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Lesions mimicking lacrimal gland pleomorphic adenoma

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ABSTRACT

Aim To report a series of patients with lacrimal gland lesions simulating the clinicoradiological features of lacrimal gland pleomorphic adenoma (LGPA).

Methods Multicentre retrospective, interventional case series. Clinical records of all patients with lesions mimicking LGPA seen in five orbital units were reviewed.

Results The study included 14 patients (seven men and seven women) with a mean age of 50.9 years. The diagnosis of LGPA was made in all cases by experienced orbital surgeons, based on clinicoradiological features, and lacrimal gland excision was performed.

Postoperative histology revealed lymphoma (four patients), chronic dacryoadenitis (three patients), adenoid cystic carcinoma (two patients), Sjogren's syndrome (two patients), cavernous haemangioma (one patient), benign lymphoid hyperplasia (one patient) and granulomatous dacryoadenitis (one patient). Comparison with the total number of histologically confirmed LGPA cases seen during the study period revealed that 22.6% of cases of suspected LGPA were misdiagnosed based on clinicoradiological criteria.

Conclusions Many different lesions may mimic the clinicoradiological features of LGPA. The accepted clinicoradiological criteria used for the diagnosis of LGPA have a high false-positive rate, even in experienced hands. Based on this study, the authors believe that fine-needle aspiration biopsy or intraoperative biopsy and frozen section diagnosis may help reduce unnecessary lacrimal gland excision.

Pleomorphic adenoma is the most common epithelial tumour of the lacrimal gland accounting for more than 50% of primary epithelial tumours.¹ The diagnosis is based on well-defined clinicoradiological criteria and management is by total excision of the tumour.^{2,3} Traditional teaching advocates a strict 'no biopsy' policy for suspected lacrimal gland pleomorphic adenoma (LGPA) to minimise the risk of recurrence or of malignant transformation.²⁻⁵ Whereas the clinicoradiological criteria for the diagnosis of LGPA are well established, their specificity is unknown, and given that the recommended treatment involves excision of the lacrimal gland, a preoperative misdiagnosis may lead to unnecessary or suboptimal surgery. We report a series of 14 patients in whom a preoperative diagnosis of LGPA made on clinicoradiological criteria was not supported by postoperative histology.

MATERIALS AND METHODS

This is a multicentre retrospective study of all patients with lacrimal gland lesions mimicking

LGPA who were seen in five orbital units: Royal Adelaide Hospital, January 1997 to October 2006 (two cases), Royal Victoria Eye and Ear Hospital, January 1986 to October 2006 (four cases), Royal North Shore Hospital, January 1996 to October 2006 (two cases), Vancouver General Hospital (University of British Columbia), Orbit Clinic, January 1994 to October 2006 (two cases) and Sydney Eye Hospital, University of Sydney, January 2000 to October 2006 (four cases). One of the patients in this series was the subject of a previous publication (case 11).⁶ Institutional Review Board/Ethics Committee approval was obtained for this study.

Experienced orbital surgeons (five different orbital surgeons were involved in this study) evaluated all the patients and the preoperative diagnosis of LGPA was based on well-established clinicoradiological features. In short, a long duration of symptoms and signs (>12 months), the absence of pain, well-circumscribed lacrimal gland mass on imaging that may indent the globe and the absence of calcification all favoured a diagnosis of LGPA. All patients underwent lateral orbitotomy and excision of the lacrimal gland, usually with preservation of part of the palpebral lobe in the superolateral conjunctival fornix but removal of the remainder of the gland including the overlying periorbita.

We reviewed the medical records of these patients to obtain the following data: patients' demographics; duration of signs and symptoms; clinical presentation; imaging findings on CT and ultrasound; histological diagnosis and outcome. The clinical and radiological findings were scored according to the algorithm devised by Rose and Wright³ (see footnote to table 1). The medical records in the five centres were also reviewed to retrieve the total number of histologically confirmed LGPA seen during the period of this study.

RESULTS

Our study included 14 patients (seven men and seven women) with a mean age of 50.9 years (median 50; range 34–68 years). The mean duration of symptoms before diagnosis was 17 months (median 12 months; range 2 weeks to 48 months). The CT findings in all cases were consistent with a diagnosis of LGPA. The most common finding was a well-circumscribed enlargement of the lacrimal gland. Indentation of the globe was seen in five cases and bone remodelling in three cases. Ultrasound examination was performed in two

Table 1 Clinicopathological summary of cases

Age, years	Symptoms	Duration	Clinical findings	Radiological findings	Score*	Histological diagnosis	Further treatment/follow-up
1 40	RUL swelling, diplopia	2 Weeks	RUL oedema, non-tender. 2 mm inf displacement right globe	Well circumscribed right lacrimal gland mass indenting globe	6	Low-grade B-cell NHL	Under observation for 7 years. No systemic disease. Developed ptosis and persistent dry eye (RE) following surgery
2 67	RUL swelling	48 Months	Right proptosis 2 mm. 3 mm inf displacement right globe. Enlarged non-tender palpable lacrimal gland	Well circumscribed right lacrimal gland mass indenting globe	8	MALT lymphoma	No systemic disease. Under observation for 5 years. Then developed posterior fossa meningioma. Lost to follow-up since chemotherapy. No systemic disease. In remission for 5 years
3 44	Recurrent corneal erosions-RE	'Several' months	Right proptosis 6 mm. 2 mm inf plus med displacement right globe. Marked restriction of elevation RE. Enlarged non-tender palpable lacrimal gland	Well circumscribed right lacrimal gland mass indenting globe	6	Follicular lymphoma	
4 62	Fullness RUL	24 Months	Right proptosis 1 mm. 3 mm inf plus med displacement left globe	Well circumscribed right lacrimal gland mass with bone remodelling in lacrimal fossa	8	Mantle-cell lymphoma	Under observation for 6 months. No systemic disease
5 54	RUL swelling	12 Months		Well circumscribed right lacrimal gland mass	6	Chronic dacryoadenitis	2 years follow-up. No problems
6 41	Proptosis LE	14 Months	Proptosis LE 3 mm	Well circumscribed left lacrimal gland mass with heterogeneous internal architecture	6	Chronic dacryoadenitis	Left upper lid retraction following orbitotomy, corrected surgically after 4 months
7 45	LUL swelling	8 Months	S-shaped LUL	Well circumscribed left lacrimal gland mass with remodelling of bony fossa	6	Chronic dacryoadenitis	Postoperative diplopia in left lateral gaze, resolved at 6 months follow-up
8 46	LUL ptosis plus swelling	18 Months	S-shaped droop LUL. Palpable non-tender mass in lacrimal fossa	Left lacrimal gland mass with globe indentation	8	Sjogren's syndrome	Prednisone x1m Developed right lacrimal gland enlargement 7 years later. Biopsy showed similar pathology. Under observation for 3 years
9 42	Vertical diplopia, LUL ptosis	12 Months	2 mm inf plus med displacement left globe. Restricted elevation and abduction. 3 mm ptosis, S-shaped droop and enlarged non-tender palpable lacrimal gland	Well circumscribed left lacrimal gland mass with globe indentation	8	Sjogren's syndrome	Under observation for 5 years
10 54	Intermittent blurring, LE	24 Months	2 mm inf plus med displacement left globe. Enlarged non-tender palpable lacrimal gland	Well circumscribed left lacrimal gland mass	8	Adenoid cystic carcinoma	Recurrence on two occasions over 7 years. Wide re-excision; further radiotherapy
11 34	Diplopia following soccer injury	2 Weeks	Proptosis RE with 5 mm inf displacement right globe	Well circumscribed right lacrimal gland mass	4	Adenoid cystic carcinoma	Lost to follow-up
12 60	Proptosis LE	'Many years'	Proptosis with inf displacement left globe	Well circumscribed left lacrimal gland mass with bone remodelling in lacrimal fossa	8	Cavernous haemangioma	No recurrence of disease for 2 years. Then discharged from follow-up
13 55	LUL swelling	3 Weeks	Left ptosis 1 mm. 3 mm med displacement of left globe	Well circumscribed left lacrimal gland mass	6	Reactive lymphoid hyperplasia	Under observation for 16 months
14 68	Proptosis RE	12 Months	Proptosis RE 3 mm	Well circumscribed right lacrimal gland mass	6	Granulomatous inflammation consistent with sarcoidosis	Postoperative dry eye. No evidence of systemic sarcoidosis

*Score: Based on Rose and Wright's³ scoring algorithm for lacrimal gland masses. One point is accorded to each of the following: duration greater than 10 months, absence of pain, absence of sensory loss, well-defined mass on imaging, bone excavation/remodelling, absence of calcification, absence of bone invasion and small tumour with long symptoms. One point is deducted for each criterion that is not met. A score of +3 to +8 was reported to favour a diagnosis of lacrimal gland pleomorphic adenoma. inf, inferior; LE, left eye; LUL, left upper lid; MALT, mucosa-associated lymphoid tissue; med, medial; NHL, non-Hodgkin's lymphoma; RE, right eye; RUL, right upper lid.

cases and in both was consistent with a diagnosis of LGPA. The clinical and radiological features of all the patients are detailed in table 1. Applying Rose and Wright's algorithm³ to the 14 cases, a mean score of 6.7 (range 4–8) was obtained, indicating a high probability of LGPA.

All patients underwent lateral orbitotomy and excision of the lacrimal gland for presumed pleomorphic adenoma. Histological examination revealed the following diagnoses: non-Hodgkin's B-cell lymphoma: four cases; chronic dacryoadenitis: three cases; Sjogren's syndrome: two cases; adenoid cystic carcinoma: two cases; granulomatous dacryoadenitis consistent with sarcoidosis: one case; benign lymphoid hyperplasia: one case; cavernous haemangioma: one case. In the last case, the diagnosis of cavernous haemangioma was evident intraoperatively. Further management was individualised according to the histological diagnosis (table 1). Four patients (26.8%) developed complications following surgery, including dry eye, ptosis, lid retraction and transient diplopia. The mean follow-up period was 3.6 years (median 3 years; range 4 months to 10 years).

During the period of the study, 48 cases of histologically confirmed LGPA were seen in the five centres (Royal Adelaide Hospital, seven cases; Royal Victoria Eye and Ear Hospital, 20 cases; Royal North Shore Hospital, four cases; Vancouver General Hospital, 11 cases; and Sydney Eye Hospital, six cases). Using figure 1, we calculated that 22.6% of patients were misdiagnosed with LGPA based on the clinicoradiological criteria.

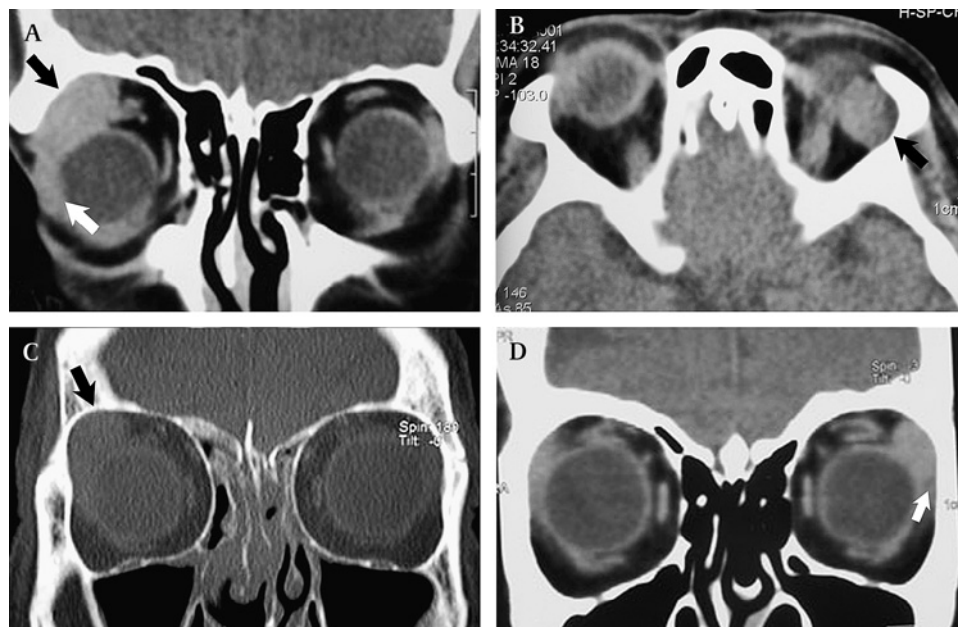
DISCUSSION

We present a series of patients with a variety of lacrimal gland lesions, with clinical and radiological features simulating LGPA. Although LGPA is the commonest epithelial tumour of the lacrimal gland, it remains an uncommon tumour overall, accounting for only 0.6% of all orbital cases.⁷ Ninety per cent of cases involve the orbital lobe of the lacrimal gland and the remaining 10% involve the palpebral lobe.¹ It is an indolent tumour, with fairly characteristic clinical and radiological features as mentioned previously, and this allows almost all cases to be diagnosed preoperatively. Definitive management is by complete excision of the tumour, which in most cases

involves total removal of the orbital lobe of the lacrimal gland along with the overlying periorbital. Incomplete removal of the tumour leads to recurrence in a significant number of cases, sometimes after decades following the original surgery.^{2–4} It is also hypothesised that incomplete resection followed by recurrence (particularly multiple recurrences) may be a risk factor for malignant transformation of the tumour¹. Biopsy is not recommended as part of the preoperative work-up, and this caveat against biopsy of lesions suspected to be LGPA arose from the study by Font and Gamel in 1978.⁴ They retrospectively analysed 136 cases of LGPA and found that 27% of the cases recurred. They calculated that previous biopsy would lead to a 5-year recurrence rate of 32%. Later series by Ni and coworkers,⁵ Garrity and Henderson² and Rose and Wright³ all found an increased risk of recurrence following incomplete excision, and based on this finding, all advised against preoperative biopsy. Therefore, based on the foregoing studies, and also because most LGPA present with characteristic clinical and radiological signs allowing accurate preoperative diagnosis, lacrimal gland excision without biopsy is the recommended treatment.^{2–5}

A review of the recent literature on LGPA, however, suggests that a significant number of cases may present with symptoms and signs not usually associated with this lesion. Sen and coworkers⁸ analysed a series of 32 cases of LGPA and found that the duration of symptoms was less than 10 months in 28% of cases. Calcification of the tumour, usually considered a sign of malignancy, has also been described in LGPA^{3 9 10} and there is a report of a case with bone destruction.¹¹ Degeneration within LGPA giving the appearance of a cystic lesion is also described.¹² Conversely, symptoms and signs said to be characteristic of LGPA may be seen in a number of other lacrimal gland lesions, as evidenced by our series. Applying traditional clinicoradiological criteria, such as the algorithm devised by Rose and Wright,³ thus often fails to distinguish between LGPA and other lacrimal gland lesions. We would like to emphasise that despite a detailed retrospective review of the case records, we were unable to discover any features that may have pointed to a different diagnosis in these cases, except perhaps for the short duration of

Figure 1 (A) A coronal CT image of case 3 showing a mass in the right lacrimal fossa indenting the globe with a relatively poorly defined inferior border (white arrow). The outer margin of the lesion with bone remodelling is marked with a black arrow. The histological diagnosis was follicular lymphoma. (B) An axial CT image of case 10 showing a well-circumscribed mass in the left lacrimal fossa with remodelling of the overlying bone (black arrow). The histological diagnosis was adenoid cystic carcinoma. (C) A coronal CT image of case 4 showing a well-circumscribed mass in the right lacrimal fossa with remodelling of the overlying bone (black arrow). The histological diagnosis was mantle-cell lymphoma. (D) A coronal CT image of case 13 demonstrating a mass in the left lacrimal fossa, note the inferior border of the mass (white arrow). The histological diagnosis was reactive lymphoid hyperplasia.



symptoms in three cases (cases 1, 11 and 13). It is also important to emphasise that five experienced orbital surgeons were involved in this study and the rate of misdiagnosis of LGPA based on clinicoradiological criteria was not significantly different between the centres.

Removal of the lacrimal gland may not result in serious morbidity, except dry eye, especially as some of the lesions mimicking LGPA, such as Sjogren's syndrome and lymphoma, may induce destruction of the lacrimal gland. However, complete excision of the lacrimal gland exposes the patient to unnecessary surgery, and also to the attendant morbidity and expense of lateral orbitotomy, including possible diplopia and temple volume deflation. This approach may also lead to suboptimal management, for example, in patients with adenoid cystic carcinoma, in whom more extensive initial surgery may have been planned if a biopsy diagnosis had been available.

It is interesting to note that in their series on LGPA, Rose and Wright³ included 10 patients who had preoperative biopsy followed by excision of the lacrimal gland and the biopsy track; none of the patients developed recurrence over a mean follow-up of 6 years. Sturgis and co-workers¹³ included three patients with LGPA in their paper on fine-needle aspiration for orbital tumours and noted no complications from the procedure. Rootman *et al*¹⁰ have stated that although inadvertent incisional biopsies are performed in 10–15% of cases, careful removal of the tumour with the biopsy track is associated with a virtually zero recurrence rate. Fine-needle aspiration biopsy (FNAB) is used routinely to diagnose salivary gland pleomorphic adenoma (SGPA) (a tumour with similar natural history to LGPA), and there has been no report of an increased risk of recurrence or malignant transformation following this procedure.^{14 15} At the same time, it is evident that incomplete excision of SGPA leads to a significant risk of recurrence, as is the case for LGPA.¹⁶ The issue of malignant transformation is more controversial, with studies suggesting that malignancy is inherently present in some SGPA and is not influenced by recurrence or incomplete excision.^{17 18} The same may also be true for LGPA.¹⁹ The literature on biopsy in LGPA has been reviewed in a recent perspective article.²⁰ Since FNAB in salivary gland lesions has a predictive accuracy of better than 80%^{14 21} it is a reasonable option to perform FNAB either preoperatively or intra-operatively in suspected lacrimal gland LGPA. In the case of a negative or suspicious result an intra-operative incisional biopsy with frozen section diagnosis may be considered.

It is clear from our study that several different lesions of the lacrimal gland can simulate LGPA clinically and radiologically. We have also seen that traditional criteria used to diagnose LGPA may have a high false-positive rate, and following a strict 'no biopsy' policy thus leads to unnecessary or suboptimal surgery in a significant proportion of patients. We therefore believe that preoperative or intra-operative FNAB, or intra-operative incisional biopsy and frozen section diagnosis are reasonable options for suspected lacrimal gland tumours. If LGPA is diagnosed, lateral orbitotomy

with complete excision of the lacrimal gland together with excision of the biopsy tract is recommended. We also feel that the role of preoperative biopsy for these lesions needs to be re-evaluated.

Competing interests PSC received funding from the Royal College of Ophthalmologists, the Dickinson Trust, Pfizer and the Ethicon Foundation for Ophthalmic Fellowship training in Adelaide. These sponsors had no role in the design or conduct of this study.

Patient consent Obtained.

Ethics approval Institutional Review Board/Ethics Committee approval was obtained for this study.

Provenance and peer review Not commissioned; externally peer reviewed.

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