

Eosinophilic meningitis secondary to allergic *Aspergillus* sinusitis

To the Editor:

Eosinophilic meningitis is an uncommon condition usually caused by helminthic parasites.¹ Nonparasitic infectious causes are rare and include coccidioidomycosis and, rarely, cryptococcosis.¹ Noninfectious causes include idiopathic hypereosinophilic syndrome, ventriculoperitoneal shunts, central nervous system leukemia or lymphoma, certain antibiotics, nonsteroidal anti-inflammatory agents, and contrast agents.¹ Allergic *Aspergillus* sinusitis (AAS) has not been previously associated with eosinophilic meningitis. We describe an unusual case of AAS that presented with cavernous sinus thrombosis, right abducent nerve palsy, and eosinophilic meningitis.

A 49-year-old Singaporean Chinese woman presented with right-sided headache of a week's duration and a 2-day history of diplopia. She had a brief upper respiratory tract illness that resolved 4 days before admission. She had no significant travel or past medical history and specifically denied symptoms of chronic or recurrent sinusitis. She had no history of unusual food ingestion.

Clinical examination revealed an alert patient with no fever or neck stiffness. She had a complete right sixth nerve palsy but no other deficits on neurologic examination.

Laboratory studies revealed a white blood cell count of $12.85 \times 10^9/L$ with 6.1% eosinophils. The cerebrospinal fluid (CSF) was clear, with a glucose concentration of 3.0 mmol/L, a protein concentration of 0.59 g/L, and a cell count of 15 white cells/ μL with 57% lymphocytes, 9% monocytes, and 34% eosinophils. No acid-fast bacilli were seen on microscopic examination. Magnetic resonance imaging of the brain showed thrombosis of the right cavernous, transverse, and sigmoid venous sinuses associated with bilateral sphenoid and ethmoid sinusitis (Fig 1). Computed tomography of the sinuses showed opacification of both sphenoid sinuses and the left ethmoid sinus. No bony erosion was noted. Her clotting and procoagulant profiles were normal. The blood cultures and the CSF bacterial, mycobacterial, and fungal cultures were negative. Her chest x-ray film was normal, and no parasites were found on stool examination. Her total serum IgE level was normal. However, the IgE-mediated test for *Aspergillus fumigatus* was strongly positive. Serology for HIV was negative.

She was initially treated for presumed basal meningitis with intravenous ceftriaxone, cloxacillin, and metronidazole. Nasopharyngoscopy revealed inflammation of the postnasal space with purulent fluid oozing from the left sphenoid ostium. Bilateral endoscopic sphenoidectomy was performed. The sphenoid sinuses were inflamed with debris, and inspissated pus was present, mainly on the left side. The intrasphenoid septum was dehiscent. Surgical enlargement of the sphenoid ostia was subsequently performed.

Histology (Fig 2) showed sheets of eosinophilic and mucinous material within which were groups of viable and

degenerate eosinophils. Gomori methenamine silver and periodic acid-Schiff stains showed numerous *Aspergillus* hyphae. There was no mucosal invasion, and allergic mucin was present. No ball-like or sheet-like mycetoma was identified.

The patient received oral antihistamines, steroids, and a short course of itraconazole after the operation. She remained well 6 months after the operation and eventually recovered her ability to abduct her right eye.

The classification of fungal sinusitis has been recently reviewed.²⁻⁵ Allergic fungal sinusitis is characterized by an allergic reaction to the fungus in the sinus rather than a fungal infection per se. It often presents as a chronic sinusitis and typically occurs in young, immunocompetent patients who are often atopic.² Multiple sinuses are frequently involved. It is postulated that the fungi incite an inflammatory reaction in the mucosa. Peripheral blood eosinophilia and a raised total IgE are often seen.^{6,7} The immunocompetent status of our patient, the peripheral and CSF eosinophilia, the presence of allergic mucin, and fungal hyphae without mucosal invasion seen on histologic examination were consistent with the allergic form of *Aspergillus* sinusitis.^{3,8} The good clinical outcome and response to anti-inflammatory therapy are also compatible with this diagnosis.

Our patient's presentation with cavernous sinus thrombosis resulting in abducens nerve palsy and CSF eosinophilia is unusual. The possibility that CSF eosinophilia was a result of a concomitant CSF infection caused by helminthes is very unlikely in view of the patient living in an urban city with no history of risk factors for *Angiostrongylus* infection. The clinical features are likely the result of the inflammatory contents of the sinus eroding through the sinus wall with leakage into the venous sinuses and subarachnoid space, which has been reported in allergic fungal sinusitis.^{2,7,9} Erosion through the intraethmoid septae, the lamina papyracea into the orbit, or even through the cribriform plate or posterior wall of the frontal sinus into the epidural space has also been reported.⁹ The process is thought to be caused by bone resorption secondary to pressure of the expanding allergic mucin mass.²

Differentiation between allergic and invasive forms of fungal sinusitis is important, because they have different prognoses and require different treatment approaches. The immunopathophysiology of allergic *Aspergillus* sinusitis is analogous to that of allergic bronchopulmonary aspergillosis. Treatment consists of surgical drainage and aeration, with oral corticosteroids to prevent recurrence. Systemic antifungal agents are not usually indicated.² There may be a role for newer, less toxic agents in refractory cases.¹⁰ By contrast, invasive variants require radical surgical debridement, systemic antifungal agents, and attempted correction of the underlying immunocompromised state. Histopathologic evaluation of surgical specimens in suspected invasive cases is critical in establishing a diagnosis.

In summary, our patient had an unusual presentation of an increasingly recognized condition with a

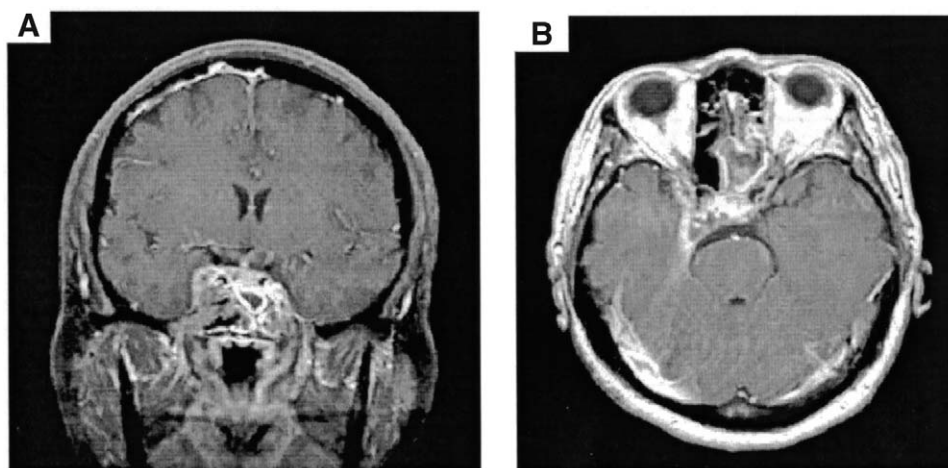


FIG 1. A, Coronal postcontrast T1-weighted image of the brain shows fluid and abnormal mucosal enhancement in the sphenoid sinus and right cavernous sinus thrombosis. B, Axial postcontrast T1-weighted image shows thrombosis of the right cavernous sinus.

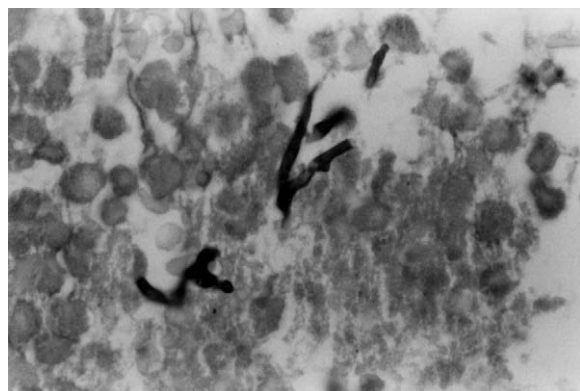


FIG 2. Photomicrograph shows branching irregular hyphae. Gomori methenamine silver (under oil immersion).

good outcome from combined surgical and anti-inflammatory therapy. Clinicians need to be aware of the expanding spectrum of AAS as we learn more about this condition.

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Soluble decoy receptor 3: Increased levels in atopic patients

To the Editor:

This is the first report to describe the serum decoy receptor 3 (DcR3) levels in atopic patients. DcR3 is a soluble molecule that lacks a transmembrane domain and was initially found by Pitti et al.¹ DcR3, also known as TR6 or M68, is a member of the TNF receptor superfamily and is also a receptor for Fas ligand and LIGHT.¹⁻³ Its expression was supposed to contribute to the ability of some tumors to escape immune-cytotoxic attack. In addition, DcR3 expression can be detected in some virus-associated lymphoma (Epstein-Barr virus or HTLV-1) as well as in