Meningococcemia With Vitreous Opacities: Endophthalmitis or Vitreous Hemorrhage?

Visual acuity after treatment with meningococcal endophthalmitis is variable. A child with meningococcemia and disseminated intravascular coagulation (DIC) developed vitreous opacities. Anterior segment inflammation was never observed.

Report of a Case. A 26-month-old, previously healthy girl became lethargic with a petechial rash that progressed to purpura. Intravenous cefotaxime sodium was given for presumed meningococcemia. Blood cultures yielded Neisseria meningitidis. Periocular ecchymoses prompted an ophthalmic consultation.

The patient was nonresponsive and was receiving mechanical ventilatory support during the examination. No relative afferent pupillary defect was present. The eyelids and conjunctiva were edematous and ecchymotic (Figure 1, left). Intracocular pressures and portable slit-lamp examination showed no abnormalities. An undilated fundus examination (due to the patient’s unstable neurologic status) of the optic discs and posterior poles of both eyes showed no abnormalities.

Multiorgan system failure developed with respiratory distress syndrome, thrombocytopenia, DIC, and acute tubular necrosis requiring hemodialysis. Her unstable neurologic status and high-frequency ventilation requirements prevented reliable sequential posterior segment evaluations. The eyelid edema and ecchymoses resolved. Four weeks after the initial examination, anterior segments were still quiet and bilateral dense vitreous opacities were seen on dilated fundus examination. Retinochoroidal thickening and vitreous cell were noted on ultrasonography. At the time, vitreous opacities were believed to be hemorrhagic, secondary to DIC, because ocular inflammation was absent. A second ultrasound examination 11 days later demonstrated bilateral vitreous opacities and a possible traction retinal detachment in the left eye.

A pars plana vitrectomy, membrane peel, gas fluid exchange, endolaser, and scleral buckle procedure were performed in the left eye. Extramacular areas of traction retinal detachment and necrotic retina were observed. The macula showed no abnormalities. Vitrectomy specimen cultures were negative but Gram stains demonstrated gram-negative intracellular organisms with vitreous hemorrhage (Figure 2). Pockets of neutrophils were observed in association with macrophages. Penicillin sodium was given intravitreally in the right eye and subconjunctivally in both eyes for possible subclinical endophthalmitis. Intravitreal antibiotics were not administered in the left eye because signs of active infection were absent and intraocular gas was present. Three weeks later, vitrectomy and scleral buckle were performed in the right eye. Intraoperative findings were similar to those in the left eye.

Postoperative visual acuity with correction was 20/40 OD and 20/80 OS. Extensive chorioretinal scarring was seen (Figure 1, right) in the mid peripheral fundus. Subsequently, visual acuity decreased in the left eye due to a posterior subcapsular cataract. Cataract extraction and intraocular lens placement were performed. Postoperatively, the patient would not fix and follow in the left eye. Amblyopia was diagnosed and full-time occlusion therapy was started.

Comment. Pain, photophobia, redness, decreased vision, and vitreal inflammation are usually present with endogenous endophthalmitis. Anterior chamber inflammation, considered typical of this condition, was never seen in our patient.

We describe the occurrence of meningococcal intracellular organisms associated with vitreous hemorrhages in a patient with meningococcemia and DIC. The most likely explanation for the patient’s ocular lesions is subclinical meningococcal en-
dophthalmitis. The intravenous antibiotics the patient received may have rendered the organisms nonviable, and the ocular findings may have been related to partially treated or subclinical endophthalmitis; however, thrombotic events from DIC could cause a similar clinical finding. If DIC were the explanation, the neutrophil-containing organisms may have entered the vitreous cavity in association with the hemorrhage. Necrotic areas of retina were likely the result of septic emboli or vascular occlusion from DIC.

To avoid amblyopia, bilateral vitrectomies were necessary to clear the visual axes. This case illustrates the importance of considering intraocular infection in the setting of meningococcal meningitis and presents alternative hypotheses to explain the clinical events.

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Conjunctival Melanoma Associated With Extensive Congenital Conjunctival Nevus and Split Nevus of Eyelid

Primary acquired melanosis and acquired conjunctival nevi are recognized to be precursors of conjunctival melanoma; however, it has not been known that congenital conjunctival nevi can be a precursor of conjunctival melanoma. We report a case of fatal conjunctival melanoma in a 72-year-old Japanese man. He was born with a large congenital black mole involving the right upper and lower eyelids and conjunctiva. He had a brown-black nodule in his inferior bulbar conjunctiva and the right parotid and submandibular lymph nodes showed marked swelling. Chemotherapy was performed to clinically diagnose metastatic conjunctival melanoma, but he died 5 months later due to systemic metastasis. Autopsy revealed conjunctival melanoma associated with extensive conjunctival nevi and split nevus of the eyelid.

Seventy-five percent of conjunctival melanomas arise in association with primary acquired melanosis. Histologic evidence of nevus or a history of a conjunctival lesion dating to childhood may be discovered in 20% to 30% of patients with conjunctival melanoma.

Report of a Case. A 72-year-old Japanese man had a large pigmented area around his right eye since birth, including the eyelid and conjunctiva. The black tone became more intense in the patient’s first decade of life and had not changed since then. He first visited our institute on March 15, 1991, with his right vision obstructed by a black-brown nodule in the inferior bulbar conjunctiva.

The visual acuity and intraocular pressure showed no abnormalities. The right eyelid, conjunctiva, and caruncle were black, and the inferior aspect of the bulbar conjunctiva had a black elevated nodule. Small cystic lesions were present in other areas of the bulbar conjunctiva (Figure 1 and Figure 2). The ocular media, fundus, and optic nerve head showed no abnormalities. The right aspect of the parotid and submandibular lymph nodes showed marked swelling that was hard and did not reduce in size despite antibiotic therapy.

Metastatic malignant melanoma of the conjunctiva was clinically diagnosed. Several treatment options, including orbital exenteration, radiation therapy, and chemotherapy, were offered to the patient and the family. They desired chemotherapy only. The patient’s condition deteriorated; he died 5 months later due to systemic metastasis of malignant melanoma.

Autopsy revealed a mass of conjunctival melanoma, composed of large epithelioid cells, in the
bulbar conjunctiva inferior to the limbus (Figure 3, Figure 4, and Figure 5). Adjacent to the nodule, a narrow zone of pigmented cells, possibly melanophages, was present in the episclera (Figure 3, Figure 4, and Figure 6), that was extensively observed around the globe. Nests of cystic compound nevus (Figure 6) were extensively present in other areas of the bulbar conjunctiva. The palpebral conjunctiva and the intraocular components showed no abnormalities. Extensive intradermal nevus composed of small round cells (Figure 7 and Figure 8) were present on the skin of the eyelids. The nevus cells had features of congenital cutaneous nevus, with deep penetration in the skin and maturation at the base.

Comment. Large congenital cutaneous nevi are associated with a risk of developing melanoma since childhood.1 Marghoob et al2 prospectively followed up 92 patients (median age, 3 years) with large congenital cutaneous nevi for an average of 5.4 years and found that the cumulative 5-year, life-table risk for the development of malignant melanoma was 4.5%. The calculated stan-
Acquired conjunctival nevi are recognized to be precursors of conjunctival melanoma, but the risk of congenital conjunctival nevus for the development of melanoma is unclear.  

Gerner et al3 studied 21 orbital melanomas. They found that 90% of patients had an associated blue nevus and 47.5% of patients had some form of congenital melanosis.

Gerner et al4 analyzed 343 surgically removed conjunctival nevi. Six cases that recurred during observation were originally classified as compound nevi. Among them, 1 recurred as malignant melanoma. They mentioned that in stationary and indolent cases in adults, excision as a routine procedure was unnecessary, since the risk of evolution of conjunctival nevus into melanoma was very low. In Japan, malignant melanoma of the conjunctiva is rare, with an estimated 6 to 7 cases per year.  

In our patient, the history indicates that large nests of nevus cells involving bulbar conjunctiva, caruncle, and eyelid skin had been present since birth. Generally speaking, large nevi are associated with a risk of developing melanoma.6 The many nevus cells of this patient probably increased the risk of developing melanoma, a condition that should be rare in Japanese patients.

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Eyelid Nodule: A Sentinel Lesion of Disseminated Cryptococcosis in a Patient With Acquired Immunodeficiency Syndrome

Cutaneous cryptococcosis is a rare infection caused by Cryptococcus neoformans an encapsulated saprophytic yeast. It is 4 to 8 µm in diameter and is surrounded by a polysaccharide capsule that lives especially well in dust and soil contaminated by the excreta of pigeons. The initial site of infection is usually the lung, where cryptococcosis occurs without symptoms and persists in a latent stage for a long time. Hematogenous dissemination of the yeast may involve any organ of the body, principally the brain (70%-90% of the cases) with meningoencephalitis or a subacute meningitis and, to a lesser extent, the skeleton, eyes, and skin. We describe a man affected by acquired immunodeficiency syndrome in whom disseminated infection with C neoformans started with a nodule on the border of his right eye.

Report of a Case. A 37-year-old man with acquired immunodeficiency syndrome had a 3-week history of a papular lesion on the border of the right side of his upper eyelid (Figure 1). The clinical suspicion was of either a molluscum contagiosum or a neoplasm derived from the meibomian glands. The lesion was surgically removed. The patient’s immunologic test results were as follows: total leukocyte count, 5 × 10^9/L; CD4+ cells, 0.019 × 10^9/L; CD8+ cells, 0.039 × 10^9/L; and the CD4+/CD8+ ratio, 0.05 (normal ratio, 1-2). The patient was taking antiretroviral therapy with indinavir (800 mg, 3 times daily), stavudine (40 mg, 2 times daily), and lamivudine (150 mg, 2 times daily). Histopathologic examination showed numerous cryptococcal organisms with large polysaccharide capsules, surrounded by a granulomatous inflammation inside the superficial and mid dermis (Figure 2). Cryptococcal antigen was detectable in serum (titer 1:8192) and cerebrospinal fluid (titer 1:512). A chest x-ray film showed interstitial thickening, but a bone scan, a computed tomographic scan of the cranium, and an ophthalmoscopic examination showed no abnormalities. Therapy with amphotericin B,
1 mg/kg per day, and flucytosine, 150 mg/kg per day, was started but after 15 days additional multiple dome-shaped, flesh-colored, umbilicated papules, and ulcerated nodules appeared on the face, arms, and the dorsal aspect of the hands. The complete clinical remission lasted 5 weeks after therapy.

Comment. Human cryptococcal disease is a potentially fatal infection that develops mainly in predisposed individuals with defective cell-mediated immunity. Since the advent of acquired immunodeficiency syndrome, cryptococcosis has become more frequent, involving from 5% to 10% of patients during their life, 10% to 15% of whom had cutaneous involvement. Most prominent on the face and neck, less frequently located on the trunk and extremities, the typical clinical cutaneous manifestations are umbilicated papules with a tiny, central hemorrhagic crust quite similar to molluscum contagiosum. Less often, violaceous papules, vesicles in a varicelliform pattern, crusted plaques, subcutaneous nodules, or cellulitis have been reported. The most frequent ophthalmic manifestations of infection with \textit{C. neoformans} involve the posterior segment of the eye with papilledema, optic nerve atrophy, endophthalmitis, and choroiditis. One existing report describes limbal and choroidal mass and another iris inflammatory mass in patients with acquired immunodeficiency syndrome.

The prognosis depends on the degree of the patient’s immunodepression, the involvement of \textit{C. neoformans}, and the prompt start of therapy. The patient we observed is interesting because he showed a single non-diagnostic lesion on the upper border of the eyelid as a sentinel lesion that preceded the spreading of the cryptococcal infection by 5 weeks. A rapid diagnosis permitted the prompt start of appropriate therapy. Notwithstanding this, our patient experienced an initial spread of cryptococcal lesions on his skin although then serum and the colony-stimulating factors titer of cryptococcal antigens were decreasing slowly. Now, after a 22-month follow-up, the patient is well. Occasional relapses of the opportunistic infection have been controlled with amphotericin B.

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**Scedosporium apiospermum of the Orbit**

\textit{Scedosporium apiospermum} is an emerging fungal pathogen commonly found in soil (even in hospital potted plants) and polluted water. Ocular infection can occur including keratitis, conjunctival mycetome, endophthalmitis, and panophthalmitis. Reports of orbital involvement have been rare. We describe a 68-year-old man with leukemia who developed an orbital subperiosteal abscess from extension of contiguous fungal pan-sinusitis. We also review the role of pharmacotherapeutics in the management of this disease. Remarkably, this patient deferred on antifungal therapy without aggressive surgical debridement.

Report of a Case. A 68-year-old man with an 8-month history of acute lymphoproliferative leukemia was seen in consultation for the hematologic service. He complained of a red, protruding left eye and progressive diplopia over 3 days. He had been admitted to the hospital with neutropenic fevers 5 days earlier.

He had left peri-orbital edema and erythema (greatest inferomedially). Palpation of the affected area revealed no crepitus or bony abnormality. Sensory divisions of the trigeminal nerve were intact. The left eye was displaced forward 2 mm and laterally 2 mm. Best-corrected visual acuity was 20/20 OD and 20/25 OS. Papillary responses were brisk with no relative afferent pupilary defect. Slitlamp examination showed no other abnormalities. Intraocular pressures were normal. Left eye abduction was notably diminished and there was a large angle esotropia. Retinal evaluation showed no abnormalities.

White blood cell count was 0.5 $\times 10^9$/L, demonstrating profound neutropenia. Computed tomographic scan (Figure 1) revealed a pansinusitis with a soft tissue density extending into the left inferomedial aspect of the orbit. Needle drainage of the left aspect of the maxillary sinus produced 30 mL of thick, yellow fluid. Initial smears demonstrated septated hyphae and were negative for bacteria.

Amphotericin B (1 mg/kg per day) was immediately started and itraconazole (400 mg/d) was added the next day. The fungus was identified as \textit{S apiospermum} (Figure 2) and the infectious disease consultant recommended aggressive treatment due to the relative in vitro insensitivity to antifungal therapy. Surgical debridement of the sinuses and orbit was recommended; however, the patient declined this procedure. By day 2 of medical therapy, the patient’s fever cleared and the edema and diplopia resolved. On the seventh day of medical treatment, there were no ocular signs or symptoms. The patient was discharged from the hospital on a regimen of identical doses of amphotericin B and itraconazole. He had no orbital recurrences and died.
bital extension of pansinusitis of *S. apiospermum* in a diabetic host. The patient had both liver and renal failure. He was treated with surgical drainage and systemic amphotericin B but died 3 months later from unrelated complications. In 1984, Anderson et al.² described the successful treatment of a 4-year-old boy who had suffered a penetrating orbital injury with orbitocranial involvement of the infection. His therapy included multiple surgical interventions and intravenous amphotericin B and miconazole.

In cases of localized disease, it seems as if local debridement of as much of the fungus as possible, combined with systemic antifungal medication, provides the best chance of cure.³,⁵ This organism is known to have relative in vitro insensitivity to amphotericin B; however, recent reports have shown good clinical responses.³ Both itraconazole and miconazole (ie, imidazoles) have shown greater effectivity in vitro and may be used as monotherapy.³,⁶ Combined treatment with amphotericin B and an imidazole seems reasonable.

In our patient, needle drainage of the involved maxillary sinus performed for diagnostic purposes also provided some therapeutic decompression. This, combined with amphotericin B and itraconazole, resolved the signs and symptoms of orbital infection. Surgical debridement may still be the treatment of choice in this disease; however, antifungal therapy alone may be reasonable in patients unwilling or unable to undergo aggressive surgery. Ideal dosage and duration of treatment are unknown, although this patient’s clinical course may provide helpful information.

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Comment. *Scedosporium apiospermum* is an opportunistic fungus commonly found in soil and decaying vegetation. In 1944, Emmons demonstrated that *S. apiospermum* is the asexual form of *Pseudallescheria boydii*. Prior to 1944, *P. boydii* was known as *Allescheria boydii*.² This organism can, in cases of penetrating injury, infect healthy individuals. Here, it produces an indurated lesion at the site of the injury.³ In immunocompromised patients, aggressive spread is common. Systemic sites of infectious mycoses in the immunosuppressed include the lungs, joints, central nervous system, sinuses, and ears.²

Orbital involvement of this organism has rarely been reported. In 1977, Gluckman et al.¹ reported orbital extension of pansinusitis of *S. apiospermum* in a diabetic host. In 1979, Gluckman et al.⁴ reported an organ system involvement of the maxillary sinuses bilaterally. Left, Periosteal thickening of the frontal and sphenoid sinuses and opacification of the left ethmoid sinus were also present (not shown). Right, A subperiosteal abscess was noted involving the left medial orbital wall.

3 months later from complications of his leukemia.


