

Relapsing migratory idiopathic orbital inflammation: six new cases and review of the literature

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ABSTRACT

Aims To present a case series of relapsing migratory idiopathic orbital inflammation.

Patients and methods Case series and review of the literature. The medical records of six patients with recurrent orbital myositis or idiopathic inflammation at different sites treated at the Goldschleger Eye Institute between April 2006 and December 2009 were collected and analysed; one patient treated at the orbital service in Priyamvada Birla Aravind Eye Hospital, Kolkata, India, was also included (June 2008 to August 2010). Orbital biopsy was performed in patients who failed to respond to steroids treatment.

Results A total of six patients with recurrent episodes of orbital myositis or inflammation were identified. Four patients had orbital myositis of one extraocular muscle at the initial episode and recurrent myositis of a different extraocular muscle on the contralateral orbit. One patient had recurrent myositis of a different extraocular muscle on the same orbit. Two patients had a third episode of recurrence on a different site, that is, an extraocular muscle or an eyelid. One patient had eyelid and soft tissue involvement on one orbit and recurrence of orbital myositis on the contralateral eyelid. Histological findings in the latter case showed small perivascular lymphocytic aggregates and scattered histiocytes. The mean time for recurrence was 7.2 months. All patients were treated successfully with oral steroids and/or intralesional triamcinolone injection.

Conclusions Idiopathic orbital inflammation or orbital myositis can recur on a different extraocular muscle and on the contralateral orbit. These cases can be successfully treated with orally administered or intralesionally injected steroids.

INTRODUCTION

Idiopathic orbital inflammation (IOI) refers to benign non-infective inflammatory conditions of the orbit without any identifiable local or systemic cause.¹ Onset is generally acute or subacute and may be focal (myositis, dacryoadenitis, anterior or apical) or diffuse. After thyroid-related orbitopathy and lymphoproliferative disease, IOI is the third most common cause of orbital inflammation, accounting for up to 6.3% of all orbital diseases.² Its aetiology is unknown, whereupon its diagnosis is one of exclusion.

The mainstay initial therapy for acute or subacute IOI is oral corticosteroids with slow tapering down. Diagnosis of IOI includes a meticulous physical exam, blood tests including CBC and a systemic work-up in order to rule out other conditions that mimic IOI, but a dramatic clinical response to medication supports the diagnosis.^{1–3} Low-dose radiotherapy has been successful in many

cases of recurrent myositis. Immunomodulatory agents have also been variably useful for treating IOI³ and intraorbital injection of steroids was described as another effective treatment.⁴

Orbital myositis is one of the acute presentations of IOI. It is an inflammatory process that primarily involves the extraocular muscles and most commonly affects young adults in the third decade of life, with a female predilection. Clinical characteristics of orbital myositis include orbital and periorbital pain, ocular movement impairment, diplopia, proptosis, swollen eyelids and conjunctival hyperaemia. The most common presentation is acute and unilateral, which initially responds to systemic corticosteroid therapy, although chronic and recurrent cases may involve both orbits. Many inflammatory, vascular, neoplastic, and infectious conditions that affect the extraocular muscles and other orbital tissue can mimic orbital myositis. The most important differential diagnoses include thyroid-related eye disease, other orbital inflammatory processes (unspecific idiopathic inflammation, vasculitis, and sarcoidosis), orbital cellulitis and orbital tumours. Steroid-sparing agents, immunosuppressants or radiation therapy may be indicated in refractory, chronic or recurrent cases.²

The purpose of the current paper is to describe a group of patients with relapsing attacks of migratory IOI who presented with each involvement in a different location in the same or fellow eye. The most common presentation was orbital myositis.

METHODS

Medical records of six patients with recurrent orbital myositis or idiopathic inflammation at different sites were collected and analysed. Five patients were treated at the Goldschleger Eye Institute between April 2006 and December 2009; one patient was treated in the Oculoplastics Orbital Services, Priyamvada Birla Aravind Eye Hospital, Kolkata, India, between June 2008 and August 2010. Data regarding symptoms on presentation, presence of double vision, results of complete eye examination and imaging studies (CT/MRI) and histology (in one patient) were retrieved and analysed.

The study was approved by the local institutional review board, Sheba Medical Center, Tel Hashomer hospital.

RESULTS

Six patients diagnosed as having IOI were the subjects of our study. They all had an unusual presentation of migratory IOI. None of them had a history of thyroid disease or trauma and there were no signs of infection, neoplasm or collagen disease.

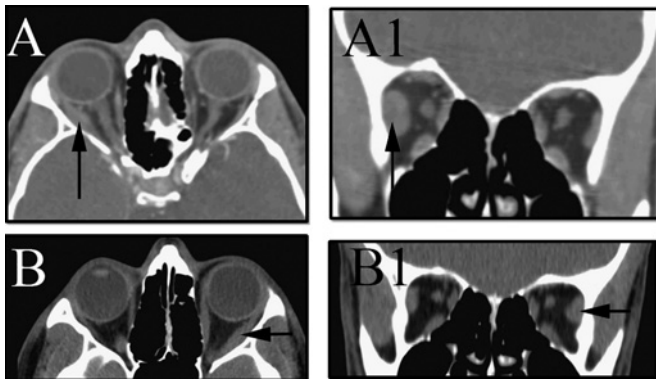


Figure 1 Patient 1—Axial CT scans of the orbit during the first episode of myositis showing right lateral rectus enlargement: (A) axial scan; (A1) coronal scan (vertical black arrows). Lower images showing CT scan of the orbit during the second relapse involving the left orbit: (B) left lateral rectus enlargement axial scan; (B1) left lateral rectus enlargement coronal scan (horizontal black arrows).

The first patient was an 18-year-old boy who was referred to our outpatient clinic complaining of right eye pain with diplopia on left gaze. On examination, there was limited adduction of his right eye. The CT scan showed enlargement and infiltration of the right lateral rectus muscle (figure 1A,A1). He was treated with 60 mg oral prednisone (his weight was 55 kg) for 3 days with a tapering down of 10 mg every 3 days. He completed his treatment course after a month. He had rapid resolution of all symptoms within days. Two months later, he presented with complaints of left eye pain with diplopia. On examination, both eyes showed full motion range and an altogether normal ocular exam. The CT scan showed enlargement and infiltration of the left lateral rectus muscle (figure 1B,B1). A second course of oral steroids, 40 mg with the same protocol of tapering down, resulted in rapid resolution of symptoms. The patient did not have any adverse events during the treatment course of steroids. The next follow-up was 3 months later with a new CT scan.

The second patient was a 17.5-year-old girl who was suffering from recurrent episodes of IOI. The first episode involved the superior rectus muscle of the left eye. She was treated with oral steroids that led to resolution of symptoms. Seven months later, she experienced an episode of inferior rectus muscle myositis of the right eye, with resolution of symptoms following oral steroid treatment. She presented to our clinic for the third time 1 year later complaining of left eye orbital pain with left lower

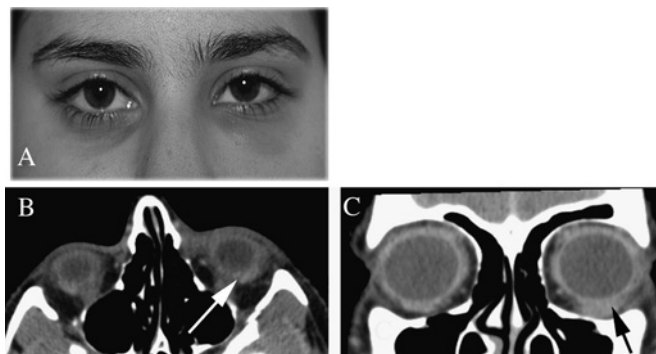


Figure 2 (A) Clinical image of patient 2 showing left lower eyelid redness and swelling. (B & C) CT scan images of patient 2 (axial and coronal sections, respectively) showing the inferior orbit soft tissue involvement (arrow).

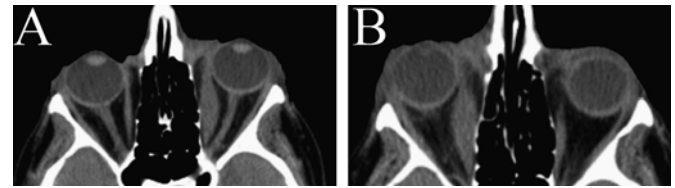


Figure 3 Patient 3—(A) Axial CT scan of the orbit showing the left medial rectus enlargement. (B) Second relapse occurred in the right medial rectus.

lid oedema. The ocular examination was unremarkable except for left lower eyelid swelling (figure 2A). A CT scan showed lower eyelid swelling and orbital fat infiltration of the left eye (figure 2B,C). She was again treated with oral steroids with complete resolution of symptoms. Her estimated weight was between 40 and 50 kg; therefore, the steroid dose prescribed was 40 mg/day for 2 weeks with tapering down of 10 mg/day every week. She had no adverse events during the treatment. She was examined in our oculoplastic department on a weekly basis. Three months after resolution of symptoms a repeated CT scan was performed.

The third patient was a 51-year-old woman who presented to our outpatient clinic complaining of left periorbital swelling. She had no complaints of pain or diplopia. CT scans showed oedema and infiltration of the medial rectus muscle (figure 3A). All the symptoms resolved following oral 80 mg/day prednisone treatment with a tapering down protocol of 10 mg/day for a week. She had no adverse events during the treatment. Seven months later, she suffered a second episode, this time presenting as right eye eyelid swelling. She had no diplopia, only pain on eye movements. Upon examination, there was full ocular motion without proptosis. CT scans showed right medial rectus infiltration (figure 3B). Clinical improvement was achieved by oral steroids at a dose of 80 mg/day for 3 days and then a tapering down protocol of 10 mg/day every 3 days until completion of the treatment. She was followed at first every week at our clinic and later on every 3 months.

The fourth patient was a 62-year-old man with a past ocular history of optic nerve fenestration in both eyes due to idiopathic intracranial hypertension 17 years earlier. He now presented to our clinic with periorbital swelling of the left eye. The ocular examination was normal except for chronic optic disc swelling of both eyes. CT scans revealed soft tissue swelling of the left eye (figure 4). Steroid treatment in a dose of 80 mg/day for 3 days and then a tapering down protocol of 10 mg/day every 3 days until completing the treatment led to partial clinical improvement. Three weeks later, he returned with bilateral eyelid swelling, and the CT scans demonstrated preseptal infiltration on the left upper lid. He underwent biopsy of the lesion with triamcinolone acetonide injection (40 mg in 1 cc) to the upper eyelid, and the histological results showed small perivascular lymphocytic aggregates (immunostains B and T) and scattered histiocytes. The right eye upper lid swelling resolved without

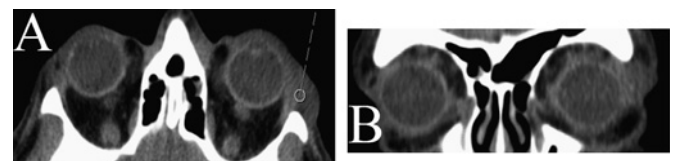


Figure 4 Patient 4. CT axial (A) and coronal (B) scans showing soft tissue swelling of the left eye.

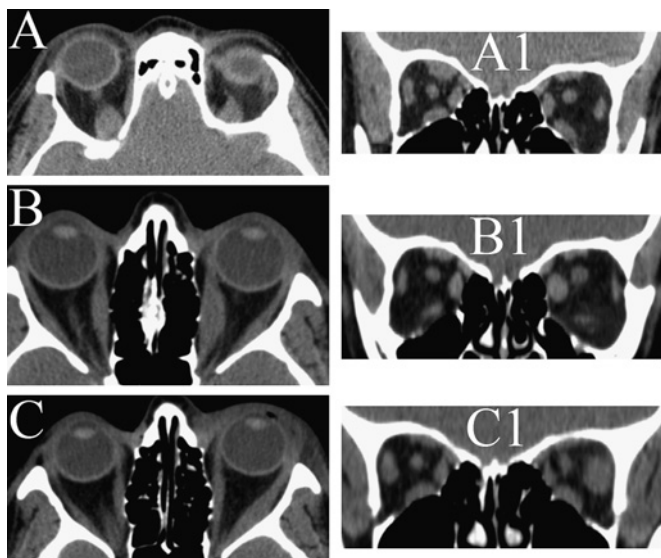


Figure 5 Patient 5—CT axial (A) and coronal (A1) scans showing enlarged superior muscle with tendon sparing of the right eye. (B/B1) Second relapse involved left medial rectus enlargement as demonstrated by CT imaging. (C/C1) Third relapse occurred in the left lateral rectus muscle.

treatment several days later. He had no adverse events during the treatment.

The fifth patient was a 46-year-old woman who presented to our clinic with right upper eyelid swelling and complaints of pain and diplopia upon ocular movements, especially on downward gaze. CT scan of the orbits showed a right enlarged superior rectus muscle with tendon sparing (figure 5A/A1). She was treated with oral steroids (40 mg/day with a tapering down of 5 mg every week) that led to dramatic improvement of her symptoms within 2 months. One month later, she returned complaining of left upper eyelid swelling with horizontal diplopia. Her ocular movements were normal. This time, the CT scan showed left medial rectus muscle enlargement (figure 5B/B1). She was again treated with a course of prednisone (40 mg/day—for 3 days and then tapering down of 10 mg/day every 3 days) that produced rapid resolution of symptoms. Five months later, she had a third episode of myositis with a similar presentation of ocular pain on left eye movements. On examination, she had a mild limitation of upgaze. The CT scan showed left lateral rectus muscle enlargement (figure 5C/C1). Thyroid function

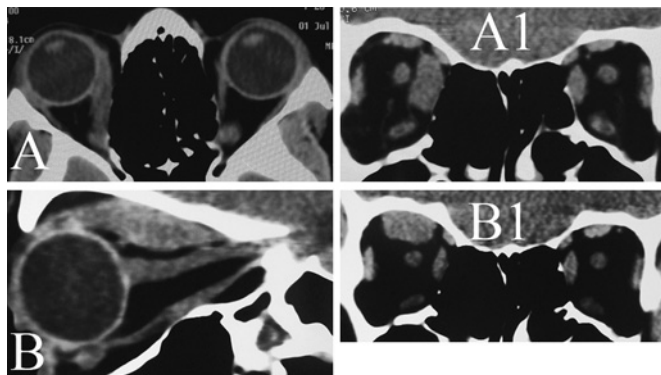


Figure 6 Patient 6—CT axial (A) and coronal (A1) scans showing an enlarged tendon involving right medial rectus muscle. (B/B1) Second relapse involved the right superior rectus muscle enlargement as demonstrated by CT imaging.

tests were normal. All the optic symptoms resolved following oral prednisone treatment (the same protocol as the second episode). After tapering down of the steroids, she complained of right ocular pain accompanied by periorbital oedema and conjunctival chemosis. She was started on methotrexate treatment 2.5 mg×3 weeks under which she did not have any further episodes of orbital inflammation. The patient did not have any adverse events to methotrexate. She was under the care of an internist because she was suffering from psoriasis.

The sixth patient was a 26-year-old Indian woman who presented to the orbital clinic with complaints of swelling of the right upper lid, congestion of the right eye with associated pain and binocular diplopia on left lateral gaze of 9 days duration. Visual acuity was 20/20 in both eyes. Examination showed a sectorally congested, slightly chemosed bulbar conjunctiva on the nasal side of the right eye. Adduction of the right eye was restricted. Resistance and tenderness were elicited on retro-pulsion of the globe. On CT imaging, the right medial rectus muscle was seen to be thickened throughout (belly and tendon involvement) (figure 6A,A1). A detailed work-up for possible systemic disorders causing orbital inflammation did not reveal any abnormality. She was treated with oral corticosteroids starting at 60 mg/day tapered 5 mg weekly with complete clinical recovery in 6 weeks. Two years later, the patient reported back at the clinic with complaints of pain in the right eye on inferior gaze with tender swelling of the right upper eyelid and the eyebrow region of 3 days' duration and binocular diplopia on inferior gaze of 1-day duration. There was no associated visual dysfunction. Clinical evaluation showed a moderately swollen, tender right upper eyelid with sulcus fullness. Unlike in the first episode, ocular movements were unrestricted in the affected eye at presentation. The rest of the clinical and systemic evaluation was unremarkable. Within the first week after presentation, however, the patient reported increased severity of diplopia and developed restriction of elevation of the affected eye. On CT imaging, the right superior rectus muscle was seen to be thickened along its entire length (figure 6B,B1). Complete regression of thickening of the medial rectus muscle (involved in the first episode) was noted. She was started on a slowly tapered course of oral corticosteroids (starting at 60 mg/day tapered 5 mg weekly) and responded dramatically to the treatment with complete regression of clinical symptoms and signs in 9 weeks.

The prednisone tapering down protocol was different for each patient. We followed a treatment protocol of prednisone 1 mg/kg with a tapering down pace of 10 mg every 3–7 days determined by the severity of clinical findings. The rationale was to taper

Table 1 Demographic data of the five patients with migratory orbital inflammation who presented to the Goldschleger Eye Institute, Sheba Medical Center (2006–2009) and one Indian patient (2008–2010)

| Case # | Pain | First episode | Second episode | Third episode | Time to first recurrence | Time to second recurrence |
|---------|------|---------------|----------------|---------------|--------------------------|---------------------------|
| 1 | + | RRL† | LLR† | | 2 months | |
| 2 | + | LSR | RIR | LLL | 7 months | 1 year |
| 3* | – | LMR | RMR | | 7 months | |
| 4* | – | LUL | RUL | | 1 week | |
| 5 | + | RSR† | LMR† | LLR† | 1 month | 5 months |
| 6* | + | RMR† | RSR† | | 26 months | |
| Average | | | | | 7.2 months | |

*Periorbital swelling on presentation.

†Diplopia on presentation.

LLL, left lower eyelid; LLR, left lateral rectus muscle; LMR, left medial rectus muscle; LSR, left superior rectus muscle; LUL, left upper eyelid; RIR, right inferior rectus muscle; RLR, right lateral rectus muscle; RMR, right medial rectus muscle; RSR, right superior rectus muscle; RUL, right upper eyelid.

down the steroids faster in the less severe cases with a fast response to therapy, and a slower tapering down in the more severe cases with a slower clinical response to therapy.

The six patients' demographic and clinical data are summarised in table 1.

DISCUSSION

We describe six patients with recurrent episodes of IOI involving mostly the extraocular muscles and soft tissues of the eyelid. All our patients responded well to oral steroids. One patient with eyelid involvement had a biopsy-confirmed diagnosis, while the others had clinical and imaging features that were indicative of orbital myositis. Two patients had a third recurrence, all three at different sites.

IOI, previously referred to as orbital pseudo-tumour, is a general term encompassing all inflammatory diseases that affect some or all of the structures contained within the orbit external to the ocular globe. In rare cases, the areas involved by the inflammatory process may extend beyond the orbit, such as into the cavernous sinus through the orbital apex. Histopathological analysis usually reveals a nonspecific, chronic, polymorphic inflammatory infiltrate, but sclerosing and non-specific granulomatous variants may be seen as well.^{5,6} Perivascular lymphocytic infiltration is described in Graves ophthalmopathy, and perivascular granulomas are described in Wegener's granulomatosis.⁷ We had one patient with eyelid involvement and biopsy-proven inflammation, but his thyroid blood tests were negative and he had no clinical features of thyroid-related eye disease.

Since any of the structures within the orbit may be involved, the presenting symptoms can be quite varied, although pain is often a prominent complaint. Four of our six patients complained of pain on the initial presentation: interestingly, all but one did not have periocular swelling.

Involvement of the extraocular muscles can result in diplopia; however, two patients in our series who did have muscle involvement had no diplopia on presentation. These patients were tested in all gaze directions; also, they did not have a compensatory head posture.

Lacrimal gland involvement often results in painful superior lateral orbital swelling, while generalised orbital tissue involvement may lead to all of the above features in addition to proptosis, chemosis, periorbital or eyelid swelling and, in severe cases, blindness due to optic nerve compression.⁸ IOI is a diagnosis of exclusion based on clinical, radiological and, if necessary, histopathological findings. The role of ocular muscle biopsy should probably be limited to atypical cases or to those unresponsive to steroid therapy, particularly to exclude the presence of a neoplastic process. Differential diagnosis of ocular myositis includes thyroid-associated orbitopathy, the most common cause of orbital disease.^{9–11} Bilateral muscle involvement, including inflammation, oedema and secondary fibrosis, is very common. Bilateral orbital inflammation is described in thyroid ophthalmopathy and in Wegener's granulomatosis.⁷ Imaging reveals fusiform posterior enlargement of extraocular muscles with relative tendon sparing.

The differential diagnosis of IOI is varied. Ocular myasthenia gravis is an isolated eye muscle weakness with blepharoptosis or ophthalmoparesis resulting in diplopia. Tolosa–Hunt syndrome manifests as painful ophthalmoplegia. Multiple combinations of cranial nerve palsies may occur, localising the pathological process to the region of the cavernous sinus/superior orbital fissure. Rare disorders, such as mitochondrial myopathies (the most common of which is late-onset bilateral progressive external ophthalmoplegia), characterised by ptosis and weakness of extraocular

muscles leading to limitation of extraocular movements with relative sparing of downward gaze, can also be misleading.

Orbital infections are included in the differential diagnosis of myositis. The differentiation may be challenging: an acute explosive disease onset, the presence of continuous pain not related to eye movements, and the association of systemic symptoms and ocular involvement point towards an infectious aetiology. Other non-inflammatory conditions that mimic orbital myositis include neoplastic disease and congenital malformations, which may present with variable degrees of proptosis and impairment of ocular movement.

It is well known that IOI tends to relapse after steroids taper. In one Chinese study that followed 209 cases of patients with IOI,¹² the recurrence rate was 41% with a mean follow-up time of 3.4 years. Those authors also found that gender and proptosis were associated with the recurrence of IOI episodes, and that men were more likely to relapse than their female counterparts.¹² Other investigators believe that recurrent episodes whether in the same or different site, could have been due to improper dosage or duration.^{13–15}

Relapsing episodes of IOI in the form of orbital myositis presenting in the same muscle but in the second eye was recently described in a 27-year-old woman who had a 2-week course of acute painful right proptosis with ptosis, medial conjunctival injection and restriction of eye movements, particularly abduction.¹³ One month later, a similar remitting painful proptosis with complete limitation of abduction developed in the fellow eye. CT scanning showed marked contrast enhancement of both medial rectus muscles, documenting the presumptive diagnosis of acute orbital myositis in the second eye.¹⁶

A report of familial incidence of IOI suggests a potential genetic predisposition in the development of orbital myositis. A relapsing episode of IOI was described in one of the family members, with each episode involving a different muscle in the second eye.¹⁷

A recent case report¹⁷ described a 12-year-old boy with bilateral involvement of several individual ocular muscles. The first episode involved the left lateral rectus and the following episode involved the right medial rectus. This boy underwent a biopsy of the extraocular muscle and the results revealed chronic inflammation with no evidence of malignancy. Paediatric IOI is characterised by a number of features that differ from the adult presentation: for example, bilateral manifestation, uveitis, disc oedema and eosinophilia are more common in children.¹⁸

Although orbital biopsy was not performed in five out of our six reported patients, the clinical presentation and imaging studies were typical of the diagnosis and we presumed that our diagnosis was correct and proceeded to administer oral steroids.

In conclusion, the purpose of this paper was to describe a series of patients with relapsing attacks of migratory IOI, each of which presented in a different location in the same eye or in the fellow eye. The most common presentation was orbital myositis.

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Competing interests None.

Ethics approval This study was conducted with the approval of the Sheba Medical Center, Tel Hashomer.

Provenance and peer review Not commissioned; externally peer reviewed.

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