Review Article

Diagnostic and Therapeutic Approaches of Orbital Inflammatory Disease: A Systematic Review

Riffat Rashid[1], Sadia Sultana[2], Farzana Afzal[3], Syeed Mehbub Ul Kadir[4]

Abstract

Background: Orbital inflammatory disease (OID) is a group of disorders characterized by in-flammation in the orbit, which can affect various orbital structures, including the extraocular muscles, lacrimal glands, and orbital fat. One specific subset, pure orbital inflammation, is char-acterized by isolated inflammatory processes within the orbital tissues without the involvement of other systemic or regional disorders. The condition typically presents with symptoms such as pain, proptosis, and diplopia. Early diagnosis and appropriate management are crucial to pre-venting permanent damage to the orbit and maintaining visual function. This review assesses the diagnostic and therapeutic approaches to pure orbital inflammation. The review found that pure orbital inflammation is primarily treated with corticosteroids, which remain the first-line therapy. Relapses may be occured after complete resolution with appropriate steroid therapy. Immuno-suppressive agents are often used to improve outcomes in cases of steroid resistance or relapse. Additionally, imaging techniques such as CT and MRI are playing a key role in diagnosing the condition by identifying the extent of inflammation. In severe cases, biologic agents, radiothera-py, or surgical intervention may be required to prevent further orbital damage or to decompress the orbit in cases of significant proptosis. Orbital inflammatory disease is a treatable but poten-tially recurrent condition that requires careful clinical management.

Key words: Orbital Inflammatory Disease, CT scan, corticosteroid, Immunosuppressive.

(J.Natl.Inst.Ophthalmol.2023;6(2):73-82)

Introduction

Orbital Inflammatory Disease (OID), also known as Idiopathic Orbital Inflammatory Syndrome (IOIS) or Nonspecific Orbital Inflammation, represents a distinct and rare subset of orbital disorders characterized by localized, noninfectious, and nonsystemic inflammation confined solely to the orbit.[1-3]

1. Associate Professor, Dept of Oculoplasty, Ispahani Islamia Eye Institute and Hospital, Dhaka, Bang-ladesh
2. Professor, Dept of Oculoplasty, Ispahani Islamia Eye Institute and Hospital, Dhaka, Bangladesh
3. Assistant Professor, Dept of Oculoplasty, Ispahani Islamia Eye Institute and Hospital, Dhaka, Bang-ladesh
4. Assistant Professor, Dept. of Oculoplasty, National Institute of Ophthalmology & Hospital, Bangla-desh.

Address of correspondence:
Dr. Riffat Rashid
Associate Professor, Department of Oculoplasty and Ocular Oncology, Ispa-hani Islamia Eye Institute and Hospital, Dhaka, Bangladesh.
Email: drriffatrashid@gmail.com
Received: 15 Aug. 2022 **Accepted:** 17 Nov. 2022

Gleason first described OID n 19034, accounting for 6% of diseases involving the orbit. This condition is enigmatic in its aetiology, with no identifiable infectious, neoplastic, or systemic autoimmune cause. OID includes a range of inflammatory responses affecting various orbital structures, such as the extraocular muscles, lacrimal gland, orbital fat, and connective tissue, which often result in significant clinical manifestations that may resemble other orbital conditions.[5] OID commonly presents a range of symptoms, including acute or subacute onset of orbital pain, proptosis, eyelid swelling, diplopia, and restricted extraocular motility.[6,7] These diverse symptoms can mimic the conditions such as thyroid eye disease, or-bital cellulitis, malignancies, or vascular lesions, making the diagnostic process complex. The pathophysiology of OID remains poorly understood, but it is thought to involve aberrant im-mune responses leading to localized inflammation.[8] The diagnostic workup for OID requires a multidisciplinary approach, incorporating clinical assessment, advanced imaging techniques, and, when necessary,

histopathological evaluation.[9] Imaging modalities such as CT or MRI play a pivotal role in identifying hallmark patterns of orbital involvement, such as soft tissue inflammation or muscle swelling with tendon involvement, helping to differentiate OID from other conditions. Histopathological confirmation is often reserved for atypical or refractory cases, where biopsy findings may reveal nonspecific chronic inflammation.[10,11] Therapeutically, OID is highly responsive to corticosteroid therapy, which remains the first-line treatment. High dose corticosteroids often result in rapid symptom resolution, providing therapeutic and diagnostic confirmation. However, long term management poses challenges, as some cases may relapse or become refractory to steroids. In these situations, alternative modalities including immunosuppressive agents, radiotherapy, or surgical decompression, along with steroids may be used at tailored doses based on the disease severity and the patient's response. Further more, careful monitoring is crucial to manage potential side effects associated with prolonged steroid use, such as osteoporosis, hyperglycemia, and gastrointestinal disturbances.[12-16] This systematic review explored the diagnostic pathways and therapeutic options for OID, emphasizing the importance of early recognition and individualized treatment approaches to optimize clinical outcomes while minimizing complications. We attempt to evaluate the diagnostic accuracy and optimize therapeutic strategies specifically for pure orbital inflammatory disease (OID).

Methodology & Materials

Search Method:

This review attempt to systematically evaluate the diagnostic accuracy and optimize therapeutic strategies for pure orbital inflammatory disease (OID). The articles assessed the studies, includ-ing randomized controlled trials (RCTs), case series, and observational studies focused on pa-tients with orbital inflammatory disease (OID), known as Nonspecific Orbital Inflammation. These were selected to ensure high quality evidence and data relevant to clinical management. The review focused on patients with pure orbital involvement, excluding those with systemic diseases like vasculitis, thyroid eye disease, or malignancies.

Outcomes included the accuracy (sensitivity, specificity, and overall diagnostic performance) of diagnostic methods and the efficacy of therapeutic approach. The main outcome measured by the improvement of the symptoms, reducing inflammation, functional recovery of the orbit, and any adverse effects related to the therapies. The studies also examined long-term outcomes, including recurrence and management of treatment-related complications.

Data collection:

We systematically gathered information by extracting specific data from various studies, following several structured steps to ensure accuracy. A comprehensive computerized database search was first conducted using targeted search terms relevant to pure orbital inflammatory disease (OID). The initial search yielded data including author names, titles, keywords, and abstracts, which were reviewed against predefined inclusion and exclusion criteria. Studies focusing on diagnostic accuracy and therapeutic strategies for pure orbital inflammation were prioritized, while studies involving systemic diseases or non-pure orbital conditions were excluded. Full text journal articles were retrieved for further examination when abstracts lacked sufficient detail.

Each study was critically assessed based on key elements such as study design, number of par-ticipants, diagnostic methods employed (e.g., imaging, biopsy, and clinical evaluation), thera-peutic interventions (e.g., corticosteroids, immunosuppressive agents, and other treatments), outcomes measured (such as symptom improvement, inflammation reduction, and orbital func-tion recovery), and the quality of the study. This evaluation ensured that only high-quality and relevant studies were included.

Table 1: Clinical Features, Diagnosis, Medical Therapy of Orbital Inflammatory Disease (OID)

Type of OID	Associated Signs and Symptoms	Imaging	Differentiating Ocular Findings
Idiopathic Orbital Inflammatory dis-ease	Acute onset pain, proptosis, eyelid swelling, red-ness, diplopia, and con-junctival injection.	MRI/CT: Diffuse orbital inflammation, enhancing soft tis-sue and fat involvement.	No systemic association; diagnosis of exclusion after ruling out specific causes.
Orbital myositis	Painful eye movement, di-plopia, restricted extraocular muscle motility, and pe-riorbital swelling.	MRI: Enlargement of one or more extraocular muscles, sparing the tendons.	Selective involvement of extraocular muscles; tendon sparing on imaging.
Dacryoadenitis	Pain and swelling in the lacrimal gland area, with associated ptosis and conjunctival erythema.	MRI/CT: Enlarged and enhancing lacrimal gland, often with smooth bor-ders.	Localized to the lacrimal gland, sometimes bilateral in systemic conditions.
IgG4-related dis-ease	Chronic, painless swelling, bilateral involvement, proptosis, and systemic signs (e.g., salivary gland enlargement).	MRI: Well defined masses with homogeneous enhance-ment may involve multiple orbital structures.	Biopsy shows IgG4 positive plasma cells, often part of systemic IgG4 related disease.
Sclerosing Orbital Inflammation	Gradual onset of painless proptosis, restricted motility, and vision loss due to compressive optic neuropathy.	MRI: Diffuse infil-trative process, with the hypointense signal on T2 weighted imaging.	Hard, fibrotic mass on palpation; poor response to corticosteroids.
Therapeutic Ap-proaches	Corticosteroid		
	Immunosuppressive agents		
	Biologic agents		
	Radiation therapy		

Diagnostic and Therapeutic Approaches of Pure Orbital Inflammatory Disease:

1. Idiopathic Orbital Inflammation:

Idiopathic orbital inflammation exhibits highly variable clinical features, ranging from diffuse to focal involvement of orbital tissues such as the lacrimal gland, extraocular muscles, and orbital fat. This condition typically presents with an abrupt onset of pain, proptosis, and inflammatory symptoms like swelling and erythema. Symptoms vary based on the location, extent of inflammation, fibrosis, and mass effect. Additional signs may include ptosis, chemosis, motility dysfunction, and optic neuropathy. In severe cases, entrapment, compression, or destruction of orbital tissues may occur due to sclerosis. While unilateral presentation is more common, bilateral cases are also seen. Symptoms usually develop acutely (hours to days), but in some cases, they may progress over weeks (subacute) or months (chronic).[17-19]

Yuen and Rubin (2003), patients were generally treated with a high dose oral steroid therapy (1.0-1.5 mg/kg/day) for one to two weeks, followed by a taper over 5 to 8 weeks. If symptoms rebounded during the steroid taper or recurred after a period of remission, the steroid dosage was increased (with a slower taper) or restarted, typically for no longer than 10 to 12 weeks. Radiation therapy usually involves low-dose irradiation, typically 15 to 20 Gy, administered over 10 days.[20]

Hsuan et al. (2006). Twenty seven patients were treated with oral prednisolone, the observed response was evaluated as good in 9 patients, partial in 11 patients, and poor in 7 patients. Six patients were treated by the second line immunosuppressive modality, and 6 received radiotherapy.[21]

There are reports [22-25] indicating an initial positive response to corticosteroids, followed by recurrence and progression of the condition. However, limited information exists on the specific tapering protocol for corticosteroid therapy. Effective immunosuppression requires an adequate dose maintained throughout the active phase of the disease. As a result, alternative agents should be considered, particularly for corticosteroid sparing approaches in managing long term disease.

Mombaerts et al. 2017,[26] convened a multinational panel of 35 experts with an average of 31 years of experience to establish diagnostic criteria for idiopathic orbital inflammation (IOI). Consensus was achieved on several key aspects: 7 of 14 clinical and radiologic items, 5 of 7 pathologic items for nonmyositic IOI, 11 of 14 clinical and radiologic items, and 1 of 5 pathologic items for myositic IOI. The panel emphasized the importance of sur-gical tissue biopsy in diagnosing nonmyositic IOI. Additionally, they agreed that up to 30 IgG4 positive plasma cells per high power field in orbital tissue are compatible with IOI.

Ding et al., 2011,[27] highlighted that idiopathic orbital pseudotumor (IOP) could affect single or multiple intraorbital structures, with the potential for extra orbital extension. Its imaging features often resemble other orbital diseases, making diagnosis challenging. Both computed tomography scan and magnetic resonance imaging are commonly employed in investigating orbital conditions.

The study by Seyahi et al., 2024,[28] provides detailed insights into the clinical features, imaging findings, histopathology, and treatment outcomes in patients with idiopathic orbital inflammatory disease. Key findings include:

a) Unilateral Disease Onset:

- 96.1% of patients (n=49) presented with unilateral involvement at onset (right: 24; left: 25).

b) Imaging Observations:

- Orbital MRI, performed in all patients, showed involvement of extraorbital muscles, periorbital skin, lacrimal gland, and optic nerve.
- PET/CT revealed FDG uptake in 15 out of 50 patients, consistent with MRI findings.

c) Histopathology:

- Biopsies (n=23, 45.1%) showed lymphocyterich infiltration with eosinophils.
- IgG4 related disease (IgG4-RD) was

ruled out in 8 biopsies examined.

d) Associated Conditions:

- Inflammatory diseases were identified in 11 patients (22%).
- Lymphoma was detected in 3 patients (1 concurrent, two during follow up).

e) Treatment and Outcomes:

- Rituximab (RTX) was administered to 44 patients (86.3%), and methotrexate (MTX) to 40 patients (78.4%).
- Median RTX courses were 2 (range: 1–6).
- Among 33 patients receiving ≥2 RTX courses, 32 showed clinical improve-ment:
  - Complete symptom resolution in 21 patients.
  - Residual sequelae (e.g., diplopia, ptosis) in 11 patients.
- MRI and PET/CT findings correlated with clinical remission.
- GC (glucocorticoid) therapy was discontinued in 24 patients (47%) treated with RTX.
- Cyclophosphamide and tocilizumab were used in RTX-refractory cases.

This study underscores the effectiveness of RTX in managing idiopathic orbital inflammatory disease, with high rates of clinical improvement and reduced dependency on glucocorticoids. It also highlights the utility of imaging modalities and the importance of histopathological evaluation to exclude IgG4-RD and identify associated conditions like lymphoma.

2. Orbital Myositis:

Orbital myositis is a distinct subgroup of idiopathic orbital inflammatory disease (IOID) characterized by inflammation targeting one or more extraocular muscles. Clinically, it manifests as pain during eye movements and diplopia, which may or may not be accompanied by general orbital inflammatory signs such as erythema and oedema. The disease is further categorized into two forms:

- Limited Oligosymptomatic Ocular Myositis: This form presents minimal symptoms, often limited to discomfort or pain with eye movement and mild diplopia, without significant signs of orbital inflammation.
- Severe Exophthalmic Ocular Myositis: This form is more pronounced and has additional features such as ptosis, proptosis, chemosis, and sometimes marked orbital inflammation.

Imaging, particularly CT scan or MRI, typically shows enlargement of affected extraocular muscles with sparing of the tendons (Fig. 2) , a key diagnostic feature distinguishing it from other orbital pathologies. Corticosteroids are the cornerstone of treatment for orbital myositis, effectively reducing inflammation and

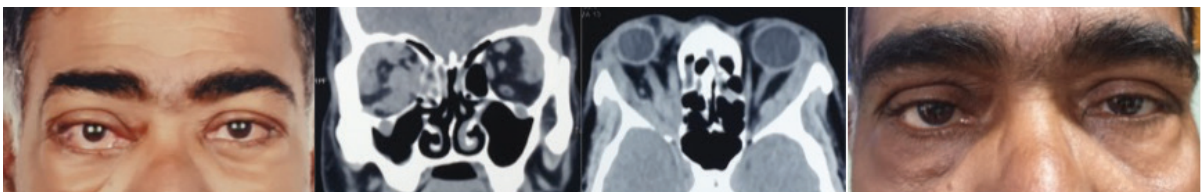

Fig 2: A 53-year-old male, presented with bilateral proptosis, ophthalmoplegia, periocular swelling and RE compressive optic neuropathy due to IOID

Corticosteroid therapy is the primary treatment for orbital myositis, with dosing tailored to the severity and extent of muscle involvement. The standard regimen typically involves oral predni-solone with a dose of 1 mg/kg/day for 1–2 weeks, followed by a gradual taper over 6–12 weeks to minimize the risk of recurrence and adverse effects. In cases requiring rapid symptom relief or severe inflammation, induction therapy with intravenous (IV)

methylprednisolone at 1000 mg/day for a few days has shown excellent efficacy.[29,30]

For patients with less extensive disease, such as single muscle involvement, some clinicians recommend lower doses of oral prednisone (20 mg/day) to reduce the likelihood of systemic side effects while still achieving effective control of inflammation.[31]

Relapses of orbital myositis during corticosteroid tapering is a significant concern, with up to 80% of patients experiencing recurrence when treated with steroids alone.[32,33] The relapse rate, however, is notably lower in cases of single muscle involvement.[34] To manage relapses and enable steroid tapering, steroid sparing immunosuppressive agents are frequently employed. Options include methotrexate, cyclosporine, cyclophosphamide, mycophenolate mofetil, azathi-oprine, and intravenous immunoglobulin (IVIG), all of which have demonstrated efficacy in reducing dependency on corticosteroids and providing symptom relief.[30]

In refractory cases or when systemic side effects of steroids are a concern, biological agents have shown promise. These include infliximab, daclizumab, rituximab, and adalimumab, with isolated case reports indicating their effectiveness in managing orbital myositis.[35-39]

Radiation therapy has also been utilized for resistant orbital myositis, yielding a good initial response. However, its efficacy in long term control of recurrences is suboptimal, limiting its util-ity.[32]

When treatment fails, or the disease exhibits a chronic relapsing course, a biopsy may be war-ranted to rule out alternative diagnoses and guide further management strategies.[34]

3. Dacryoadenitis:

Dacryoadenitis is a subtype of nonspecific orbital inflammatory syndrome (NSOIS) that manifests as isolated inflammation of one or both lacrimal glands (Fig.1), accounting for up to 50% of idiopathic orbital inflammation cases.[40-42] Risk factors for poor prognosis include chronic disease, extension to the orbital apex, and sclerosing histology.[40,42]

Corticosteroids have been the historical cornerstone of treatment, with induction doses of 0.6–1 mg/kg/day of oral prednisone, followed by a 6–10 week taper.[43] However, corticosteroid monotherapy often leads to suboptimal outcomes, with over 50% showing incomplete initial responses and recurrence rates ranging from 40% to 80%.[44,45]

Fig 1: A 37-year-old female, presented with bilateral proptosis, ophthalmoplegia, periocular swelling due to Dacryoadenitis. Left eye incision biopsy was done to confirm diagnosis. CT scan of the orbit revealed that the enlarged both lacrimal glands.

Surgical intervention, particularly excisional biopsy combined with debulking of the orbital part of the lacrimal gland, has emerged as a highly effective alternative. In a study by Mombaerts et al., 80% of patients achieved complete symptom relief, with only 8% recurrence following sur-gery. Notably, prior corticosteroid therapy was associated with surgical failures, leading to the recommendation of debulking surgery as a first-line treatment. In cases of surgical failure, treatments such as radiation therapy, rituximab, methotrexate, and intralesional steroids have been utilized effectively.[46]

Adjunctive therapies, such as azathioprine, have also been reported to enhance outcomes when combined with surgery.[34] Furthermore, a study by Mohammad et al. demonstrated promising results with intralesional betamethasone (2–4 ml) and oral indomethacin, achieving rapid symp-tom resolution within a week and no

recurrences over a follow up of up to 96 months.[43,46,47]

4. IgG4-related disease:

IgG4 related disease (IgG4-RD) is an idiopathic inflammatory disease characterized by tissue infiltration with IgG4 bearing plasma cells and fibrosis, often involving multiple systemic sites. In the orbit, it can affect the lacrimal glands, extraocular muscles, and soft tissues.[48-51] As a relatively new entity, IgG4-RD has redefined some cases previously classified under idiopathic orbital inflammation. However, no universally accepted diagnostic criterion exists, with multiple diagnostic frameworks currently in use.

Corticosteroids are the primary treatment modality for IgG4-RD, achieving symptomatic improvement in 95% of patients, as reported by Wu et al. Nevertheless, disease relapse remains a significant challenge, with 72% of patients experiencing recurrence after corticosteroid taper-ing.[52]

Methotrexate, cyclosporine, and azathioprine have been explored for steroid sparing therapy but demonstrate limited efficacy.[53] Among advanced therapies, rituximab has shown promise; in a small trial by Wallace et al., 6 out of 16 patients achieved disease resolution, and 8 showed symptomatic improvement.[54-56] Additional studies corroborate rituximab's effectiveness, positioning it as a key option for refractory or relapsing cases.

In cases of visionthreatening complications due to mass effect, surgical decompression may help prevent further vision deterioration, although its benefits are typically temporary.[54]

5. Sclerosing orbital inflammation:

Sclerosing Orbital Inflammation (SOI) accounts for approximately 5–8% of orbital inflammatory diseases (OID).[57] It typically presents with a gradual onset of dull pain, proptosis, and double vision, with progressive replacement of orbital structures by fibrosis, leading to significant functional disability. Histopathological findings often show dense collagen deposits and a sparse inflammatory response of lymphocytes, plasma cells, histiocytes, eosinophils, and neu-trophils.[57,58]

Due to the rare nature of SOI, treatment strategies are mainly derived from case report and case series. Corticosteroids are usually used as the first line therapy for SOI, but the results with steroids alone have been mixed.[57,59-61] A systematic review by Pemberton and Fay (2012) found that 9/21 patients achieved complete symptom relief (no recurrence) with steroids, while 5/21 patients had a partial response (some improvement but with possible recurrence), and 7/21 experienced no improvement or disease progression. Steroid dosing ranged from 30 to 150 mg/day, and the duration of the treatment ranged from 1 to 144 months, although recurrence rates were likely higher, given the lack of specified follow up time.[52] A study by Hsuan et al. suggested that earlier detection and treatment with corticosteroids may improve the response, with patients presenting with shorter disease duration before treatment tending to show better outcomes.[60]

Debulking surgery is a second key treatment for SOI. In a study by Hsuan et al., 2/4 of patients who underwent surgical debulking with corticosteroid therapy experienced complete symptom relief, and 1/4 had a partial response.[60] Similarly, Pemberton and Fay found that 3/8 patients responded well to surgery and corticosteroids, 5/8 had a partial response, and none experienced no response.[61] Debulking surgery is the only treatment that effectively reduces the mass of inflammatory tissue in the orbit.

In steroid-refractory cases, radiotherapy has been used with mixed results. Lee et al. reported a complete response in 15/22 patients and a partial response in 3/22, with 14 patients free from disease progression or recurrence at a median follow-up of 34 months. Additionally, radiother-apy combined with surgical debulking showed no recurrences in six patients.62 However, other studies have found partial or no response to radiotherapy.[57,60,61]

Chemotherapeutic and biological agents such as cyclophosphamide, azathioprine, cyclosporine, methotrexate, infliximab, and rituximab have been used with variable results.[39, 61, 63, and 64] A case study noted near complete resolution of SOI with a combination of systemic steroids, CyberKnife surgery, and rituximab.[62] Similarly, Pemberton and Fay reported favourable re-sponses in patients receiving a combination of azathioprine

and steroids, with one patient showing a partial response.[60] In one instance of sclerosing myositis, a combination of infliximab, methotrexate, and systemic corticosteroids led to complete resolution of pain, although diplopia and motility deficits persisted in the primary position.[39]

Overall, steroid therapy and surgical debulking offer the most effective current treatment for sclerosing orbital inflammation. Radiation therapy and azathioprine show promise, but their results remain inconsistent. Given the mixed responses to various treatments, a tailored approach that combines steroids, surgery, and, when necessary, radiation therapy or azathioprine may provide the best outcomes for patients with SOI.

Our current review has several limitations. It focuses exclusively on pure orbital inflammation without considering the broader spectrum of associated or underlying systemic conditions. Orbital inflammatory diseases (OID) often occur in conjunction to other systemic conditions, such as autoimmune diseases or malignancies, and these comorbidities can influence both the presentation and treatment outcomes. By excluding these broader contexts, the study may not fully capture the complexity and variability of OID or the potential impact of systemic diseases on orbital inflammation.

Conclusion

Orbital inflammatory diseases (OID) represent a diverse group of conditions, including idiopathic orbital inflammation (IOI), orbital myositis, dacryoadenitis, IgG4 related disease (IgG4-RD), and sclerosing orbital inflammation (SOI), which can impair the function and structure of the orbit, leading to symptoms such as pain, proptosis, and diplopia. Corticosteroids are the mainstay of treatment for many OID subtypes; however, long term management often requires additional immunosuppressive therapies to prevent relapses. Radiotherapy and chemotherapeutic agents show potential in certain cases, although further studies are needed to optimize their role in treatment. Surgical interventions, particularly debulking surgery, remain vital for managing sclerosing inflammation or when medical treatments are ineffective.

References

1. Swamy BN, McCluskey P, Nemet A, Crouch R, Martin P, Benger R, Gabriel R, Wakefield D. Idiopathic orbital inflammatory syndrome: clinical features and treatment outcomes. Br J Ophthalmol. 2007;91:1667-1670
2. Kapur R, Sepahdari AR, Mafee MF, Putterman AM, Aakalu V, Wendel LJ, Setabutr P. MR imaging of orbital inflammatory syndrome, orbital cellulitis, and orbital lym-phoid lesions: the role of diffusion-weighted imaging. AJNR Am J Neuroradi-ol. 2009;30:64-70.
3. Sepahdari AR, Aakalu VK, Setabutr P, Shiehmorteza M, Naheedy JH, Mafee MF. Indeterminate orbital masses: restricted diffusion at MR imaging with echo-planar diffusion-weighted imaging predicts malignancy. Radiology. 2010;256:554-564
4. Yuen SJ, Rubin PA. Idiopathic orbital inflammation: distribution, clinical features, and treatment outcome Arch Ophthalmol. 2003;121:491-499.
5. Nonspecific orbital inflammation (idiopathic orbital inflammation, orbital inflammatory syndrome, orbital pseudotumor) - EyeWiki [Internet]. Eyewiki.org. 2024 [cited 2024 Dec 29]. Available from: https://eyewiki.org/Nonspecific_Orbital_Inflammation_(Idiopathic_Orbital_Inflammation,_Orbital_Inflammatory_Syndrome,_Orbital_Pseudotumor)
6. Zakir R, Manners RM, Ellison D, Barker S, Crick M . Idiopathic sclerosing inflamma-tion of the orbit: a new finding of calcification. Br J Ophthalmol 2000; 84: 1322–1324.
7. Billing KJ, Hsuan J, Selva D. Idiopathic sclerosing inflammation of the orbit: a case of the steroid-responsive disease in a patient with autoimmune hemolytic anaemia. Eur J Ophthalmol 2005; 15: 263–266.
8. Idiopathic Orbital Inflammation: Diagnosis and Management [Internet]. American Academy of Ophthalmology. 2022 [cited 2024 Dec 29]. Available from: https://www.aao.org/eyenet/article/idiopathic-orbital-inflammation-diagnosis
9. Ferreira, T.A., Saraiva, P., Genders, S.W. et al. CT and MR imaging of orbital inflam-mation. Neuroradiology 60, 1253–1266 (2018). https://doi.org/10.1007/s00234-018-2103-4
10. Weber AL, Romo LV, Sabates NR. Pseudotumor of

the orbit. Clinical, pathologic, and radiologic evaluation. Radiol Clin North Am 1999; 37: 151–168, xi.

11. Orbital inflammatory syndrome (OIS): Diagnosis, treatment, and referral guidelines [In-ternet]. Harvard.edu. [cited 2024 Dec 29]. Available from: https://eye.hms.harvard.edu/book/ois-diagnosis-treatment-and-referral-guidelines

12. Rubin PA, Foster CS. Aetiology and management of idiopathic orbital inflammation. Am J Ophthalmol 2004; 138: 1041–1043.

13. Jacobs D, Galetta S. Diagnosis and management of orbital pseudotumor. Curr Opin Ophthalmol 2002; 13: 347–351.

14. Wirostko BM, Wirostko E, Wirostko RF. Orbital pseudotumors treated with systemic corticosteroids. Ophthalmology 1996; 103: 1519–1520.

15. Notter M, Kern T, Forrer A, Meister F, Schwegler N. Radiotherapy of pseudotumor orbitae. Front Radiat Ther Oncol 1997; 30: 180–191.

16. Isobe K, Uno T, Kawakami H, Ueno N, Kawata T, Abe H et al. Radiation therapy for idiopathic orbital myositis: two case reports and literature review. Radiat Med 2004; 22: 429–431.

17. Mottow LS, Jakobie FA. Idiopathic inflammatory orbital pseudotumor in childhood, I: clinical characteristics. Arch Ophthalmol. 1978;961410-1417

18. Mottow-Lippa L, Jakobiec FA, Smith M. Idiopathic inflammatory orbital pseudotumor in childhood, II: diagnostic tests and biopsies results. Ophthalmology. 1981;88565- 574

19. Berger JW, Rubin PAD, Jakobiec FA. Pediatric orbital pseudotumor: case report and review of the literature. Int Ophthalmol Clin. 1996;36161- 177

20. Yuen SJA, Rubin PAD. Idiopathic Orbital Inflammation: Distribution, Clinical Fea-tures, and Treatment Outcome. Arch Ophthalmol. 2003;121(4) :491–499. doi:10.1001/archopht.121.4.491

21. Hsuan JD, Selva D, McNab AA, Sullivan TJ, Saeed P, O'Donnell BA. Idiopathic Sclerosing Orbital Inflammation. Arch Ophthalmol. 2006; 124(9):1244-1250

22. Levine MR, Kaye L, Mair S, Bates J. Multifocal fibrosclerosis: report of bilateral idio-pathic sclerosing pseudotumor and retroperitoneal fibrosis. Arch Ophthal-mol 1993;111841- 8437.

23. Rootman JMc, Carthy M, White V, Harris G, Kenerdell J. Idiopathic sclerosing in-flammation of the orbit: a distinct clinicopathologic enti-ty. Ophthalmology 1994;101570- 584

24. Mombaerts I, Schlingemann RO, Goldschmeding R, Koornneef L. Are systemic corti-costeroids useful in the management of orbital pseudo-tumors? Ophthalmology 1996;103521- 528

25. Kennerdell JS. The management of sclerosing nonspecific orbital inflamma-tion. Ophthalmic Surg 1991;22512- 518

26. Mombaerts I, Bilyk JR, Rose GE, et al. Consensus on Diagnostic Criteria of Idiopathic Orbital Inflammation Using a Modified Delphi Approach. JAMA Ophthal-mol. 2017;135(7):769–776. doi:10.1001/jamaophthalmol.2017.1581

27. Ding ZX, Lip G, Chong V. Idiopathic orbital pseudotumour. Clinical radiology. 2011 Sep 1;66(9):886-92.

28. Seyahi E, Toker Dincer Z, Sarici A.M, Mangan M.S, Arslan S, Sahin O.E, Aydin Ulgen O, Fresko I. AB1386 Idiopathic Orbital Inflammatory Disease: A Multidiscipli-nary Approach To Diagnosis, Follow-Up, and Treatment. Annals of the Rheumatic Diseases 2024;83:2046-2047

1. Montagnese F, Wenninger S, Schoser B. "Orbiting around" the orbital myositis: clinical features, differential diagnosis and therapy. J Neurol. 2016;263(4):631–640.

2. Schoser BG. Ocular myositis: diagnostic assessment, differential diagnoses, and thera-py of a rare muscle disease - five new cases and review. Clin Ophthalmol. 2007;1(1):37–42.

3. Lacey B, Chang W, Rootman J. Nonthyroid causes of extraocular muscle disease. Surv Ophthalmol. 1999;44(3):187–213.

4. Mombaerts I, Koornneef L. Current status in the treatment of orbital myo-sitis. Ophthalmology. 1997;104(3):402–408.

5. Yan J, Wu P. Idiopathic orbital myositis. J Craniofac Surg. 2014;25(3):884–887.

6. Rootman J. Diseases of the orbit: a multidisciplinary approach. 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 2003.

7. Garcia-Pous M, Hernandez-Garfella ML, Diaz-Llopis M. Treatment of chronic orbital myositis with daclizumab. Can J Ophthalmol. 2007;42(1):156–157.

8. Harris GJ. Idiopathic orbital inflammation: a pathogenetic construct and treatment strat-egy: the 2005 ASOPRS foundation lecture. Ophthal Plast Reconstr Surg. 2006;22(2):79–86.

9. Hernández-Garfella ML, Gracia-García A, Cervera-Taulet E, García-Villanueva C, Mon-tero-Hernández J. Adalimumab for recurrent orbital myositis in Crohn's disease: report of a case with a 3-year follow-up. J Crohns Colitis. 2011 Jun;5(3):265-6. doi: 10.1016/j.crohns.2011.02.010. Epub 2011 Mar 10. PMID: 21575896.

10. Lim L, Suhler EB, Smith JR. Biologic therapies for inflammatory eye disease. Clin Ex-periment Ophthalmol. 2006;34(4):365–374.

11. Sahlin S, Lignell B, Williams M, Dastmalchi M, Orrego A. Treatment of idiopathic scle-rosing inflammation of the orbit (myositis) with infliximab. Acta Ophthalmol. 2009 Nov;87(8):906-8. doi: 10.1111/j.1755-3768.2008.01320.x. PMID: 18631325.

12. Bijlsma WR, Van 't Hullenaar FC, Mourits MP, Karmann R. Evaluation of classification systems for

nonspecific idiopathic orbital inflammation. Orbit. 2012 Aug;31(4):238-45. doi: 10.3109/01676830.2012.681749.

13. Mombaerts I. The many facets of dacryoadenitis. Curr Opin Ophthalmol. 2015;26(5):399–407.

14. Yuen SJ, Rubin PA. Idiopathic orbital inflammation: distribution, clinical features, and treatment outcome. Arch Ophthalmol. 2003;121(4):491–499.

15. Andrew NH, Kearney D, Sladden N, McKelvie P, Wu A, Sun MT, McNab A, Selva D. Idiopathic Dacryoadenitis: Clinical Features, Histopathology, and Treatment Outcomes. Am J Ophthalmol. 2016;163:148-153.e1. doi: 10.1016/j.ajo.2015.11.032.

16. Mombaerts I, Schlingemann RO, Goldschmeding R, Koornneef L. Are systemic cortico-steroids useful in the management of orbital pseudotumors? Ophthalmology. 1996 Mar;103(3):521-8. doi: 10.1016/s0161-6420(96)30663-5.

17. Swamy BN, McCluskey P, Nemet A, Crouch R, Martin P, Benger R, Gabriel R, Wakefield D. Idiopathic orbital inflammatory syndrome: clinical features and treatment outcomes. Br J Ophthalmol. 2007 Dec;91(12):1667-70. doi: 10.1136/bjo.2007.124156.

18. Mombaerts I, Cameron JD, Chanlalit W, Garrity JA. Surgical debulking for idiopathic dacryoadenitis: a diagnosis and a cure. Ophthalmology. 2014 Feb;121(2):603-9. doi: 10.1016/j.ophtha.2013.09.010.

19. Leibovitch I, Prabhakaran VC, Davis G, Selva D. Intraorbital injection of triamcinolone acetonide in patients with idiopathic orbital inflammation. Arch Ophthalmol. 2007 Dec;125(12):1647-51. doi: 10.1001/archopht.125.12.1647. PMID: 18071116.

20. Stone JH, Zen Y, Deshpande V. IgG4-related disease. N Engl J Med. 2012;366(6):539–551.

21. Andrew N, Kearney D, Selva D. IgG4-related orbital disease: a meta-analysis and re-view. Acta Ophthalmol. 2013;91(8):694–700.

22. Kubota T, Moritani S. Orbital IgG4-related disease: clinical features and diagno-sis. ISRN Rheumatol. 2012;2012:412896.

23. Lindfield D, Attfield K, McElvanney A. Systemic immunoglobulin G4 (IgG4) disease and idiopathic orbital inflammation; removing 'idiopathic' from the nomenclature? Eye (Lond). 2012;26(5):623–629.

24. Plaza JA, Garrity JA, Dogan A, Ananthamurthy A, Witzig TE, Salomão DR. Orbital in-flammation with IgG4-positive plasma cells: manifestation of IgG4 systemic disease. Arch Ophthalmol. 2011 Apr;129(4):421-8. doi: 10.1001/archophthalmol.2011.16. PMID: 21482868.

25. Wu A, Andrew NH, McNab AA, Selva D. IgG4-Related Ophthalmic Disease: Pooling of Published Cases and Literature Review. Curr Allergy Asthma Rep. 2015 Jun;15(6):27. doi: 10.1007/s11882-015-0530-4. PMID: 26141575.

26. Wallace ZS, Deshpande V, Stone JH. Ophthalmic manifestations of IgG4-related dis-ease: a single-centre experience and literature review. Semin Arthritis Rheum. 2014;43(6):806–817.

27. Carruthers MN, Topazian MD, Khosroshahi A, Witzig TE, Wallace ZS, Hart PA, Desh-pande V, Smyrk TC, Chari S, Stone JH. Rituximab for IgG4-related disease: a prospec-tive, open-label trial. Ann Rheum Dis. 2015 Jun;74(6):1171-7. doi: 10.1136/annrheumdis-2014-206605.

28. Wu A, Andrew NH, Tsirbas A, Tan P, Gajdatsy A, Selva D. Rituximab for treating IgG4-related orbital disease: experience from five cases. Eye (Lond). 2015 Jan;29(1):122-8. Doi: 10.1038/eye.2014.251.

29. Rootman J, McCarthy M, White V, Harris G, Kennerdell J. Idiopathic sclerosing inflam-mation of the orbit. A distinct clinicopathologic entity. Ophthalmology. 1994 Mar;101(3):570-84. doi: 10.1016/s0161-6420(94)31298-x. PMID: 8127579.

30. Garner A. Pathology of 'pseudotumours' of the orbit: a review. J Clin Pathol. 1973;26(9):639–648.

31. Chen YM, Hu FR, Liao SL. Idiopathic sclerosing orbital inflammation–a case series study. Ophthalmologica. 2010;224(1):55–58.

32. Hsuan JD, Selva D, McNab AA, Sullivan TJ, Saeed P, O'Donnell BA. Idiopathic scle-rosing orbital inflammation. Arch Ophthalmol. 2006 Sep;124(9):1244-50. doi: 10.1001/archopht.124.9.1244. PMID: 16966618

33. Pemberton JD, Fay A. Idiopathic sclerosing orbital inflammation: a review of de-mographics, clinical presentation, imaging, pathology, treatment, and outcome. Ophthal Plast Reconstr Surg. 2012;28(1):79–83.

34. Lee JH, Kim YS, Yang SW, Cho WK, Lee SN, Lee KJ, Ryu MR, Jang HS. Radiotherapy with or without surgery for patients with idiopathic sclerosing orbital inflammation re-fractory or intolerant to steroid therapy. Int J Radiat Oncol Biol Phys. 2012 Sep 1;84(1):52-8. doi: 10.1016/j.ijrobp.2011.11.031.

35. On AV, Hirschbein MJ, Williams HJ, Karesh JW. CyberKnife radiosurgery and rituximab in the successful management of sclerosing idiopathic orbital inflammatory disease. Ophthalmic Plast Reconstr Surg. 2006 Sep-Oct;22(5):395-7. doi: 10.1097/01.iop.0000231549.24125.7a.

36. Patel AK, Hoch S, Shindler KS. Mycophenolate mofetil treatment of steroid-resistant idiopathic sclerosing orbital inflammation. Clin Experiment Ophthalmol. 2011;39(9):912–913.