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CLINICAL VIGNETTE

From Botulism to Blindness

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Abstract

We present a patient who was admitted to the hospital with an acute bilateral orbital cellulitis after recent botulinum toxin injection. The infection led to blindness due to corneal sloughing despite aggressive antibiotic treatment with steroids. We propose a mechanism of post-streptococcal syndrome resulting from botulinum injection, which may have triggered these events.

Case Report

A 52-year-old woman presented to the ED with a two-day history of rapidly decreasing visual acuity associated with painful bilateral lower extremity rash and arthralgias. Five days prior, she developed fevers and chills, while gradually developing periorbital swelling. The rash erupted in concert with the eye symptoms, involving localized to her back and lower extremities. She also had a painfully swollen right ankle. Ten days prior to presentation, the patient attended a "Botox Party" in the Philippines. She received botulinum A toxin injections for rhytides around her eyes bilaterally. She reports these injections were administered using a new sterile needle and a new vial. Her husband was the second patient who received similar injections reportedly from the same vial. He denied any symptoms and was at patient's bedside on presentation. The patient denied contact lens use, ocular trauma or instrumentation of the eye, nose, or throat, and denied recent sinus and upper respiratory infections. The remainder of medical history was non-contributory.

On physical exam there was prominent bilateral periorbital swelling causing closure of her eyes and significantly limiting her extra ocular movements. The conjunctiva was markedly injected with opacified cornea and sloughing sclera. Her pupils were non-reactive and cloudy, and she could only detect light. She had a serpeginous erythematous tender macular-papular rash primarily on the medial bilateral lower extremities. Her right ankle was edematous, tender to palpation diffusely, and erythematous. The remainder of the physical exam was unremarkable. The patient was initially treated with intravenous fluids and started on ceftriaxone,

doxycycline, and vancomycin covering most gram-positive, and gram-negative bacteria.

Lab analysis revealed a white blood cell count of 39.7 with a left shift. The erythrocyte sedimentation rate was markedly elevated at >130 and c-reactive protein was elevated to 198. Chest film was normal, and CT scan of the brain showed evidence of bilateral post-septal cellulitis. The MRI study of her head and face showed enhancement of the choroid, abnormal soft tissue around the globes with intraconal fat stranding and enhancement that extended along the optic nerve sheaths, consistent with an infectious etiology.

An extensive infectious disease work-up was performed, with a positive beta hemolytic streptozyme test, positive antistreptolysin O titer (ASO) of 783, and antideoxyribonuclease-B titer (anti-DNase B, or ADB) positive at >1000. Vitreous culture was positive for Group A, beta hemolytic streptococcus. However, all bacterial, viral, and fungal cultures of the throat, blood, and urine were repeatedly negative. An autoimmune workup was negative. Methylprednisolone was started on hospital day #14 to decrease orbital swelling. On day #19 her left cornea ruptured requiring emergent conjunctival patch surgery. She was continued on intravenous steroids and antibiotics with minimal response to the inflammatory process or improvement in ocular symptoms. She was discharged with plans for a corneal transplant, pending resolution of the inflammation.

Discussion

This case of apparent post-streptococcal uveitis is unique, not only for its rarity (some 30 cases have been reported¹), but also because of the novel possible mechanism of streptococcal infection. It serves as reminder that routine procedures always carry the risk of inciting pathogenesis. Without a history of a prior strep infection or sinus disease, the most plausible sequence of events is the introduction of group A, beta-hemolytic strep (*streptococcus pyogenes*) into the bilateral pre-septal areas during injection of botulinum toxin. This initial infection

could have triggered an acute post-streptococcal syndrome, leading ultimately to corneal melt and bilateral blindness.

The uveitis and concurrent presentation with fever, rash, and arthralgias are consistent with post-streptococcal syndrome, however the bilateral orbital cellulitis and strep-positive vitreous culture are not. Orbital, or post-septal, cellulitis is more aggressive than peri-orbital (pre-septal) cellulitis. It presents classically with a unilateral, painful, swollen eyelid, proptosis, conjunctival chemosis, limited eye movement, pupillary defects, color vision impairment, and decreased visual acuity. Sixty to 80% of cases of orbital cellulitis arise from sinusitis, but can also occur after surgery, trauma, or from the progression of pre-septal cellulitis. Staphylococcus and Streptococcus are the most frequent pathogens in adults, and orbital cellulitis is most common between November and December². Bilateral orbital cellulitis is very rare, but has been reported after strabismus surgery when an underlying sinus infection was present³. A case of bilateral MRSA (methicillin-resistant staph. aureus) orbital cellulitis was reported after a patient lanced a pustule on his nose. He presented two days later with fevers, chills, and a leukocyte count of 24,000. Blindness ensued despite aggressive treatment with antibiotics and steroids, due to retinal and optic nerve infarction⁴.

Group A streptococcus is a gram positive bacteria with certain cell wall proteins that appear to cause post-infection inflammation⁵. Purified streptococcal M protein has been shown to induce non-immune human T cells to proliferate, making it a "superantigen"⁶. The theory of "molecular mimicry" stipulates that similarities between M proteins and host proteins can activate T cells which now have a specificity for self-antigens⁷. Injecting rabbits with streptococcal wall fragments resulted in joint disease⁸, while intravitreal injection of peptidoglycan-polysaccharide complexes from group A streptococci caused chronic intraocular inflammation⁹. Later work proved immune cross-reactivity of several of the more than 80 M proteins with human retina proteins, including a uveitogenic retinal antigen that reacted with anti-streptococcal M antibodies¹⁰. The exact proteins and mechanisms involved in post-streptococcal syndrome, including poststrep uveitis, have not been determined⁴. Individual leukocyte haplotypes, the virulence of the pathogen and the location of immune complex deposition may determine the specific features of the syndrome. The ocular manifestations are variable, and include conjunctival hyperemia, anterior scleritis,

corneal precipitates, choroiditis, and retinal involvement¹.

Most cases of post-streptococcal uveitis resolve uneventfully with intense topical steroid therapy, although vitritis, retinitis, and glaucoma are not unusual⁴. We found only one other case of post-streptococcal uveitis progressing to a necrotizing anterior scleritis, though it did not progress to perforation. The reported patient did not have ocular involvement until more than a month after she presented with Streptococcal Toxic Shock Syndrome with positive blood cultures, multi-organ failure, and eventual necrotic vasculitis requiring multiple limb amputations¹.

Our patient presented with clear evidence of streptococcal infection by ASO and ADB titers, 36,000 white count, and positive vitreous culture. The positive vitreous culture and bilateral orbital cellulitis, with negative blood and throat cultures suggest that the initial infection was localized to the eyes or orbits, and the history of recent needle injection in the area is the most likely explanation.

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