Orbital Polymyositis and Giant Cell Myocarditis

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Background: Orbital polymyositis associated with giant cell myocarditis rarely has been reported in the literature. The authors report the clinical, neuroradiographic, and histopathologic features of the only patient to survive this usually fatal syndrome after cardiac transplantation.

Findings: This 22-year-old white woman presented in 1991 with periorbital redness, swelling, and pain in both eyes that was unresponsive to antibiotic therapy. Results of her examination were significant for limited extraocular movements, ptosis, erythema, edema, chemosis, and exophthalmos. Electrocardiogram and chest x-ray were normal. Orbital computed tomographic scan showed swelling of the extraocular muscles up to and including their insertions. The patient was given the diagnosis of orbital polymyositis and her condition improved clinically and radiographically while taking parenteral steroids. One month after discharge, the patient was in cardiogenic shock. Endomyocardial biopsy showed giant cell myocarditis, and the patient underwent emergent cardiac transplantation. Despite a complicated postoperative course, the patient has done remarkably well.

Conclusion: Although this disorder is rare, this case suggests the need for a high index of suspicion for giant cell myocarditis in patients with inflammatory orbital polymyositis. In non-Graves orbital polymyositis the patient should be questioned and instructed concerning the signs and symptoms of congestive heart failure. Chest x-ray, Holter monitoring, and electrocardiogram also should be performed and be repeated with an echocardiogram if there are any cardiac symptoms. In addition, early endomyocardial biopsy should be considered in the proper clinical setting, allowing timely diagnosis and expeditious cardiac transplantation.

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The association of giant cell myocarditis with orbital polymyositis is, indeed, a rare disorder. To our knowledge, there have been only two1,2 such cases reported in the literature. Because of the lethal nature of giant cell myocarditis, there is need to exert extra caution when dealing with patients who have orbital polymyositis in the absence of Graves disease.

Case Report

A 22-year-old white woman was admitted to Columbia-Presbyterian Medical Center on September 16, 1990, with a 3-week history of periorbital redness, swelling, itching, and pain on extraocular movement in the right eye which was greater than in the left. Six days before admission, she was seen by a local pediatrician who initiated warm soaks and cefadroxil (Duricef) (500 mg orally twice daily). The next day, her symptoms worsened; the tense right upper lid was drained unsuccessfully, and the left upper lid was injected with triamcinolone. The antibiotic was changed to amoxicillin (500 mg orally 3 times daily). Two days before admission, she felt better, but by the day of admission fever, right leg tenderness, diffuse periorbital pain, proptosis, conjunctival injection, and pain in adduction developed. She became dizzy and weak and was brought to the emergency room. Her medical history was significant for asthma, vitiligo, and multiple food allergies.

On admission, her oral temperature was 37.5°C. The infectious disease service was consulted, and bilateral orbital cellulitis
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Figure 1. Initial clinical presentation demonstrates marked ptosis, moderate lid erythema and edema, and exophthalmos in the right eye which was greater than in the left eye.

was suggested. Oxacillin (2 g intravenously every 4 hours) and ceftazidine (1 g intravenously every 8 hours) were initiated. High-resolution orbital computed tomography (CT) was ordered, and the ophthalmology service was consulted.

On bedside examination, her near visual acuity was 20/30 in the right eye and 20/20 in the left at 14 inches. The pupils were equal and reactive to light and accommodation. There was no relative afferent pupillary defect. Color vision by American Optical Hardy Rand Ritter Color Plates was 3.5/6 in the right eye and 2/6 in the left. The extraocular movements were painful and limited to 1 mm in all fields of gaze in the right eye greater than the left.

Results of the external examination showed ptosis, moderate erythema, edema, mild chemosis, and exophthalmos in the right eye greater than the left (Fig 1). The corneas were clear, and anterior chambers were deep. The intraocular pressure and results of the funduscopic examination were normal.

Orbital CT scans showed moderate preseptal swelling and swelling of the extraocular muscles up to and including their insertions as seen on the axial views (Fig 2). The muscles, particularly the right and left medial recti, have a tapering outline, with the greatest swelling seen in the middle of the muscle but with some extension of the swelling into the muscle insertions. The right lateral rectus is the exception, having a uniform degree of swelling throughout. Coronal views showed enlargement of all of the extraocular muscles in both eyes (Fig 3).

Laboratory investigation showed a leukocyte count of 15,000 with 58% neutrophils, 2% bands, 1% metamyelocytes, 19% lymphocytes, 8% monocytes, and 12% eosinophils. The erythrocyte sedimentation rate was 3 mm/hour. The creatinine phosphokinase was 197 U/l (normal, 1–50 U/l). Thyroid function studies were within normal limits. Anti-thyroglobulin antibody, anti-microsomal antibody, antinuclear antibody, latex fixation, antidi­double-stranded DNA antibody, and lupus anticoagulant were negative. Serum electrophoresis showed an increase in the alpha 1 and alpha 2 fractions. Total hemolytic complement was within normal limits. Cultures of the eyelids, conjunctivae, blood, and urine were negative. No parasites were detected in the stool, and Lyme, Trichinella, and Toxoplasma gondii titers were negative. Electrocardiogram and chest x-rays were normal.

In view of the CT and laboratory findings, the diagnosis of orbital polymyositis was made, and the patient was given a total of 400 mg parenteral methylprednisolone over 3 days with marked improvement clinically and radiographically (Fig 4). Her medication then was switched to oral prednisolone (80 mg daily), and she was discharged 1 month after admission with a tapering regimen.

Figure 2. High-resolution orbital computed tomographic scan in axial projection shows moderate preseptal inflammation and swelling of the extraocular muscles up to and including the insertions.

Figure 3. High-resolution orbital computed tomographic scan in coronal projection shows inflammation of all of the extraocular muscles in both eyes.
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In mid-October 1990, an exotropia of 18 prism diopters developed. Palpebral fissures measured 5 mm in the right eye and 4.5 mm in the left, with levator function measuring 7 and 10 mm, respectively. The exotropia increased to 45 prism diopters by mid-November. Exophthalmometry readings measured 19.5 mm in the right eye and 20.5 mm in the left at a base of 106 mm.

One month after discharge, the patient was in cardiogenic shock. The echocardiogram showed global hypokinesis (Fig. 5). Viral titers for cytomegalovirus, Epstein-Barr virus, Mycoplasma, and coxsackievirus were negative. An endomyocardial biopsy showed evidence of muscle necrosis, and one half of the specimen was infiltrated with lymphocytes, monocytes, numerous eosinophils, and prominent multinucleated giant cells (Fig 6). Histologic features were compatible with giant cell myocarditis.

The patient failed to respond to immunosuppressive therapy, including high-dose steroids, cyclosporine, and azathioprine. After 1 week, she underwent cardiac transplantation. Her post-operative course was complicated by a duodenal ulcer, Salmonella sepsis, and cardiac rejection despite high doses of steroids and cyclosporine. In January 1991, she started taking FK-506 and has done remarkably well. Her last examination was on January 20, 1993. She currently is taking FK-506 orally twice daily, prednisolone (5 mg orally twice daily), ciprofloxacin (orally every day), ranitidine (orally every day), calcium (Oscar-cal) (orally every day), and multiple vitamins. Her best-corrected visual acuity is 20/20 in both eyes. Results of the neuro-ophthalmic examination are within normal limits. Results of the slit-lamp examination show early posterior subcapsular cataracts. The intraocular pressure and results of the dilated fundus examination are normal.

Results of recent laboratory studies are normal, including a negative test for anti-acetylcholine receptor antibodies.

Discussion

The association of orbital polymyositis and giant cell myocarditis has been presented in two isolated case reports in the literature.1,2 Klein et al2 and Kattah et al3 have described two women with orbital myositis in whom fatal cardiac arrhythmias later developed. At autopsy, both patients were found to have a giant cell myocarditis identical to that seen in our patient. Biopsy of extraocular muscles in the patient described by Klein et al2 showed minimal extraocular muscle inflammation and no giant cells, whereas extraocular muscle biopsy done in Kattah et al’s2 patient showed intense mononuclear cell inflammation with giant cells. The differences in the histology of the extraocular muscles in these two patients suggest that they were at different stages of the same pathologic process.

Giant cell myocarditis is a rare, idiopathic, and usually fatal syndrome that can either cause sudden death or rapidly progressive congestive heart failure and arrhythmia.3,4 Unless endomyocardial biopsy is performed, giant cell myocarditis usually is diagnosed at autopsy. Histopathologically, there is a mononuclear cell infiltration accompanied by multinucleated giant cells and myocyte necrosis, with areas of myocyte regeneration and fibrosis.5

There is considerable debate in the literature about the origin of the giant cells in giant cell myocarditis. It has been argued that the giant cells are derived from myocardial fibers either as a result of degeneration or regeneration3,6,7 or from histiocytes.8,9 Features that suggest a myogenic derivation include a smooth transition between giant cells and the myocardium, direct contact between giant cells and myofibrils and lipofuscin granules within the giant cells.4 Other studies using immunohistochemical techniques maintain that the giant cells arise from histiocytes and are therefore inflammatory in nature. Theaker et al demonstrated positive staining of giant cells with monoclonal antibodies EBM11 and KB90, which are specific macrophage markers not found on myocytes. They also found negative staining for desmin, a myocyte marker, on the giant cells.8 In a similar manner, Hales et al9 demonstrated positive staining of giant cells with monoclonal antibodies to MAC387, another specific macrophage marker.

The differential diagnosis of idiopathic giant cell myocarditis includes infection with spirochetes, fungi, my-
Figure 6. Cardiac muscle demonstrates the cardinal histologic features of giant cell myocarditis, including extensive myocyte damage with replacement by granulation tissue and marked mononuclear cell infiltration with multinucleated giant cells (arrows) (hematoxylin-eosin, X200).

cobacteria, foreign body reaction, and sarcoidosis. In our patient, no infectious agent was isolated from the myocardium, making infection unlikely. Differentiating cardiac sarcoidosis from giant cell myocarditis can be difficult to impossible if no lung manifestations of sarcoidosis are present. In our patient, sarcoidosis was unlikely in view of her normal chest x-ray and normal angiotensin-converting enzyme level.

Because giant cell myocarditis has been found in association with different autoimmune conditions such as thymoma, myasthenia gravis, systemic lupus erythematosus, dermatomyositis, ulcerative colitis, thyroid disease, and pernicious anemia, it has been postulated that giant cell myocarditis may arise from an organ-specific autoimmune response. Namba et al noted that the autoimmune conditions associated with giant cell myocarditis often precede the myocardial manifestation by many years. Humbert et al reported a man with ulcerative colitis, by use of immunofluorescence techniques, to have both immunoglobulins in the myocardium and circulating specific antimyofibril antibodies. The presence of anti-heart antibodies, however, does not necessarily establish an autoimmune basis for the condition. Our patient had a history of vitiligo, a disease that is thought to have an autoimmune basis, lending more credence to the association of giant cell myocarditis with autoimmune diseases.

Computed tomography and magnetic resonance imaging permit the identification of the anatomic nidus primarily involved in idiopathic inflammation, and consequently, the antiquated term pseudotumor has been supplanted by orbital myositis, dacryoadenitis, perineuritis, scleritis, and lymphoid hyperplasia. The radiographic and clinical separation of these entities is not artificial. Neither are they necessarily the clinical expression of the identical inflammatory process, in that they differ in their clinical response to one mode of therapy.

Several radiographic features have emerged for each entity. In orbital myositis, and as was observed in our patient, one sees diffuse enlargement of one or more extraocular muscles with extent up to and including the muscle insertion. This is in contrast to the true taper of Graves orbitopathy in which the muscle insertion is spared. Alteration of the orbital fat lucency also is seen in orbital myositis, and spill-over onto the globe may give a positive ring sign. Unique to the myositis seen in association with myocarditis, every extraocular muscle was involved, including the obliques. Nonspecific radiographic signs include occlusive and constrictive changes in the proximal segment of the superior ophthalmic vein when venography and magnification arteriography are used.

Neuroradiographic imaging generally is confirmatory and orbital biopsy, therefore, unnecessary. Orbital myositis is notable for chemosis, proptosis, bulbar pain, episcleral injection of the involved muscle(s), unimpaired vision, and rapid and dramatic response to corticosteroid treatment. Orbital myositis generally is idiopathic, although a case has been reported in association with Lyme disease.

Myasthenia gravis rarely causes inflammation of muscles. Russell described lymphocyte infiltration into extraocular muscles along with skeletal muscle fiber necrosis and inflammatory myocardial fiber necrosis and phagocytosis without giant cells in several patients with myasthenia gravis and thymoma. Burke et al reported giant cell myocarditis and skeletal myositis in a patient with myasthenia and malignant thymoma. Extraocular muscles were involved clinically but were not examined histologically. In our patient, there was no evidence of thymoma radiographically. In addition, serologic testing failed to demonstrate anti-acetylcholine receptor antibodies.

Graves disease can cause progressive myocarditis and skeletal myositis in conjunction with extraocular muscle infiltration. One case has been reported in which both the heart and skeletal muscle contained giant cells. The clinical, laboratory, and radiographic findings in our patient are not consistent with Graves disease.

Both polymyositis and dermatomyositis can cause ophthalmoplegia and ptosis. However, granulomatous inflammation with giant cells are not present in the myocardium.
Although an extraocular muscle biopsy was not performed in our patient, it is clear that our patient, and those described by Klein and Kattah, represent three reports of idiopathic orbital polymyositis with associated giant cell myocarditis. Although this disorder is rare, these three cases indicate the need for a high index of suspicion for giant cell myocarditis in patients who present with inflammatory orbital panmyopathy, particularly in association with eosinophilia. We suggest that in non-Graves orbital polymyositis the patient be questioned and instructed concerning the signs and symptoms of congestive heart failure. Chest x-ray, Holter monitoring, and electrocardiogram should be performed and be repeated together with an echocardiogram if there are any cardiac symptoms. In addition, early endomyocardial biopsy should be considered in the proper setting, allowing timely diagnosis and expeditious cardiac transplantation.

References