A case of middle cerebral artery aneurysm secondary to Acute Invasive Fungal Rhinosinusitis

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ABSTRACT

Acute Invasive Fungal Rhinosinusitis (AIFRS) is a life-threatening disease process which primarily affects immunocompromised patients. AIFRS can be complicated by angioinvasion and can cause arterial aneurysms. Arterial aneurysms secondary to AIFRS have been most commonly reported in the literature as occurring in the internal carotid artery, adjacent to the cavernous sinus. The following report details a case of middle cerebral artery aneurysm secondary to AIFRS, which has not been well-reported in the literature.

1. Introduction

Invasive fungal rhinosinusitis remains a life-threatening, albeit curable, disease that carries the potential for misdiagnosis. Acute invasive fungal rhinosinusitis (AIFRS) primarily occurs in immunocompromised patients, such as those with under-controlled diabetes, HIV, hematological malignancies, or those undergoing chemotherapy. In patients with uncontrolled diabetes, zygomycetes is the most commonly isolated organism, due to its preference for the acidic environments seen with diabetic ketoacidosis (DKA) [1]. In patients with non-diabetes-related immunosuppression, aspergillus is more commonly isolated. Diagnosis can be complicated by many things, beginning with the relatively non-specific presenting symptoms of most patients. While there are no pathognomonic symptoms for AIFRS, 50–65% of patients present with facial edema, pain, nasal obstruction, and fever [2]. More serious signs of invasion include cranial nerve deficits suggestive of cavernous sinus involvement [3]. Invasion out of the sinuses can lead to orbital apex syndrome (OAS), which is characterized by progressive loss of vision, ophthalmoplegia, and proptosis [4]. Imaging of the head and sinuses is an important initial step in diagnosing AIFRS. While CT findings again are relatively non-specific, further evaluation with contrast-enhanced MRI will better reveal the extent of fungal invasion outside of the sinuses and into the orbit, brain, or soft tissues [2]. When AIFRS progresses on imaging to invade neurovascular structures, it can often be mistaken for a malignancy [5]. Additionally, in rare cases, invasive cerebral fungal infections can lead to mycotic aneurysm formation in affected vessels [6]. This has been most commonly reported in segments of the internal carotid artery (ICA), adjacent to the cavernous sinus [7]. In situations where AIFRS is suspected, endoscopic nasal biopsy should be performed in order to confirm the diagnosis [2]. Because of the potentially quick progression of AIFRS, this diagnosis necessitates early surgical intervention and treatment with antifungal medications. Here we will discuss the case of a 53-yo female who presented to the ED with a 2-day history of right upper/lower extremity weakness, facial numbness, and double vision and was found to have an invasive soft tissue mass in the right infratemporal fossa as well as a right middle cerebral artery saccular aneurysm.

2. Case presentation

Patient is a 53-year-old female with a past medical history significant for uncontrolled type II diabetes mellitus, multiple previous episodes of diabetic ketoacidosis (DKA), homelessness, and a history of medication noncompliance who presented to the emergency department after being found down by a neighbor. For the purpose of clarity on the patient’s clinical course, day 0 will be defined as the first day of the patient’s hospital admission. On day 0, she presented to the emergency department with complaints of a 2-day history of right upper and lower extremity weakness, facial numbness, and double vision in her right eye. On review of systems, she endorsed 2 days of headaches, body aches, nausea, vomiting, and post-nasal drip with foul smell, as well as a 30-lb weight loss within 2 months. Of note, she had previously been admitted on day 14 for DKA, at which point she was found to have an HbA1C of 14. In the emergency department on day 0, her initial blood glucose level was 406.
Complete neurologic exam on day 0 revealed mild dysarthria, complete limitation of abduction of her right eye consistent with lateral rectus dysfunction as well as some depression in vision of her right eye, reduced sensation bilaterally in the V2–V3 distribution, and slightly asymmetric facies. Flexible nasal endoscopy revealed significant obstructive nasal mucus crusting in the right nostril.

CT angiogram of the head and neck with and without contrast revealed a soft tissue mass in the right infratemporal fossa as well as the parapharyngeal space with a multi-compartment extension, suspicious for a skull base lymphoma versus nasopharyngeal carcinoma versus infectious etiology. Additionally, the angiogram revealed occlusion of the right carotid canal, causing complete occlusion of the right cervical internal carotid artery (Fig. 2a and b). There was also a notable 5 × 6 mm saccular aneurysm in the M1 segment of the right middle cerebral artery (MCA) (Fig. 2). Also notable was a 5 × 9 mm pseudoaneurysm of the right maxillary artery. Because CT appeared nondiagnostic, follow-up MRI with contrast was recommended which revealed ill-defined edema of the right infratemporal fossa and enhancement extending through multiple compartments, as well as cavernous sinus extension with right ICA thrombosis (Fig. 3 and 4). The aggressive nature and rapid onset of the mass suggested a possible neoplastic process, such as lymphoma or nasopharyngeal carcinoma, or given the patient’s history, a possible infectious process such as invasive fungal sinusitis. Of note, none of these findings had been present on CT scans obtained 2 months...

Fig. 1a and 1b. CT Maxillofacial WO contrast
1a: 2 months prior to admission showing scattered ethmoid air cell (long arrow) and sphenoid sinus (short arrow) mucosal thickening, mild in degree. The remainder of imaged paranasal sinuses and right mastoid air cells are clear.
1b: CT on day 0 showing opacification of multiple right-sided mastoid air cells (bold arrow) as well as post-obstructive fluid in both the sphenoid sinus (short arrow) and right maxillary sinus (long arrow).

Fig. 2a and 2b. CTA of the head/neck on day 0 with contrast revealing complete occlusion of the right internal carotid artery (circle demonstrates area lacking blood flow compared to the left) as well as a 5 × 6 mm saccular aneurysm in the M1 segment of the right middle cerebral artery (bold arrows).
On day +2, the decision was made to take the patient to the operating room for endoscopic nasal surgery with intraoperative biopsy. Due to the aggressive nature of the disease along the skull base, the decision was made to forego extensive debridement as morbidity risks outweighed benefit. Frozen sections were obtained intraoperatively and revealed invasive fungal disease with angioinvasion and erosion of bone. The 2 final specimens, removed from the maxillary and sphenoid sinuses, underwent GMS staining which resulted on day +8 and demonstrated branched fungal hyphae morphologically suggestive of Zygomycetes. Pathology also noted that there was invasion of the adjacent bone in both specimens, as well as acute bone inflammation. The final pathologic report only stated that the fungi was morphologically consistent with zygomycetes and did not specify whether there was septation or irregular branching. We were able to reach the pathologist responsible for this report, who stated that by “morphologically suggestive of Zygomycetes”, he meant that the specimen was non-septate and had irregular branching, distinguishing this from aspergillus.

The patient was started on IV amphotericin B 0.25 mg/kg q24 on day +2, as per recommendations from infectious diseases. Once final pathology was confirmed on day +8 as described above, infectious diseases recommended an increase of the IV amphotericin B dose to 1 mg/kg q24. In order to prepare for patient’s potential discharge, infectious diseases discontinued amphotericin B on day +11 and began PO Cresemba, or Isavuconazonium. The dosage on this medication was 372 mg PO every 8 hours. This medication was continued on discharge.

On day +23, she was again admitted for DKA, at which time her physical exam revealed some medial deviation of the right eye as well as residual mucor in the right nostril. An eschar was also noted on her right earlobe. Repeat maxillofacial CT at that time revealed resolution of the rim-enhancing fluid collection in the tissues beneath the right skull base and improved right paranasal sinus disease; however, there was unchanged opacification of the right mastoid air cells and middle ear cavity from eustachian tube obstruction. There was also unchanged

Fig. 3a, 3b and 3c. T1 and T2 Flair MRI of the head on day 0 with contrast revealing ill-defined edema of the right infratemporal fossa (star region) and enhancement extending through multiple compartments.
hypoenhancement of the right cavernous sinus and intracranial right ICA, compatible with chronic occlusion of the structures. There are multiple concerns listed in the chart regarding patient’s compliance with isavuconazonium treatment, as she continued to return secondary to DKA and diabetes medication noncompliance. The patient’s complex home life as well as her difficult nature have complicated management of both her mucormycosis and diabetes, and these conditions will unfortunately continue to cause her grief until she is able to achieve compliance with treatment.

3. Discussion

While AIFRS can be cured with antifungal medications and debridement, treatment can sometimes be delayed by misdiagnosis. This is in part due to the variation in initial presentation of these patients. While early presentation can be rather non-specific, the presence of more alarming symptoms, such as vision changes or facial paresthesias should clue physicians into the possibility of AIFRS, as these symptoms are often signs of advanced disease [5]. Our patient’s initial symptoms of cranial nerves V2, V3, and VI weakness, as well as her history of multiple recent episodes of DKA helped us to further develop our differential and include AIFRS.

Our initial CT angiogram findings did lead to some uncertainty regarding the diagnosis, as the soft tissue mass was not confined to the infratemporal fossa, but also invaded the parapharyngeal space as well as appeared to have multi-compartment extension. These findings broadened the differential to include skull base lymphoma, nasopharyngeal carcinoma, and infectious causes, such as AIFRS. While there is no pathognomonic CT finding for AIFRS, the most common finding in early disease is unilateral thickening of the nasal mucosa [9]. More interesting, perhaps, were our CTA findings of multiple aneurysms. Infectious aneurysms are thought to make up only 2–5% of intracranial aneurysms [6]. Our images show that, while the ICA continues to be the vessel most commonly affected in cerebral mycotic aneurysms, there is the possibility of involvement of other nearby vessels, such as the middle cerebral artery, as seen in our patient. In our review of the literature, we found evidence of 12 published cases in which fungal infections involving the sphenoid sinuses led to internal cerebral arterial aneurysms, but we were unable to find published cases in which AIFRS led to middle cerebral arterial aneurysms [7]. Furthermore, our images exemplify the aggressive nature of AIFRS and emphasize the importance of early nasal biopsy in distinguishing between malignant and infectious processes, as the treatment and prognosis for these conditions differs significantly.

Acute Invasive Fungal Rhinosinusitis continues to be a life-threatening complication of diabetes mellitus, and this diagnosis must always be on our differential for patients who present with repeat episodes of diabetic ketoacidosis. CT is often nondiagnostic and findings can broaden the differential, and this case shows that there are a myriad of possible findings on imaging of these patients, such as middle cerebral arterial aneurysms. While patients present with a wide range of symptoms, it is important to consider AIFRS as our diagnosis and complete the proper workup, including nasal biopsy, as antifungal medications can lead to cure and resolution of symptoms.

Declaration of competing interest

There are none.

Acknowledgements

There are none.

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