Idiopathic (non-specific) orbital inflammation

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Abstract

Orbital inflammatory disease is a broad spectrum of orbital diseases comprising of infections and inflammations which may pose potential threat to life and/or vision. It is difficult for the clinician to diagnose these conditions based on clinical examination alone. Imaging features may overlap posing further diagnostic dilemma. Idiopathic orbital inflammation, also known as non-specific orbital inflammation, is one of the commonest diseases encountered in oculoplastic practice characterized by an inflammatory process involving 1 or more orbital tissue without any associated local or systemic cause. IOI is a diagnosis of exclusion and a variety of mimics need to be excluded to facilitate timely and appropriate management of patients with IOI. We comprehensively review the clinico-radiologic and histopathologic features of IOI with an emphasis on its differential diagnosis.

Keywords dacryoadenitis; idiopathic; inflammation; myositis; non-specific; orbit; sclerosing

Background

Orbital inflammatory disease is a term applied to a diverse group of inflammatory conditions which involve 1 or more tissues in the orbit. Idiopathic orbital inflammation (IOI) is the third most frequently encountered orbital disease after thyroid related orbitopathy and orbital lymphoproliferative disease.[1–5] Diagnosis is one of exclusion based on clinical history, examination, clinical course, radiological findings, histopathologic assessment and response to steroid therapy. Differential diagnoses include various local and systemic inflammatory conditions, infections and neoplasms. IOI varies widely in clinical presentation and course. Treatment is with corticosteroids but relapses can occur further complicating the clinical course.

This review discusses the general approach to evaluating and managing IOI and reviews and the different orbital diseases which mimic IOI.

Historical perspective & nomenclature

Proptosis has been conventionally considered as a *prima facie* evidence of an orbital neoplasm. In 1850, it was observed that a patient with proptosis due to a presumed orbital neoplasm showed significant improvement that was attributed to use of homeopathic remedies.[6] Panas, in 1895, coined the term 'pseudoplasm' to describe such cases.[7] In 1903, Gleason found only inflamed extraocular muscles (EOM) in a patient whom he surgically explored for a clinically suspected orbital tumor. He named the condition as 'idiopathic myositis of EOM.'[8] Bosse – Hucchmein made similar observations and used the term 'chronic orbital myositis'.[9] The condition was characterized as a distinct entity in 1905 by Birch-Hirschfeld who used the term 'orbital pseudotumor' to describe one of his patients having an orbital mass resembling an orbital tumor clinically but was an inflammatory lesion.[10] Since then, several terminologies have been used to describe this entity. These are listed in Table 1. At present, idiopathic orbital inflammation, nonspecific orbital inflammation and orbital inflammatory pseudotumor can be used interchangeably although 'idiopathic orbital inflammation (IOI)'is the most preferred terminology.

Definition

Idiopathic orbital inflammation is now considered as a distinct clinical entity. However, authors have used varied definitions for this disease process.[24] IOI can be defined as a *non-specific, non-neoplastic, non-granulomatous inflammatory disease involving one or more orbital structures without any associated local or systemic cause*.

Terminologies for idiopathic orbital inflammatory disease

Authors	Year	Terminology
Panas[7]	1895	Pseudoplasm
Gleason JE[8]	1903	Idiopathic myositis
Busse O and Hochheim W[9]	1903	Chronic orbital myositis
Birch-Hirschfeld[10]	1905	Orbital pseudotumor
Verebely[11]	1926	Cellulitis fibroplastic
Resse AB[12]	1951	Orbital granuloma
Umiker[13]	1954	Inflammatory pseudotumor
Easton JA and Smith WT[14]	1961	Non-specific orbital granuloma
Coop ME[15]	1961	Orbital lipogranuloma
Hogan MJ and Zimmerman LE[16]	1962	Inflammatory non-neoplastic pseudotumor
Jakobiec FA and Jones IS[17]	1979	Idiopathic inflammatory orbital pseudotumor
Henderson JW[18]	1980	Lymphocytic inflammatory orbital pseudotumor
Abramovitz JN[19]	1983	Sclerosing orbital pseudotumor
Kennerdell JS and Dressner SC[20]	1984	Non-specific orbital inflammatory syndrome
Jakobiec FA and Font RL[21]	1986	Idiopathic orbital inflammation
Henderson JW[22]	1994	Non-vasculitic inflammatory orbital tumor
Rootman J et al.[23]	1994	Idiopathic sclerosing orbital inflammation

Table 1

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Epidemiology

The true incidence of IOI is unknown due to lack of agreement on a single definition. Three of the largest surveys on orbital masses published in the literature report orbital pseudotumors (orbital myositis excluded) to have an incidences of 4% (Mayo Clinic, Rochester, US), 11% (Orbital Centre, Amsterdam, Netherlands) and 12% (Moorfields Eye Hospital, London, UK).[22,24,25] Rootman et al. (British Colombia, Canada) and Yuen et al. (Boston) report incidences of 6.5% and 6%.[1,3] IOI occurs in any age-group but is most seen in adults with a peak incidence between 40 and 60 years of age with no racial or gender predominance.[22] Cases of 'pseudotumor' have been reported in children with the youngest being 3-month-old.[26–28]

Aetiopathogenesis

To date, researchers have not been able to elucidate the exact pathogenesis of IOI. Several factors including infectious, autoimmune, genetic and environmental factors have been proposed as causative agents. Few observers have documented a recent history of upper respiratory tract (URT) in patients with IOI.[26,29] It has been postulated that IOI results from an autoimmune response triggered by infectious agents.[30] Presence of cell wall –deficient bacteria in leucocytes of patients with chronic IOI, association between herpes zoster ophthalmicus and IOI and the association between IOI and recent URT infection support this hypothesis.[31–36] Parvovirus B19, Epstein–Barr virus, Human Herpes virus –6 have been identified in biopsies of IOI patients using polymerase chain reaction.[37] Lower socio-economic status, high body-mass index (BMI), obesity and use of biphosphonates have been associated with an increased risk of IOI.[38] IOI has also been associated with several systemic immune-mediated diseases such as Crohn disease, systemic lupus erythematosus (SLE), rheumatoid arthritis, diabetes mellitus, myasthenia gravis and ankylosing spondylitis.[3,14,39–41] Mombaerts and Koornneef reported a concurrent autoimmune disorder in 10% of patients with IOI.[42] Chemotherapeutic drugs and lithium have also been associated with IOI.[43,44] Autoimmunity has been suggested as a causative factor but not yet proved convincingly. Circulating antibodies against eye muscle antigens have been reported in patients with orbital myositis.[45] Mombaerts et al. and Rootman et al. proposed aberrant immune-mediated production of fibrogenic cytokines which result in fibrosis seen in sclerosing orbital inflammation.[23,46]

Classification systems in IOI[3,20,46–61]

Basis of classification	Categories	Definition
Onset	Acute	Onset within 14 days
	Sub-acute	Onset within 15 days to few weeks
	Chronic	Onset within few weeks to months
Location	Diffuse	Nonlocalized enhancing mass obscuring orbital structures in variable extent, possibly expanding from the apex to the posterior margin of the globe or appearing to mold itself along fascial planes, the globe or the orbital bones.
	Extraocular muscle	Relatively diffuse enlargement of one or more extraocular muscles (with or without the involvement of the associated tendons) accompanied by some spillover of the inflammatory process into orbital fat bordering the muscle, blurring the margin of the muscle.
	Lacrimal gland	Diffuse, oblong enlargement of the lacrimal gland with preservation of the shape of the gland that may be accompanied by an inflammatory reaction in the periglandular tissue, blurring the gland margin.
	Optic nerve	Enlargement and enhancement of the optic nerve sheath, without nerve fiber involvement, and possible streaky inflammatory densities in the contiguous orbital fat.
	Sclera	Enlargement of the scleral uveal rim may be associated with edema extending into Tenon's space. Including periscleritis and sclerotenonitis.
	NOS (not otherwise specified)	Impossible to classify elsewhere.
Histopathology	Classic	Chronic inflammatory infiltrate with small well differentiated mature lymphocytes, admixed with plasma cells, neutrophil and eosinophil granulocytes, occasionally with histiocytes and macrophages.
	Granulomatous	Various cellular response, mainly histiocytic infiltration and multinucleated giant cells, sometimes with well-formed noncaseating granulomas.
	Sclerosing	Interstitial connective tissue is disproportionately great and inflammatory infiltrate is paucicellular. Includes fibrosis (loosely attached immature collagen bundles with multiple fibroblasts) and sclerosis (more hyalinized connective tissue with few fibroblasts).
	NOS (not otherwise specified)	Impossible to classify elsewhere.

Table 2