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Orbital lymphoma versus reactive lymphoid hyperplasia: an analysis of the use of computed tomography in differential diagnosis

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Abstract

Computed x ray tomography (CT) studies of 40 patients with proptosis or periorbital swelling, in whom biopsy showed lymphoma in 23 and reactive lymphoid hyperplasia in 17, were analysed in an attempt to identify radiological differences between the two conditions. The results indicate that homogeneity of an orbital mass is a sensitive but non-specific indication of lymphoma, 75% of lymphomatous masses and only 23% of reactive lesions being homogeneous. Bone destruction was seen only in cases of lymphoma, but was rare. Other radiological features of the mass or the affected orbital structures did not allow discrimination of tumour from a reactive lesion.

Localised lymphocyte proliferation within the orbit, sufficient to cause proptosis or swelling and developing in the absence of an identifiable cause, is well recognised. However, this proliferation may be a reactive hyperplasia, presumed to be inflammatory and falling into the broader category of orbital granuloma or pseudotumour, or neoplastic, in the form of non-Hodgkin's lymphoma.[1] It is important to distinguish these two conditions to orientate appropriate treatment.

Although an early publication[2] indicated that computed x ray tomography (CT) was 'of little value in the diagnosis and management of lymphoproliferative diseases' of the orbit, this technique has now become the standard method of examination, providing a valuable means of investigating orbital masses, the orbital skeleton, and the surrounding soft tissue structures.[3] The differentiation between lymphoma and reactive hyperplasia, among the most common conditions causing patients to present with proptosis or periorbital swelling, has traditionally been on clinical grounds – reactive hyperplasia, like inflammation, tending to cause pain and lymphoma being relatively painless,[4] though the distinction is not absolute.[5] Response to systemic steroids can be confusing.[5] The 'non-specific' CT appearances have been described previously,[6] and little attempt has been made to differentiate benign from malignant lymphoproliferative lesions.[7,8]

The aim of this study was to identify, without reference to the clinical or demographic data, radiological characteristics which might aid in differential diagnosis.

Table 1 CT characteristics of orbital masses

	Lymphoma (28)	*Hyperplasia (21)*
Size		
2 cm or less	8 (29%)	9 (41%)
2·1–4 cm	17 (61%)	9 (41%)
more than 4 cm	3 (11%)	4 (18%)
Shape:		
round	3 (11%)	0
moulded	17 (61%)	13 (59%)
irregular	8 (29%)	9 (41%)
Texture:		
homogeneous	21 (75%)	5 (23%)*
Site:		
postseptal only	4 (14%)	4 (18%)
preseptal only	1 (4%)	1 (5%)
both	23 (82%)	17 (77%)
intraconal only	3 (11%)	1 (5%)
extraconal only	21 (75%)	15 (68%)
both	4 (14%)	6 (27%)
quadrant:		
superomedial	15 (54%)	12 (55%)
superolateral	25 (89%)	19 (86%)
inferomedial	12 (43%)	6 (27%)
inferolateral	18 (64%)	13 (59%)
Number of quadrants:		
one	2 (7%)	6 (27%)
two	14 (50%)	7 (32%)
more than two	12 (43%)	9 (41%)
mean	2·50	2·27
Extraorbital spread:		
intracranial only	1 (4%)	1 (5%)
extracranial only	7 (25%)	4 (18%)
both	0	0

*p<0·01

Material and methods

RADIOLOGICAL

The CT examinations of the orbits of 40 patients, comprising 50 abnormal orbits, were examined retrospectively. Since patients had been referred from several hospitals, there was no standard technique, but in general thin (2 mm) axial sections were obtained through both orbits in the plane of the optic nerves, targeted to include the pituitary fossa. Coronal images were obtained by scanning directly in the coronal plane or by computer reformation where axial sections were sufficiently thin; three patients had only axial images. Only contrast-enhanced images were obtained in the majority of cases: nine patients were examined without and three before and after intravenous contrast medium.

The histological diagnosis was not known by the radiologists at the time of review of the images, the criteria for which were as follows. The maximum diameter of the mass was measured, by means of the computer generated scale of the imager, to the nearest 5 mm; its shape was recorded as rounded, moulded to adjacent structures, or irregular; its margin as well or poorly defined and its texture as homogeneous or otherwise, regardless of the regularity of its borders. The overall radiographic density of the mass, compared with that of the adjacent brain, was noted before and/or after intravenous contrast medium, and the pattern of contrast

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Table 2 Effects of orbital mass on normal structures

	Lymphoma (28)	*Hyperplasia (21)*
Globe:		
displacement	18 (64%)	20 (91%)
distortion	0	0
incorporation	0	0
nil	10 (36%)	2 (9%)‡
Optic nerve:		
displacement or distortion*	4 (14%)	3 (14%)
incorporation†	3 (11%)	5 (23%)
nil	21 (75%)	14 (64%)
Lacrimal gland:		
displacement or distortion*	3 (11%)	3 (14%)
incorporation †	19 (68%)	15 (68%)
nil	6 (21%)	4 (18%)
Muscles:		
displacement or distortion*	4 (14%)	9 (41%)
incorporation†	15 (54%)	9 (41%)
nil	6 (21%)	4 (18%)
Number of muscles involved:		
none	6 (21%)	4 (18%)
one	8 (29%)	8 (36%)
more than one	14 (50%)	10 (45%)
mean	1·92	2·55
Bone		
remodelling	3 (11%)	1 (5%)
lytic destruction	2 (7%)	0
thickening	2 (7%)	5 (23%)
nil	23 (82%)	16 (73%)

*Excludes incorporation.
†Includes displacement or distortion.
‡$p<0·05$.

enhancement was recorded as uniform, inhomogeneous or focal. The site of the mass in relation to the orbital septum, muscle cone, and quadrant (superolateral, inferomedial, etc) was noted, together with spread outside the orbit superficially or towards the paranasal sinuses or cranial cavity. Involvement of normal orbital structures, such as the optic nerve or muscles, was assessed as displacement or distortion by the mass or incorporation into it. Effects on the bony skeleton were recorded as remodelling, lytic destruction, or thickening of bone. The orbital fat was assessed for evidence of focal or generalised alteration in radiographic density. The results were subjected to statistical analysis by the χ^2 test.

HISTOLOGICAL

Tissue was obtained by open biopsy under direct vision in all cases, fixed immediately in formol–saline, and subjected to histopathological examination. Sections were cut from paraffin embedded material and, in addition to conventional haematoxylin and eosin staining, were stained for the presence of Ig light chains κ and λ by an immunoperoxidase technique. The criteria for recognition of neoplastic proliferation were based on a fairly uniform accumulation of lymphocytes with diffusely distributed immature cell forms, a dearth of other types of leucocycte, and a mono- or markedly oligoclonal light chain profile in the cytoplasm of the antibody-forming cells. Reactive lymphocyte proliferation was identified by the presence of germinal centres (though these were not invariable), of macrophages in moderate numbers and, less commonly, of eosinophils and neutrophils, and of a polyclonal light chain pattern. For the purposes of this study lesions which could not confidently be assigned to one or other group were excluded.

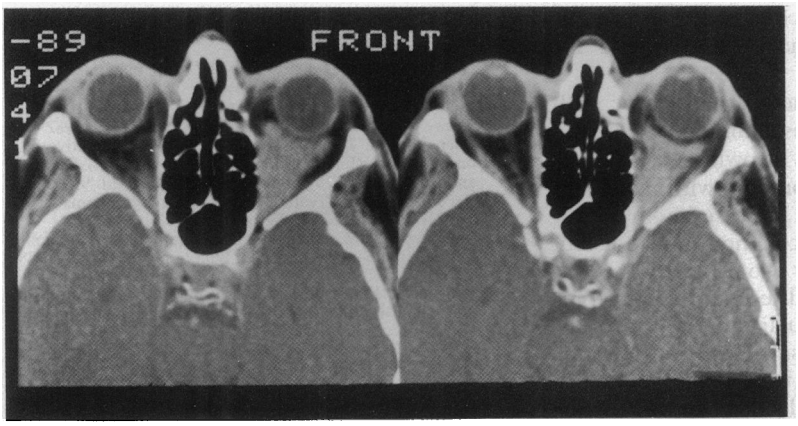

Figure 1 Lymphoma of the left orbit: 2 mm contiguous axial CT sections after intravenous contrast medium (Somatom DRH, Siemens). The abnormal soft tissue is of homogeneous radiographic density.

Results

Tables 1 and 2 show the frequency of the radiological findings in the two disease groups, expressed as the numbers of abnormal orbits showing a particular characteristic. Some data are not included: insufficient patients were examined both before and after intravenous contrast medium for useful assessment of enhancement; there was no discernible alteration of fat density in any patient; all but one of the masses were well defined. Five (22%) patients with orbital lymphoma and five (29%) with reactive lymphoid hyperplasia had bilateral masses. Mucoperiosteal thickening, presumed to represent simple inflammatory change, was present in the paranasal sinuses of four patients (17%) with lymphoma and two (12%) with reactive disease.

Discussion

The CT appearances of lymphoid orbital masses are well documented[9] and common manifestations of non-specific orbital inflammation have been described. Thus it is usually possible to distinguish inflammatory or reactive lymphoid masses from inflammatory changes in Graves' disease.[10] Several workers have suggested features which may discriminate inflammatory or reactive masses from lymphoma: scleral thickening[11] and infiltration of retrobulbar fat[12] are suggestive of the former, while remodelling or destruction of the orbital skeleton may suggest neoplasia.[1 13] In general, however, the appearances are too variable for accurate diagnosis, and biopsy is essential.[2 14]

In this study neoplasms (57%) showed a slight predominance over reactive hyperplasia, as in most large series; McNally *et al*[15] found 64 of 100 patients with orbital lymphoproliferative lesions to have lymphomas. Our CT findings were broadly in agreemnt with those of Yeo *et al*,[8] who did not, however, differentiate radiologically between the 15 cases of lymphoma and 12 of lymphoid hyperplasia in their series. Thus less than 10% of the masses were solely intraconal, and the majority involved several quadrants, superior lesions being more frequent than those lying below the globe. The masses tended to conform to the shape of the globe. It has been

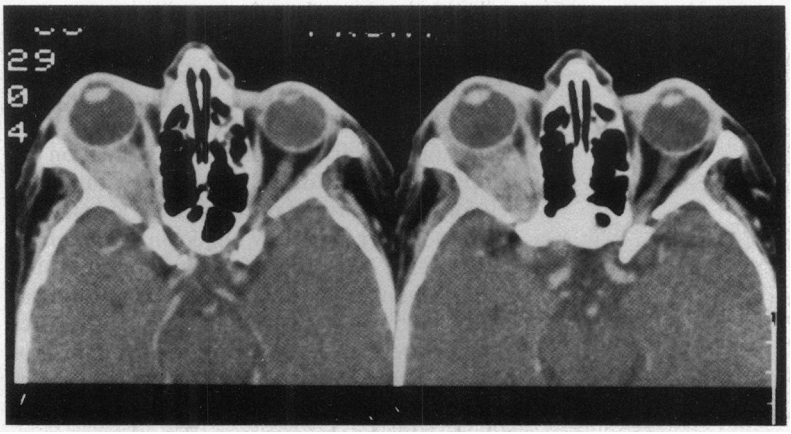

Figure 2 Reactive lymphoid hyperplasia of the right orbit: CT as in Figure 1. The radiographic density of the mass lesion is more inhomogeneous, although the variability is not marked.

suggested that, as the orbit itself contains no lymphatics, postseptal lesions are more likely to be neoplastic and preseptal lesions to be reactive,[16] but this was confirmed neither by our findings nor in a smaller series reported previously.[17]

It is evident from our findings that no single radiological feature is a reliable discriminator betwen lymphoma and lymphoid hyperplasia. Homogeneity of texture was significantly more frequent ($p<0.01$) in patients with lymphoma (Fig 1) than in those with reactive lymphoid masses (Fig 2), in accordance with the reported finding of lower CT attenuation values in inflammatory masses than in lymphoma, attributed to inflammatory infiltration of the intraconal fat cells.[18] There are, however, several potential pitfalls in this observation: in all cases examined the degree of inhomogeneity was minor, and occasionally difficult to discern; the orbital soft tissue structures are particularly liable to streak artefacts and artefacts due to beam hardening and scatter, because of the adjacent bone; partial volume effects diminish resolution, tending to increase apparent inhomogeneity, especially with small masses. Nevertheless, if a standardised scanning technique is employed, the texture of the mass may provide a clue to the differential diagnosis.

Displacement of the globe was significantly more common ($p<0.05$) in patients with reactive lymphoid lesions, but was frequent in both groups, since the presence of proptosis or periorbital swelling was one of the criteria for inclusion.

Although bone destruction may occur with other types of orbital pseudotumour,[2] among lymphoproliferative cases Knowles and Jakobiec[1] observed bone destruction only with malignant lymphoma; this was also the case in our series, but it was insufficiently common to be a useful finding, occurring in only two patients.

In one series lymphoid lesions affecting predominantly the extraocular muscles involved almost exclusively the superior rectus/levator palpebrae complex, and were mainly benign;[19] we confirmed the predilection for the upper orbit, but not the predominance of reactive lesions. Lacrimal gland involvement is also more commonly due to lymphoma than to lymphoid hyperplasia,[20] but our findings point to this being simply a manifestation of the relative frequency of the two conditions.

In common with previous workers we did not find bilaterality helpful for discrimination.[2 17] This is not surprising, since the proportion of patients with unilateral and bilateral lymphoproliferative lesions who subsequently develop lymphoma in other sites is identical.[15] No other radiological criteria were of discriminatory value, emphasising the fact that although orbital CT is of proved utility for orientating biopsy, planning radiotherapy,[21] and monitoring treatment, it is not useful in differential diagnosis.

Although a minority also advise local irradiation for benign lesions,[22] most workers reserve radiotherapy for malignant lymphoma when localised to the orbit.[23] Biopsy and immunohistochemical examination of the type described here thus remain essential.[17 24] While it is therefore convenient and, for the purposes of management, important to make a clear distinction between benign, reactive lesions and those which should be considered as malignant neoplasms, with potential for dissemination,[15] sometimes more than five years after the initial presentation,[25] this consideration should not obscure the possibility that lymphoproliferative orbital disease may represent a continuous spectrum. Thus there is evidence that lesions beginning as polyclonal reactive processes can succumb to malignant transformation with light chain restriction.[5] Moreover, it appears that a proportion of patients will have masses which, although initially presumed to be inflammatory, harbour a clone of neoplastic cells which will proliferate alongside the reactive lymphocytes.[26] Development of contralateral monoclonal lymphoma in a patient presenting with a polyclonal reactive lesion is also described,[15] and there are even reports, though poorly documented, of patients with benign orbital lesions who subsequently developed systemic lymphoma.[22] Such overlap would go some way to explaining the inability of radiological techniques to establish a reliable distinction between the two ends of the spectrum as specifically represented here: had more histologically indeterminate proliferations been included in the study, the degree of radiological differentiation would probably have been even more blurred.

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