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Aspergillus Terreus Brain Abscess Complicated by Tension Pneumocephalus in a Patient with Angiosarcoma

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Conflict of interest: None declared

Patient: Male, 67
Final Diagnosis: *Aspergillus terreus* brain abscess complicated by tension pneumocephalus
Symptoms: Blurred vision • hemiparesis
Medication: —
Clinical Procedure: —
Specialty: Infectious Diseases

Objective: Rare co-existance of disease or pathology

Background: *Aspergillus terreus* is an evolving opportunistic pathogen, and patients with *A. terreus* often have poor outcomes due to its intrinsic resistance to several systemic antifungal agents. Here we present a unique case of intracranial abscesses of *A. terreus* in a patient with recurrent angiosarcoma, complicated by development of tension pneumocephalus.

Case Report: A 67-year old gentleman with history of scalp angiosarcoma with wide excision two years prior presented to the hospital for left arm clumsiness, altered mental status, and low-grade fever. *Staphylococcus aureus* and *Proteus mirabilis* bacteremia was detected, and Computed Tomography (CT) of the head showed right frontal lobe abscesses. He was started on steroids, intravenous vancomycin and cefepime, and was eventually discharged. He presented to the hospital again due to persistent and worsening symptoms. MRI showed progression of the brain lesions, and surgical biopsy and culture of lesions revealed *A. terreus* and gram-positive cocci. He was started on trimethroprim/sulfamethoxazole and voriconazole and symptoms improved. On post-op day four, he acutely decompensated with total loss of left arm strength; MRI demonstrated tension pneumocephalus. Conservative management was undertaken with continuous supplemental oxygen. Serial x-ray imaging over the next week demonstrated resolution of the pneumocephalus, and the patient was able to regain all proximal lower and upper extremity strength.

Conclusions: Never before has a case of *A. terreus* been associated with angiosarcoma or tension pneumocephalus in the literature. Proper identification and prompt diagnosis of species is crucial in the immunocompromised patient. Tension pneumocephalus should be included in the differential diagnosis of nontraumatic hemiparesis for emergent evaluation and management.

MeSH Keywords: Aspergillosis • Aspergillus • Hemangiosarcoma • Neuroaspergillosis • Pneumocephalus

Full-text PDF: http://www.amjcaserep.com/abstract/index/idArt/900425

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Background

Aspergillus terreus is a saprophyte that has mainly been associated with immunocompromised patients, and has been reported up to 15–23% percent of hematologic malignancy patients with invasive aspergillosis (IA) [1]. Although not as prevalent as other etiologies of IA, with *A. fumigatus* being the most common, patients with *A. terreus* often have worse outcomes due to intrinsic resistance to amphotericin B [1]. Here we present an unusual case of a patient with intracranial *A. terreus* abscesses, which was further complicated by tension pneumocephalus after surgical evacuation.

Case Report

A 67-year old Caucasian man with a history of hypertension, dyslipidemia, and myocardial infarction with stent placement, was diagnosed with angiosarcoma of the scalp in 2013. At the time of diagnosis, the patient had a 30-pack-year smoking history, and no other significant alcohol or substance abuse history. He underwent wide excision of scalp in October 2013 with revision for positive margins. Attempted closure of scalp wound via flap had failed twice, and patient had an epithelialized skull. Post-operatively, he underwent radiation therapy with 60 Gy over 6 weeks over 30 fractions to the surgical bed and margin using intensity modulated radiation therapy (IMRT) with image guidance, followed by chemotherapy with 6 cycles of single agent paclitaxel, 80 mg/m^2 for four weeks per cycle. However re-staging scans and biopsy in February 2015 showed metastatic disease with lymphadenopathy in the posterior triangle bilaterally, and he was treated with doxorubicin 75 mg/m^2 single agent for 5 cycles total. Re-staging imaging showed further progression, and a concurrent chemotherapy with radiation therapy approach was used, with dose-reduced paclitaxel for 3 cycles at 60 mg/m^2, and radiation therapy with 66 Gy in 33 fractions using IMRT.

In September 2015, he presented with left arm clumsiness, altered mental status with mild confusion but otherwise no neurological dysfunction, and low-grade fever. Summary of clinical course is shown in Figure 1. Blood cultures were positive for methicillin-sensitive *Staphylococcus aureus* and *Proteus mirabilis* bacteremia. A Computed Tomography (CT) of the head revealed 2 right frontal lobe lesions with surrounding vasogenic edema. Brain MRI showed ring-enhancing intra-axial abscesses on the right side without evidence of recurrent scalp tumor. The source of the bacteremia was thought to be secondary to his large scalp wound or a possible brain abscess. He was empirically treated with dexamethasone 2 mg once daily by mouth, intravenous vancomycin 1.75 mg every 12 hours, intravenous cefepime 2 mg every 8 hours, and metronidazole 500 mg three times daily by mouth, each for four-week duration.

One month later, he presented with acute left-sided weakness in upper and lower extremity, left-sided facial droop, symptoms of high order executive dysfunction such as word-finding difficulties, persistent low-grade fever, blurry vision, and vomiting. Vitals on admission included temperature of 36.6°C, pulse of 79 beats per minute, respiratory rate of 20 breaths per minute, and blood pressure of 142/89 mmHg. Physical

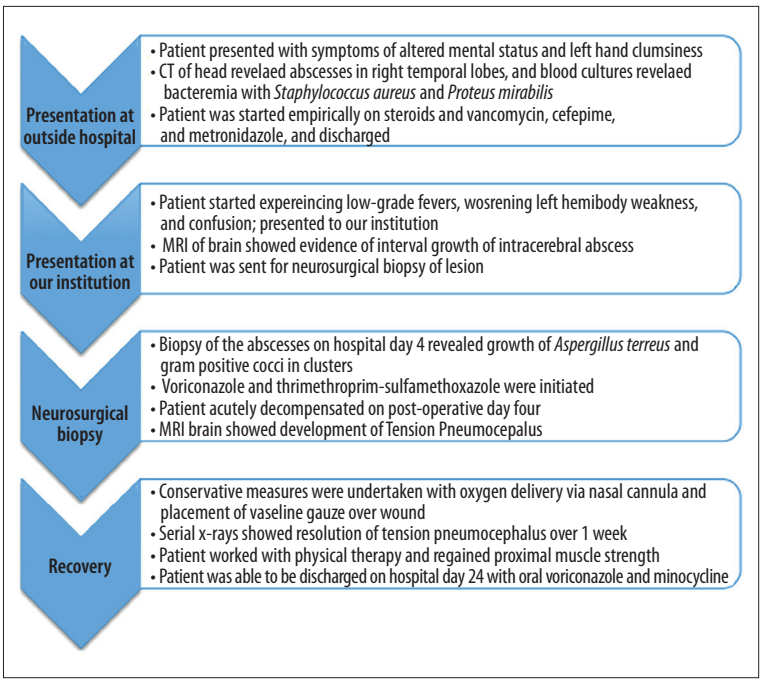

Figure 1. Summary of clinical course. Description of sequence of events from hospital stay.

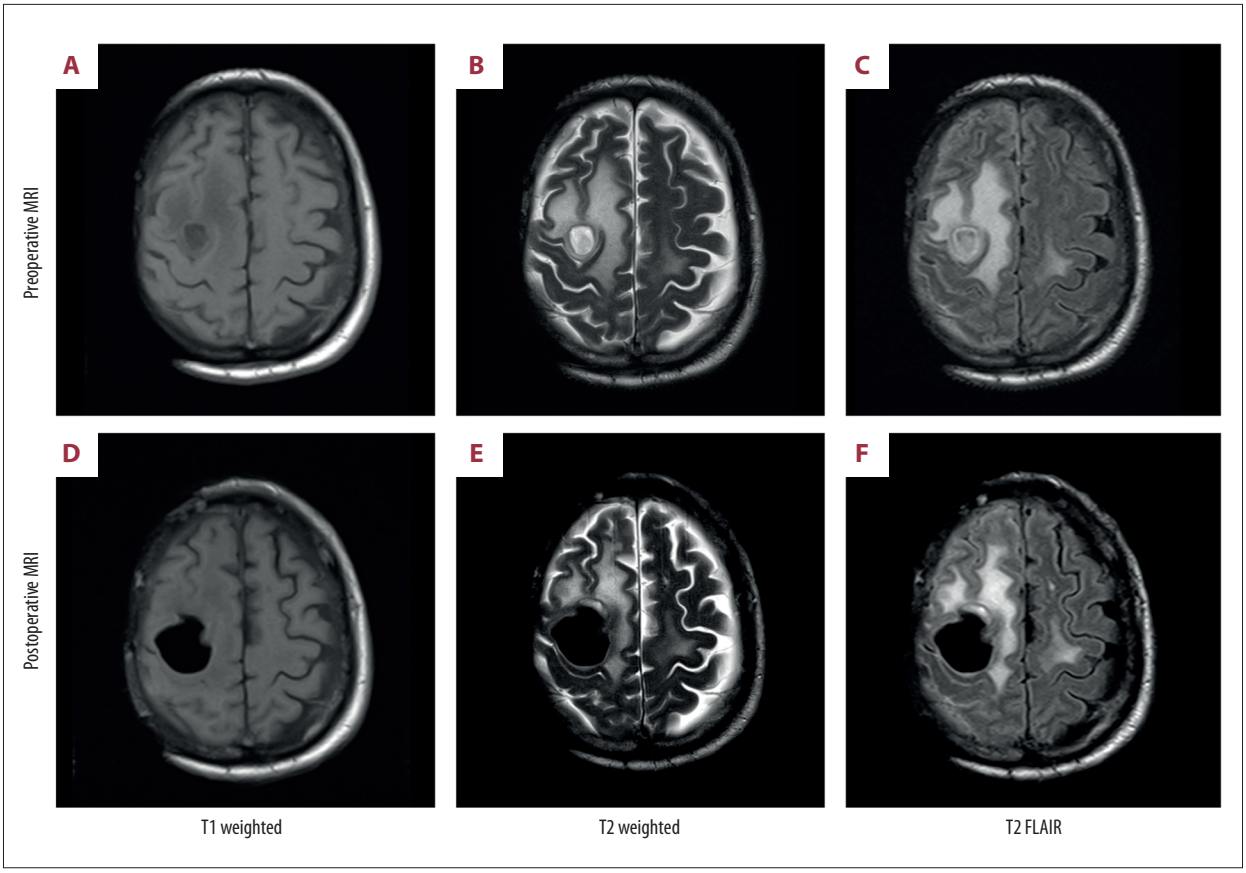

Figure 2. Pre- and post-operative T2-weighted MRI brain. (**A–C**) Pre-operative MRI from hospital day 2 which demonstrates abscess in the temporal lobe area surrounded by significant vasogenic edema; T1-weighted (**A**), T2-weighted (**B**), and T2 FLAIR (**C**) images included. (**D–F**) Post-operative MRI from hospital day 9 showing expansion of space from evacuated abscess, demonstrating tension Pneumocephalus; T1-weighted (**D**), T2-weighted (**E**), and T2 FLAIR (**F**) images included.

examination revealed 4/5 strength of left upper and lower extremities, bradykinesia, diminished alternating movements in left hand, and word-finding difficulties. The remainder of the neurological exam was intact. Laboratory values revealed leukopenia with WBC 3.41 k/uL, normocytic anemia with hemoglobin 11.0 g/dL, hematocrit of 32.9, and mean cell volume 85.0 FL. Other laboratory values, including platelet count, electrolytes, creatinine, and liver enzymes, were without significant abnormality (data not included). Repeat MRI showed an interval progression of the brain lesions, with increase in size of right frontal abscess and associated vasogenic edema (Figure 2A). Therefore, he was empirically started intravenous vancomycin 1.75 mg every 12 hours, intravenous cefepime 2 mg every 8 hours, and intravenous dexamethasone 4 mg twice daily. Subsequent blood cultures were negative.

He underwent a stereotactic right frontal craniectomy, biopsy, and drainage of the abscesses. The biopsy of the abscess wall was sent for both permanent fixation and culture. Four to five mL of yellow purulent material was drained from another frontal abscess, and cultures were sent. Biopsies of the bone, dura mater, and arachnoid mater did not reveal any evidence of recurrent malignancy. Deep wound cultures grew *A. terreus* and gram-positive cocci in clusters and his antibiotic therapy was changed to trimethroprim/sulfamethoxazole 320–1600 mg twice daily and Voriconazole 200 mg twice daily.

He initially improved clinically, but on post-operative day four, he acutely decompensated with total loss of left arm strength and increased left-sided facial droop. Repeat MRI brain demonstrated that the dominant ring-enhancing lesions had been completely removed, with a large amount of air under tension in the corticectomy defect, with questionable midline shift. The diagnosis of tension pneumocephalus was made based on these radiologic findings (Figure 2B). Conservative management was undertaken with continuous supplemental oxygen via nasal cannula at 4 L/hr, and triple layer of vaseline gauze was placed over scalp wound to prevent further accumulation of air. Serial x-ray imaging of the head over the next week demonstrated resolution of the tension pneumocephalus by post-operative day eight (Figure 3). On post-operative day nine, basic metabolic panel revealed that patient had

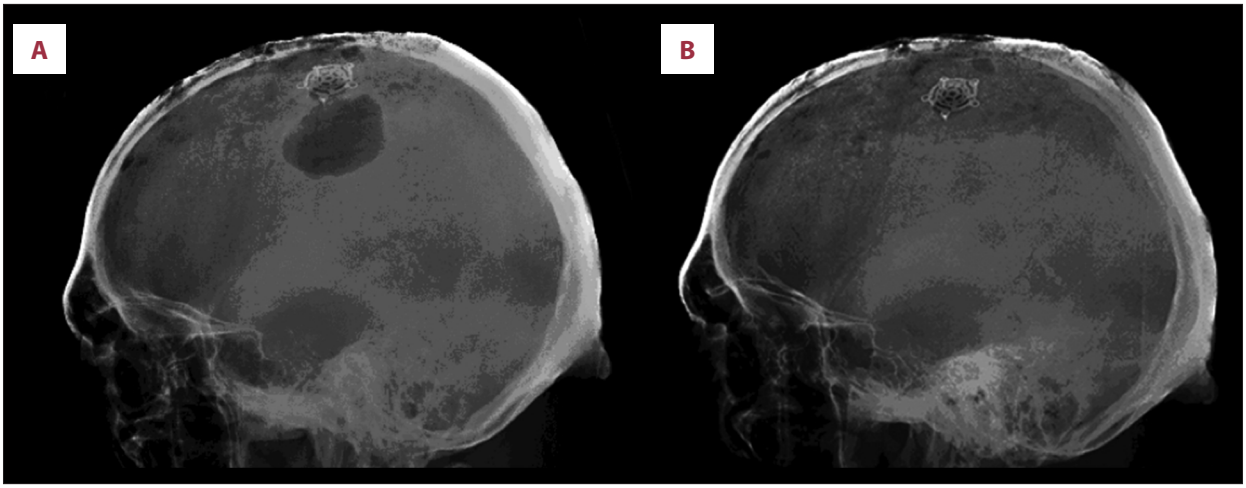

Figure 3. Serial Post-operative X-ray Imaging. (**A**) X-ray image from post-operative day 6 revealing intracranial air from tension pneumocephalus and right frontal-parietal craniotomy site with dressing. (**B**) X-ray image from post-operative day 10 demonstrating resolution of tension pneumocephalus.

hyperkalemia with potassium of 5.1 mEq/L. Patient was given kayexalate 30 mg, and trimethroprim-sulfamethoxazole was discontinued as it was thought to be likely causative agent. Minocycline 100 mg capsule twice daily was initiated for antibiotic coverage.

With physical and occupational therapy, the patient was able to regain proximal muscle strength, though he continued to suffer from loss of fine motor skills and wrist strength. He was able to stand with assistance and ambulate with a rolling walker, and was eventually discharged on hospital day 24 to a sub-acute rehabilitation facility to continue physical and occupational therapy. Dexamethasone 4 mg was tapered over a 2-week course after discharge, and he was continued on oral voriconazole 250 mg twice daily by mouth and minocycline 100 mg twice daily by mouth to complete a six-month course with scheduled follow up brain imaging. Our patient is currently followed as an outpatient in neuro-oncology, infectious disease, and sarcoma clinic.

Discussion

Aspergillus terreus is a very unusual cause of central nervous system (CNS) invasion, though the highest prevalence has been found in patients with hematologic malignancy. Few reports have been made directly linking *A. terreus* with CNS infections. *A. terreus* was recently reported as a cause of meningitis in an immunocompetent adolescent patient [2]. Furthermore, another recent case report detailed *A. terreus* in a brain abscess in a patient with glioblastoma multiforme; the authors concluded that in patients with brain tumors who receive steroids for management of cerebral edema, as our patient had, they maybe more susceptible to infection with this species [3].

A patient with Acute Myelogenous Leukemia (AML) was found to have *A. terreus* growing in bilateral brain abscesses, thought to have arisen hematogenously from a pulmonary infection after induction chemotherapy [4]. Our case is very unique in that *A. terreus* has never been associated with angiosarcoma of the scalp as per our review of the literature [5]. Of course, our patient had a much higher chance of intracranial infection considering that full scalp flap closure was never achieved, thus greatly increasing the risk of contamination.

CNS aspergillosis has shown to have poor response to amphotericin B treatment, but this lack of response is further complicated in patients with *A. terreus,* as it is inherently resistant [5–7]. A recent retrospective study reviewing 20 years of hematologic malignancy patients at one institution showed that patients with *A. terreus* had a significantly higher mortality rate in comparison with other *Aspergillus* species, with 51% versus 30% [1]. Azole therapies, such as voriconazole used in this patient, have shown promise in patients with *A. terreus.* One study showed that in retrospective analysis of 83 cases, patients who received voriconazole had higher survival rates in comparison to those who received amphotericin B at 12 weeks of therapy (64.7% *vs.* 26.2%) [8].

Another unique aspect of this case is that never has *A. terreus* been associated with tension pneumocephalus in the literature. Pneumocephalus is characterized by the accumulation of intracranial air, and it is considered to be under 'tension' when air accumulates but is unable to escape the cranial vault. In our patient, the tension pneumocephalus most likely developed secondary to the neurosurgical biopsy; however, cases have been reported of tension pneumocephalus being caused by fungal sinusitis as well [9,10]. Of note, in our review of the literature one case recently described the development

of tension pneumocephalus in a patient with scalp angiosarcoma as well [11].

Tension pneumocephalus can cause rapid clinical deterioration due to increase in intracranial pressure due to mass effect, and can lead to brain stem herniation, coma, and death. For patients with tension pneumocephalus, immediate neurosurgical intervention is most likely required to alleviate the elevated intracranial pressure if midline shift is present. Evacuation of accumulated air can be accomplished by drilling a burr hole, using needle and syringe aspiration, and then closing the dural defect [12]. Conservative management involves placing the patient in Fowler position at 30 degrees, avoiding any behaviors that would increase intracranial pressure like valsalva, coughing, or sneezing, and either using hyperbaric oxygenation or continuous normobaric oxygenation [12]. Increasing the oxygenation is thought to enhance reabsorption of nitrogen into the blood, which in turn decreases the volume of the accumulated air. Thus, the fact that our patient had complete resolution of his tension pneumocephalus via conservative management alone is yet another reportable factor of this case.

Conclusions

Here we present an unusual case of *Aspergillus terreus* brain abscess in an angiosarcoma patient, further complicated by tension pneumocephalus after evacuation. Never before has *A. terreus* been associated with angiosarcoma or with tension pneumocephalus. We believe this case highlights the importance of proper identification of infectious species in immunocompromised patients with brain abscesses in order to initiate appropriate antibiotic therapy, especially in patients with scalp defects, due to the open and contaminated nature of the wound. Furthermore, it is important to note that due to the fact that complete dural closure after biopsy and aspiration of brain abscesses cannot be achieved, close attention should be paid to evaluate for symptoms of pneumocephalus.

Conflicts of interest

None.

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