dothelial cells (Figure 3B). The VEGF from the subretinal fluid was below the detectable levels by enzyme-linked immunosorbent assay (Quantikine Human VEGF Immunoassay; R&D Systems, Inc, Minneapolis, Minn).

Comment. This patient demonstrated rapid fibrosis of an occult fibrous neovascular membrane. The histopathology of the present lesion contained microvascular channels, a prominent fibrotic response, hypercellularity of the tissue comprising both inflammatory and endothelial cells, and expression of PDGF B within vascular channels. A hypercellular response was most prominent in that portion of the scar adjacent to the RPE. Part of the cellular responses appeared to be a prominent inflammatory component consisting of CD68+ macrophages. This finding suggests that these cells may participate in the evolution of fibrous neovascular membranes and support the inflammatory paradigm of CNV in AMD. The origin of vascular elements contributing to the subretinal fibrovascular membrane in AMD remains uncertain. In the present case, endothelial cells located within the microvascular channels were strongly positive for CD34+ and vWF. Many individual cells isolated within the fibrous matrix of this membrane were CD34+ but vWF negative. In addition, many endothelial marker positive cells were identified as isolated, individual cells rather than embedded in a neovascular channel. These findings, in this case, suggest that a cellular rather than a vascular invasion may have played a role in the pathogenesis of the neovascular structures. In addition, while vWF staining is specific to endothelial cells, CD34+ also serves as a marker for hematopoietic stem cells. Recently, work with stem cells has highlighted the capacity of these cells to differentiate into vascular elements both in vitro and in vivo under the influence of VEGF and PDGF. Whether this process occurs in the pathogenesis of CNV remains speculative.

Consistent with a previous report on cytokine production in CNV undergoing involution, this case exhibited a lack of VEGF expression both by immunohistochemistry and quantitative enzyme-linked immunosorbent assay. However, prominent PDGF staining was detected within the vascular channels. In summary, this surgically excised fibrovascular membrane demonstrates additional findings that add to our knowledge of the molecular biology of neovascular AMD.

Karl Csaky, MD, PhD
Judit Baffi, MD, PhD
Chi-Chao Chan, MD
Gordon A. Byrnes, MD
Bethesda, Md

None of the authors has a proprietary interest in any test or product described within this article.

Corresponding author and reprints: Karl Csaky, MD, PhD, Bldg 10, Room 10N119, NEI/NIH, 9000 Rockville Pike, Bethesda, MD 20895-1857 (e-mail: kcsaky@helix.nih.gov).


Blindness From Septic Thrombophlebitis of the Orbit and Cavernous Sinus Caused by Fusobacterium nucleatum

Fusobacterium organisms are obligate anaerobic gram-negative bacilli belonging to the family Bacteroidaceae. Of the 15 species recognized, Fusobacterium nucleatum and Fusobacterium necrophorum are the most frequently isolated species from clinical specimens. These species are most commonly found in the mouth and to a lesser extent in feces and the urogenital tract but rarely give rise to severe disease. We describe a previously healthy 55-year-old woman with a history of severe periodontal disease who developed septic thrombophlebitis of the orbit and cavernous sinus caused by F. nucleatum. We are unaware of previous reports of septic thrombophlebitis of the orbit and cavernous sinus caused by F. nucleatum.

Report of a Case. A previously healthy 55-year-old woman had a 1-month history of left-sided headaches that were treated with pain medications. Her medical history was notable for severe periodontal disease and a previous partial thyroidectomy for a benign mass. The patient subsequently developed severe left orbital pain. Computed tomography and magnetic resonance imaging of the orbits and brain were performed, and the findings demonstrated cavernous sinus enlargement and enhancement on the left side. Thoracoabdominal computed tomography and cerebrospinal fluid evaluation results were negative. Infectious and noninfectious inflammatory processes, including Tolosa-Hunt syndrome and granulomatous diseases, were considered in the differential diagnosis, and the patient was treated with antibiotics and high doses of steroids. One week prior to admission to our institution, she developed bilateral proptosis and intractable pain. She was referred to our institution for further evaluation and treatment.

On examination she had bilateral proptosis with severe periorbital edema and erythema with conjunctival hyperemia and chemosis. She was unable to open her eyes. Her visual acuity was counting fingers OU, but this could not be assessed reliably because of poor patient cooperation due to extreme pain. Extraocular motility was markedly limited in all fields of gaze bilaterally. The pupils measured 2 mm bilaterally with normal pupillary light reaction. Additional magnetic resonance images of the brain and orbits were obtained. Compared with the magnetic resonance images obtained 1 week earlier, there was now involvement of the right cavernous sinus (Figure 1). Proposis of both globes with reticulated abnormal enhancement of the retrobulbar fat in both or-
bits was also noted. There was shaggy enhancement involving the optic nerve sheaths and the walls of the enlarged superior ophthalmic veins (Figure 2). The paranasal sinuses were clear. Magnetic resonance angiography revealed diffuse narrowing of the petrous, cavernous, and supraclinoid segments of the left carotid artery. The most likely diagnosis based on the clinical findings and imaging studies was cavernous sinus thrombosis, secondary to an infectious or inflammatory process. The differential diagnosis included orbital apex syndrome caused by an infectious process such as mucormycosis or a fungal species; inflammatory processes, including Tolosa-Hunt syndrome; primary or metastatic malignancy; vasculitis; hypercoagulative states; and granulomatous diseases, including sarcoidosis.

The patient was afebrile with a white blood cell count of 18,000/µL. On the day of admission, she underwent a bifrontal craniotomy and decompression of the left optic nerve within the bony canal. Culture and biopsy specimens were obtained from the orbits and cavernous sinus. Intraoperative findings were remarkable for pale, firm orbital fat with multiple adhesions and considerably swollen and tense periorbita on the left side. No frank pus was seen. Frozen section examination findings from the left orbital fat biopsy revealed an acute inflammatory infiltrate with numerous neutrophils and scattered lymphocytes and macrophages without serious vasculitis. Gram stain showed gram-positive cocci. Postoperatively, the antibiotic regimen was changed to intravenous vancomycin hydrochloride, ceftriaxone sodium, and clindamycin empirically.

Physical examination findings remained the same during the first postoperative day. Visual acuity was counting fingers OU. Two days after surgery, the patient had no light perception bilaterally. Fundus examination findings were normal without disc edema. During the first postoperative week, she showed clinical improvement with marked decrease in proptosis, periocular edema, and chemosis. Right optic disc edema was noted 5 days postoperatively. Histopathological analysis of the surgical specimens revealed septic thrombosis in the left orbital fat and acute inflammation with numerous neutrophils and scattered lymphocytes and macrophages in dura of the cavernous sinus. The specimen from the right orbital fat showed fat necrosis. No granulomatous, primary vasculitic, or neoplastic process was noted. Findings on chest radiography and cardiac echocardiography were within normal limits. Results of a workup for hypercoagulability and antineutrophil cytoplasmic antibodies were negative. Culture specimens from the left orbit grew F nucleatum and rare α streptococci 7 days after the operation. The F nucleatum culture results were sensitive to clindamycin. Blood culture findings remained negative during the entire follow-up. Panorex dental radiography revealed localized periodontal erosive changes with loss of the bony root of the right mandibular canine tooth. The patient was treated with intravenous clindamycin for 1 more week and was discharged after 2 weeks of hospitalization. At the time of discharge, the periorbital edema, erythema, and chemosis were totally resolved with minimal residual bilateral proptosis. Ocular motility was within normal limits bilaterally. Visual acuity remained no light perception with nonreactive, dilated pupils bilaterally.

Comment. Fusobacterium nucleatum can form aggregates with other bacteria in periodontal diseases and can behave synergistically with other bacteria in mixed infections. Devitalized tissue may provide a suitable environment for the growth of these organisms. The production of proteolytic enzymes by Fusobacterium organisms may allow for invasion of regional veins, even without tissue necrosis.

Fusobacterium nucleatum was reported to be associated with gingivitis, periodontal disease, abscesses, and venous thrombosis in various anatomic locations associated with septicemia.1,2 We are unaware of previous reports of septic thrombophlebitis of the orbit and cavernous sinus caused by F nucleatum. Two hypotheses can be considered for the pathogenesis of the thrombophlebitis of the cavernous sinus: (1) recent infection of a preexisting cavernous sinus thrombosis (however, our patient’s hypercoagulopathy study results were normal, and the condition resolved with appropriate antibiotic treatment without anticoagulation); (2) more likely is that the fusobacterial infection arose in the periodontal space and spread secondarily to involve the cavernous sinus and orbits. This latter possibility is supported by the fact that F nucleatum has thrombogenic ability.3 We realize, however, that an infectious process arising primarily in the cavernous sinus cannot be completely excluded.
Cavernous sinus thrombophlebitis can progress very rapidly—often in a matter of hours—and even with appropriate surgical and antibiotic treatment, it can be fatal or result in serious complications. Esardco et al reported a case of orbital cellulitis caused by F necrophorum that required 3 urgent surgical interventions and 30 days of intravenous antibiotic treatment. Despite this intensive treatment, the patient’s vision did not fully recover. Early examination of the patient with only a 1-day history of proptosis may have allowed early diagnosis and treatment and possibly helped to preserve sight.

This case also illustrates the prolonged period that may be required to isolate Fusobacterium organisms. It is therefore imperative that cultures be allowed a prolonged incubation period so that important pathogens are not missed following isolation of rapidly growing pathogens, resulting in inappropriate antimicrobial therapy.

Although rare, F nucleatum can be a cause of severe septic thrombophlebitis of the orbit and cavernous sinus, which, despite intensive treatment, may result in severe morbidity.

Yonca Ozkan Arat, MD
Debra J. Shetlar, MD
James E. Rose, MD
Houston, Tex

The authors have no relevant financial interest in this article.

Corresponding author: Yonca Ozkan Arat Medicine, Scurlock Tower, 6560 Fannin St, Suite 902, Houston, TX 77030.


Orbital Abscess Following Subtenon Triamcinolone Injection

Orbital infections are often associated with pain, erythema, swelling, and warmth of the periorbital tissue and may affect pupillary responses, ocular motility, and visual acuity. The most common cause is sinusitis; however, inoculation as a result of trauma or bacteremia or as an extension from adjacent infected teeth, lacrimal sac, or eyelids has also been described. Abscess formation is a potential complication that often requires surgical drainage in addition to systemic antibiotic therapy. In this report, we describe an orbital abscess that developed following a subtenon injection of triamcinolone acetone without associated signs or symptoms of inflammation.

Report of a Case. We evaluated a 90-year-old woman for a progressively enlarging orbital mass. She had macular edema secondary to a branch retinal vein occlusion in the left eye that was unresponsive to treatment with laser photocoagulation. She subsequently had 2 subtenon triamcinolone injections performed 1 month apart in a standard manner by passing a 25-gauge needle through the superotemporal conjunctival fornix. Three weeks after the second injection, the patient noted a left orbital mass that became progressively larger without any associated pain, discharge, diplopia, or change in visual acuity.

Visual acuity was 20/100 OS. There was a soft, well-demarcated, 2- by 3-cm mass located in the superotemporal left orbit with blepharo-phtosis but no erythema, warmth, or tenderness (Figure 1). Exophthalometry measurements were 21 mm OD and 23 mm OS. The pupil reactions were normal without an afferent defect, and motility was full in all directions of gaze. Funduscopy revealed a laser grid pattern along the superotemporal arcade and macular edema but no optic nerve swelling.

A computed tomographic scan with contrast was obtained and revealed a low-density mass with an enhancing rim just above the lacrimal gland but with no intraconal extension, bone erosion, or paranasal sinus disease (Figure 2). Seven milliliters of green, purulent fluid was removed by fine-needle aspiration. A stab incision was made into the mass, and loculations were disrupted by curettage. A drain was inserted, and the patient was given an oral course of clindamycin hydrochloride because of a previous peni-

Figure 1. Mass involving superotemporal orbit with blepharo-phtosis but no erythema or edema.

Figure 2.