

Commentary

Why “orbital pseudotumour” is no longer a useful concept

After 20 years of experience and more than 3000 orbital cases, one of the single most frustrating aspects of a referral based practice in orbit is the avidity ophthalmologists have for the diagnosis “orbital pseudotumour” and the laxity of clinical evaluation caused by misunderstanding this antiquated concept. If one looks at the historic trends in medical understanding, the last century was dominated by the clinical definition of disease, which gradually gave way in this century to specific diagnoses based on pathological, anatomical (imaging), and systemic associations of disease. The final decades of this millennium have been characterised in medical diagnostic sciences by increasing specificity brought about by immunopathological and molecular genetic techniques, which clearly will link to prevention and specific treatment based on the ultimate pathogenesis of disease. It is against this background that I disparage the use of the term “orbital pseudotumour” since its definition is of such diverse character that it no longer serves a useful purpose. In fact, its use contributes to intellectual laxity in clinical analysis and may have significant negative consequences as a result of delay and confusion in diagnosis and management of patients.

The term was put forward at the turn of the century by Birch-Hirschfeld as a negative entity when on surgical exploration of the orbit no distinct tumour was found.¹ The confusion caused by this definition is compounded by the wide variety of pathological entities that have been included in subsequent years.^{2–3} Historically, under the rubric “pseudotumour,” descriptions have included entities that affect different anatomical structures in the orbit, such as the muscles, lacrimal gland, periosteum, optic nerve, etc, and the clinical disorders described range from acute inflammations to asymptomatic, infiltrative, and non-infiltrative masses.^{3–5} The so called histological features may be simulated by a wide range of different and specific aetiologies, including trauma, adjacent sinusitis, leaking dermoid cysts, retained foreign body, thrombophlebitis, and lymphangioma.^{6–7} Systemic disorders associated with “pseudotumour” include endocrine exophthalmos, periarteritis nodosa, multifocal fibrosclerosis, sarcoidosis, Wegener’s granulomatosis, dysproteinaemia, amyloidosis, Riedel’s thyroiditis, lupus erythematosus, retroperitoneal fibrosis, mediastinal fibrosis, sclerosing cholangitis, and Dupuytren’s contracture.

A long list of modern authorities bemoan the use of this term based on its contribution to diagnostic confusion both clinically and pathologically, and ask us to relinquish its use in favour of more positive nomenclature.^{8–9} As a practising orbitologist, I can only reflect on the diversity of underlying disorders sent for referral under this rubric in which failure of recognition can have serious consequence for the patient. These disorders have included such conditions as lymphoma, idiopathic sclerosing inflammation, Wegener’s granulomatosis, myositis, granular cell tumour, thyroid orbitopathy, metastatic adenocarcinoma, angio-lymphoid hyperplasia with eosinophilia, leucocytoclastic vasculitis, a host of dermatological inflammatory disease, and sarcoidosis, to name just a few.

Upon analysis of my own experience, I have been struck by the increasing specificity in the diagnosis of orbital inflammatory disorders over time that have been brought

about by improved imaging and investigative criteria, including histopathological and systemic testing. We have seen a significant shift in the specific identification of orbital inflammatory and non-inflammatory disorders that belie the use of any concept that would lead to a “lumping” of these entities. We have seen a clearer definition of lymphoproliferative disorders^{10–17} in particular, as well as vasculitides,¹⁸ sclerosing inflammatory disease,^{19–20} and a multiplicity of primary, secondary, and haematological tumours.

I prefer classifying groups of diseases on a much more specific basis that reflect not only their clinical but their underlying pathophysiological character. In particular, in the so called “inflammatory pseudotumour” category, we believe that it is appropriate to identify and specify lymphoproliferative disorders as clinically, histopathologically, and molecularly separate and different from inflammatory disorders. In addition, we now can identify specific inflammatory disorders, such as Wegener’s granulomatosis, vasculitis, collagen diseases, sarcooidal reactions,²¹ and xanthogranulomatous diseases, based on histopathology and systemic evaluative testing. There remain a number of non-specific inflammatory disorders that presently can be defined only from an anatomical point of view. Yet even within this group, biopsy will reveal a wide range of pathological processes or disease constellations, which suggest that some more specific identity should be sought and can be found based on pathology and/or systemic findings. Further, more specific pathological identification can be obtained by using an algorithm based on the patterns of pathological infiltration and the constellation of clinical and imaging findings.^{18–20} For instance, a pathological infiltrate that is dominated by mixed inflammation associated with features of necrosis and intense perivascular infiltration belies an underlying process (possibly vasculitic) that is vastly different from one that is dominated only by an acute lymphocytic infiltration, just as a lesion dominated by foamy histiocytes, cholesterol granulomas, fibrosis, and a lymphocytic background would belie a different kind of process.²²

How then can we deal with the diagnosis of diseases of such diverse character and aetiology? The best way is to try to define the clinical and pathophysiological patterns or processes involved in an individual case, and then proceed to a specific diagnosis based on imaging, systemic evaluation, testing, and biopsy when necessary. The major clinical processes that can be easily discerned include inflammatory, infiltrative, mass effect, and vascular change.

Inflammatory signs and symptoms consist of pain, warmth, loss of function, and mass effect. These inflammatory disorders can be divided into acute, subacute, and chronic change. Aetiologically, the categories are distinct and imply different types of pathology. Infiltrative change, on the other hand, is characterised by evidence of destruction, entrapment, or both, suggesting neoplasia or a chronic infiltrative or desmoplastic inflammatory process. Mass effect consists of displacement with or without signs of involvement of sensory or neuromuscular structures. Finally, vascular change consists of alteration in the character, size, or structural integrity of vessels. Defining the clinical features of a disease process in the

context of inflammation, infiltration, mass effect, or vascular change leads to a logical differential diagnosis, particularly when contextualised within specific imaging, systemic findings, blood chemistry, and age specific diseases.

In our experience, the so called "pseudotumour" cases that are referred run the gamut from acute and subacute inflammations, to infiltrations, and to masses. Acute or subacute inflammations are aetiologically caused by either infections and infestations, or specific inflammatory disorders. The remaining group could be classified as originating from acute and subacute non-specific inflammations. These in turn could be investigated to identify when possible specific location, clinical features, imaging features, and associations (for example, sarcoid, sclerosing inflammation, Wegener's granulomatosis, etc). The acute and subacute non-specific inflammations can be divided according to clinical syndromes, including locations based on anterior, diffuse, myositic, lacrimal, and apical infiltrations. Infections and infestations can be treated specifically on diagnosis, and the specific inflammatory disorders (based on specific histology and/or constellations of systemic and local findings) would be treated on the basis of their distinct identification. The non-specific inflammations characteristically are treated with non-specific anti-inflammatory measures and, if they progress or fail on treatment, should be followed with biopsy to continue the effort to define the disease by recognising non-specific and ambiguous characterisation. It is likely that in the future, the nature of these disorders will also become more specific as will the treatment. However, there are in my opinion two particular anatomical locations where the diagnosis of non-specific inflammation should be made extremely cautiously and may more often require biopsy because of the risks of misdiagnosis. These are lesions of the lacrimal gland and orbital apex. In my experience, inflammatory lacrimal lesions are associated with a specific diagnosis or systemic disorder in 50% cases, which suggests that it is appropriate to biopsy. Apical inflammations, on the other hand, are part of a group of differential diagnoses where misdiagnosis is very frequent; one should be very reluctant to use non-specific inflammation as a diagnostic category and should go to extra lengths to specify the disease in this location.

On the other hand, the chronic inflammatory processes are usually characterised by infiltrative phenomena that require biopsy in order to proceed appropriately. As for systemic associations with clinical inflammatory disease, one has to consider thyroid orbitopathy, vasculitides (in which case, an ischaemic phenomenon may be associated), collagen diseases, and more rarely cancers, structural disorders, and vascular disease.

Finally, mass effect as the primary clinical phenomenon can be divided into those that are infiltrative and non-infiltrative. Infiltrative masses are primarily neoplasia and chronic inflammations, and are less frequently

lymphoproliferations and depositions. Thus, all usually require biopsy and are then dealt with accordingly. Masses that behave as well defined lesions with or without functional deficit may include neoplasia, lymphoproliferations, some chronic inflammations, vascular entities, and some structural lesions. In these instances, exploration with or without extirpative biopsy may be required to obviate the process.

The above arguments prompt me to challenge the ophthalmic and orbital community to move with science towards a more specific definition of disease, and to give up paying homage to a term simply because it exists in the lexicon, particularly if it continually confuses the issue and leads to inappropriate care of patients.

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