Endogenous Aspergillus Uveitis Following Heart Surgery

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Eleven cases of endogenous Aspergillus infection of the eye have been reported. In eight, the fungus was identified by histologic examination alone, supported in the other three by culture of Aspergillus from sputum, from pleural exudate at autopsy, and from a thoracotomy specimen during life as well as several organs at autopsy. Uveitis has also been reported in a patient with an Aspergillus abscess in the lung, but no pathologic examination of the eye was possible.

This communication reports a case of intraocular aspergillosis following heart surgery in which uveitis was the presenting sign of endocarditis with septic embolism.

Report of a Case

This 40-year-old white woman underwent open-heart surgery June 10, 1966 at another hospital for replacement of her mitral valve, deformed by rheumatic heart disease, with a Starr-Edwards prosthesis. Postoperatively, she was maintained on anticoagulants warfarin sodium (Coumadin Sodium) and digoxin. She made a good recovery and was well until the middle of August, when pain and blurred vision in her right eye developed. Ophthalmological examination on Aug 22 revealed a marked exudation in the anterior chamber and cellular infiltration of the vitreous, as well as a very low intraocular tension. She was treated with 6 mg of oral dexamethasone (Decadron) daily and local 1% atropine and 0.1% dexamethasone drops to the right eye. When this regimen failed to control the intraocular inflammation, the oral dexamethasone was increased to 12 mg daily, and 1 cc of methylprednisolone acetate (Depomedrol) was injected subconjunctivally. Because of the possibility of a low grade systemic bacterial infection and her severe mental depression, she was hospitalized. Although several blood cultures were sterile, treatment with penicillin 4.8 million units daily was started and dexamethasone reduced to 1.5 mg daily orally.

After the appearance of an hypopyon in the left eye, the patient was referred for consultation to Arthur G. DeVoe, MD. Examination on Sept 7, 1966, showed the vision reduced to ability to count fingers in the right eye and light perception with poor projection in the left. In the right eye, there was a marked subconjuncti-
val hemorrhage in the region of the methylprednisolone acetate injection. The cornea was clear. Slit-lamp examination showed 3+ cells and 1+ flare in the anterior chamber. The pupil was widely dilated. The lens showed early cortical opacities. The entire vitreous was seeded with innumerable cells, which were gathered in cloud-like clumps between 5 and 8 o'clock in the peripheral vitreous. The optic disk and vessels could just be distinguished. Intraocular tension by applanation was 4 mm Hg.

The left eye showed a moderate ciliary injection. There was a 3 mm hypopyon, 4+ cells, 2+ flare, and clumps of fibrin in the anterior chamber. The pupil was widely dilated, and the lens showed diffuse cortical cataract. The vitreous was so densely seeded with cells that the optic disc could not be seen. Intraocular tension was 4 mm Hg by applanation. During the examination, it was apparent that the patient had difficulty carrying out manipulative acts with her hands, and partially lost her sense of balance. In addition, she suffered from severe headaches and neck pain.

At the Neurological Institute the patient had few neurological signs, although numerous petechiae were noted all over her back. The heart sounds reflected the presence of the mitral valve prosthesis. The hematocrit was 30% and the white blood cell count was in the range of 20,000 with 85% neutrophils. The platelet count was 273,000. The prothrombin time was markedly elevated to 50 seconds. The sedimentation rate was 69 mm after one hour. Urinalysis showed 100 mg/100 cc albumin and many red cells per high power field. Lumbar puncture showed opening pressure of 220, closing pressure of 210 with xanthochromic fluid, 4 white blood cells, 3,100 crenated red blood cells, protein 55 mg/100 cc, and glucose 76 mg/100 cc. The electroencephalogram was diffusely abnormal.

The clinical diagnosis was hemorrhage into the brain substance secondary to treatment
with anticoagulants or to subacute bacterial endocarditis with emboli to the brain. Because of the association of severe bilateral uveitis with abnormality of hearing and vague neurological symptoms, a diagnosis of Vogt-Koyanagi-Harada's disease was considered. The prothrombin time returned to normal range after treatment with menadione sodium bisulfate (Hykinone) and phytonadione (Mephyton). Despite repeatedly negative blood cultures, 2 gm of streptomycin intramuscularly and 40 million units of penicillin by continuous intravenous drop were given daily.

During her remaining week of life, the patient lost all vision, had intermittent seizures and a fever ranging between 99.5°F (37.5°C) and 102°F (38.9°C) rectal. On Sept 15, the patient died.

At autopsy hyphae of *Aspergillus fumigatus* were identified microscopically within a large thrombus attached to the mitral valve prosthesis, and the fungus was cultured from both the thrombus and from heart blood. Numerous abscesses with surrounding growth of hyphae could be identified in the brain and in both eyes but not in other organs examined. There was an extensive subarachnoid hemorrhage.

**Ophthalmic Pathology (Case 13697).**—The globes were fixed in formaldehyde solution (formalin) and sectioned horizontally into two callots and central section. In the right globe the most striking gross finding was an arborescent white mass in the anterior vitreous, adherent to the ciliary body. A similar mass arose from the posterior retina of the left globe extending anteriorly into the vitreous cavity (Fig 1).

Microscopic examination of the right globe showed an abscess between the sclera and ciliary body which extended into the vitreous cavity. No fungi could be identified in the ciliary body or in the center of the large vitreous abscess. However, on the border of this abscess and around numerous smaller abscesses, branching hyphae could be identified in sections stained by PAS (Fig 2) or Gomori methenamine silver nitrate (Fig 3) methods. The hyphae were 4μ to 7μ in diameter, possessed numerous transverse septa, and branched in a dichotomous manner at 45° angles characteristic of *A fumigatus*. Unusual forms of a fungus presumed to be *A fumigatus* were found in areas of tissue necrosis in the anterior chamber, iris, and vitreous (Fig 4). The retina was extensively infiltrated by hyphae and was detached. The pigment epithelium was intact in all but one area of chorioretinal necrosis. The choroid was infiltrated by inflammatory cells but revealed no hyphae. The sclera and optic nerve were normal. Microscopic examination of the left eye showed a similar *Aspergillus* infection, although less extensive.

**Comment**

It is surprising how rarely the eye has been involved in systemic mycotic infections. Embolism to the retina from fungus endocarditis following heart surgery has been reported only once. However, a history of recent open-heart surgery in a patient with severe uveitis should provoke a careful search for endocarditis as a possible source of septic emboli. Repeated blood cultures may be reported negative for bacteria, but should be tested for the presence of fungus. Isolation of a fungus from serial blood cultures in a patient with signs of embolism and changing cardiac murmurs would establish the diagnosis of mycotic endocarditis. In spite of the gravity of the intraocular inflammation, steroids should not be given until endocarditis is ruled out. In addition to systemic steroids, this case was treated with a subconjunctival injection of methylprednisolone in the right eye. Microscopic examination showed the entire anterior segment of the right eye to be filled with fungus, in contrast to the left eye. Anterior chamber tap of the right eye might have provided a positive culture during life, but this procedure is seldom helpful even in experimental intraocular mycosis.
Summary

Bilateral posterior uveitis was the first sign of generalized mycosis in a patient who had undergone open-heart surgery two months previously.

Cultures taken at autopsy from heart blood and from a thrombus surrounding the mitral valve prosthesis all grew Aspergillus fumigatus. Characteristic hyphae were identified microscopically in sections from the thrombus, brain and both eyes. Systemic steroids and antibiotics had been used in an attempt to control the uveitis before the grave nature of the underlying disease was suspected.

Arthur G. DeVoe, MD, permitted the reporting of the ophthalmic aspects of this case and George H. Newman, MD, provided the culture obtained at autopsy. Identification of the fungus from the eye and mitral valve was confirmed by Margarita Silva, MD, director of the Mycology Laboratory of the College of Physicians and Surgeons.

Generic and Trade Names of Drugs

Warfarin sodium—Coumadin Sodium, Panwarfin, Prothromadin.
Dexamethasone—Decadron, Deronil, Gamma-cortin, Hexadrol, Dexameth.
Phytonadione—Mephyton, Konakion, Aquamephyton, Mono-Kay.
Methylprednisolone acetate—Depo-Medrol, Medrol Acetate Veriderm.

References