplastine time (APTT) and prothrombin time (PT) ratios are maintained at 1.5-2.0 and 1.3-1.5 for intravenous heparin and coumarins, respectively, safety is
ensured. In our case, the patient’s age, DM, HTN, and cavernous sinus thrombophlebitis contributed to a high risk of stroke.

Conclusion

Cavernous sinus thrombosis is rare and likely caused by sphenoidal or ethmoidal sinusitis. Otolaryngologists are not familiar with this disease; therefore, a team of multidisciplinary specialists composed of a neurologist, neurosurgeon, otolaryngologist, and an infectious disease specialist may be needed to treat the disease. Discussion with a radiologist for the differential diagnosis should be emphasized. Delayed diagnosis or treatment can result in severe morbidity or mortality. Although noninvasive sphenoid fungal ball is mostly found in immunocompetent patients, transformation into the invasive form should be considered in immunocompromised patients. Since the year 2000, cases have been described of invasive fungal disease in immunocompetent patients with initial neurological symptoms and lethal outcomes unless treated with rapid surgical intervention and antifungal treatment. Any sign of isolated sphenoidal disease with neurological signs in immunocompromised patients should be regarded as urgent. In fact, any sinusitis in immunocompromised patients demands careful attention and follow-up.

References


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