Pleomorphic adenoma of the lacrimal gland: is there a role for biopsy?

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Abstract

Aim **To review the literature on biopsy of lacrimal gland pleomorphic adenoma (LGPA) and to examine the validity of the prohibition against biopsy in LGPA.**
Method **Literature review.**
Results **LGPA is usually diagnosed preoperatively based on clinical and radiological characteristics, as current teaching advises complete excision without prior incisional biopsy. The caveat against biopsy is based on older studies that reported increased recurrence rates with increased risk of malignant transformation after incomplete excision or biopsy. On the basis of a detailed examination of the literature on biopsy of both LGPA and pleomorphic adenoma of the salivary glands, it appears that there is no clear evidence to support the claim that biopsy increases the risk of recurrence or of malignant transformation of LGPA.**
Conclusion **Lacrimal gland tumours are uncommon lesions and optimal management depends to a great extent on a definite preoperative diagnosis. Preoperative biopsy should therefore be considered in all lacrimal gland mass lesions and management should be tailored to the biopsy findings. If surgical resection is then required, it may be prudent to excise the biopsy tract to ensure complete removal of the tumour.**
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Introduction

Pleomorphic adenoma (benign mixed tumour) of the lacrimal gland accounts for approximately 12–25% of all lacrimal tumours.[1,2] It is well recognised that lacrimal gland pleomorphic adenomas (LGPAs) should be excised completely with a margin of normal tissue as incomplete resection may lead to recurrence, often decades later.[3–9] Furthermore, it has been suggested that there is a significant risk of malignant transformation associated with longstanding or recurrent disease.[3–5] Incisional biopsy is believed to increase the risk of recurrence due to disruption of the pseudocapsule and tumour spillage.[3–5] Hence, the traditional recommendation is that incisional or needle biopsy is strictly contraindicated.[3–9] Insofar as the characteristic clinical and radiological features of LGPA generally make a strong presumptive diagnosis possible, in the majority of cases it is possible to proceed to complete excision with confidence. However, in a number of cases (approximately 15%, unpublished observations), this approach will expose the patient to the morbidity of a lateral orbitotomy and result in unnecessary removal of the orbital lobe of the lacrimal gland. Additionally, this approach may result in less than optimal treatment if the tumour is malignant. Therefore, in selected cases, a preoperative biopsy will help the clinician choose the correct management strategy. This approach is strongly supported by the extensive literature on salivary gland tumours, which are essentially similar to tumours of the lacrimal gland.[10–14] Hence, we question the justification of the 'no biopsy' recommendation in the context of LGPA and examine the validity of the available published evidence.

Review of the literature

One of the earliest studies suggesting an association between biopsy and high recurrence rate of LGPA was the extensive series by Font

and Gamel[5] in 1978. The authors recommended a strict 'no biopsy' policy in the management of LGPA after performing a retrospective analysis of 136 cases of LGPA in the Registry of Ophthalmic Pathology at the Armed Forces Institute of Pathology, which received referral cases from various national and international institutions including Africa and India. It was found that 30 out of 113 follow-up cases (27%) had recurrence. There was no breakdown of percentage of recurrence with reference to different types of management. Furthermore, in the biopsy group, the biopsy and excision method, particularly its completeness, were not described. Actuarial method was used to derive the 5-year recurrence rate. The analysis found that 5-year recurrence rate was 13% overall, 32% for the biopsy prior to excision group, 3% for the excision with the pseudocapsule intact group, 21% for excision with capsule broken group, and 40% for those who had resection after first recurrence. Given that the sample population was recruited from various institutions, it is probable that significant selection biases may have occurred. Furthermore, treatment biases may have included different surgeons, different surgical techniques, biopsy methods and, most importantly, completeness of tumour excision in the biopsy group. Although this large study provided valuable information in the management of LGPA, it is possible the higher recurrence rate in the biopsy group may warrant alternative explanations considering the study method, selection and treatment biases.

A clinicopathological analysis of lacrimal gland tumours published by Ni et al[6] four years later recommended that every effort must be made to remove the tumour with the capsule intact to avoid recurrence and malignant transformation. In their study, there were 88 cases of pleomorphic adenomas of which 72 cases (82%) had ruptured pseudocapsules. Follow-up data were available in 73 cases. They found that the 5-year recurrence rate was 22% and attributed it to the excision technique considering the very high incidence of ruptured pseudocapsules detected histopathologically. However, the authors did not specify the surgical technique used and did not comment on the history of past biopsy prior to surgery.

Henderson[7] reported 25 cases of LGPA from the Mayo Clinic that investigated surgical management of LGPA and recurrence. In total, 14 of the 15 patients who had undergone complete resection had no recurrence with a mean follow-up of 9.7 years (range 3–21 years) and the remaining patient was living after surgery but no data were available concerning tumour recurrence. Four patients did not have an intact removal of their tumour at initial surgery. In two of these four patients, the tumour capsule ruptured with escape of contents into the surgical field. They had no recurrence after follow-up of 9 and 10 years, respectively. One patient had a thorough piecemeal excision as the tumour was necrotic and no recurrence was detected 8 years after surgery. One patient had an incisional biopsy with frozen section histology followed by complete excision and no recurrence was detected after 15 years of follow-up. The remaining six patients had recurrent tumour when they were first seen in Mayo Clinic. These six cases all had had incisional biopsy and incomplete removal of tumour elsewhere, often after an anterior orbitotomy. Therefore, the authors concluded that it is 'the surgeon who makes the initial surgical approach who has the best chance of anyone to cure the disease by complete, intact removal of tumour'.

Rose and Wright[8] in 1992 published a 21-year (1969–1990) case series of 78 patients with LGPA. In total, 63 pleomorphic adenomas (8 palpebral and 55 orbital) were completely excised without prior biopsy. Four had 'possible' intraoperative spillage of tumour cells. The mean follow-up intervals were 1.9 years for the 8 palpebral pleomorphic adenomas and 1.5 and 7.8 years for the 26 and 29 patients with orbital pleomorphic adenomas who underwent partial (with preservation of the palpebral lobe) and total adenectomy, respectively. Overall, no recurrence occurred in the group who underwent total excision without biopsy. Of the 15 patients who had biopsy before surgery, 10 subsequently underwent lateral orbitotomy and total dacryoadenectomy together with excision of the biopsy track, and no recurrence was detected at a mean follow-up of 6 years (range 5–20 years). With regard to the five other patients who underwent incisional biopsies, one developed malignant transformation 44 years after the initial surgery; four had incomplete excision, of whom two developed recurrence of tumour. In the patient who developed malignant change, the initial surgery was performed over four decades prior to presentation and no details were provided on the technique or adequacy of excision. It is notable that neither the 4 patients with intraoperative tumour spill nor the 10 patients who had biopsy followed by complete excision developed recurrence. In contradistinction, recurrence occurred in 50% of those who had incomplete excision. This study demonstrated the high risk of recurrence following incomplete removal of LGPA, but not following tumour spill or biopsy. In fact, in a subsequent reply to a letter to the editor, the authors stated they could not conclusively recommend against biopsy based on the findings of their study.[15]

Recurrence of pleomorphic adenomas after incomplete excision has also been recently reported in a 16-year (1977–1993) series of 42 cases in Tianjin Medical University, China.[9] The follow-up periods ranged from

0.5 to 17 years (mean 4.5 years). The study reported that eight (19%) cases had recurrence secondary to incomplete excision of tumour. Seven of the eight recurrences (87.5%) had multiple surgeries, two had four surgeries, and five had five surgeries. Recurrence in one case was suggested to be due to intraoperative tumour spill 17 years previously. None of the 42 cases had an incisional biopsy before surgery. The authors emphasised the importance of an initial complete excision of tumour to prevent recurrence; but recommended against biopsy by referring to the study by Rose and Wright[8] without adding any further definitive evidence against biopsy.

Rootman has suggested that difficult cases may be biopsied,[16] but individual case reports have produced mixed results on recurrence following incisional biopsy of LGPA. In 2001, Lakhey *et al*[17] published a case that had preoperative fine-needle aspiration biopsy (FNAB) followed by en bloc excision through lateral orbitotomy, and complete excision was confirmed histologically. There was no recurrence after 15 months of follow-up. On the other hand, in 2002, Becelli *et al*[18] reported a case of recurrent pleomorphic adenoma and recommended against incisional biopsy. The patient had an incisional biopsy followed by excision 15 days later. Details of the excision were not provided in the article. The patient noted recurrence 3 years later, but only re-presented 7 years later with extensive tumour that required radical exenteration. In their conclusion, the authors recommended against incisional biopsy and claimed that injury to the capsule by the initial biopsy led to dissemination of tumour cells in the adjacent orbital tissues and exposed the patient to a risk of relapse. However, the claim is not substantially supported by the information provided because tumour recurrence in this case could be attributed to a number of factors, including incomplete resection during the first surgery, the incisional biopsy, or the natural history of the tumour.

It is instructive at this point to briefly review the literature on salivary gland pleomorphic adenomas (SGPAs), tumours that demonstrate a similar natural history to those in the lacrimal glands,[18,19] first recognised by Warthin.[20] Fine-needle aspiration cytology/biopsy (FNAC/FNAB) is extensively used in the diagnosis of salivary gland tumours without any apparent adverse long-term consequences.[21] The technique has a high degree of sensitivity and specificity, with the diagnostic accuracy improving over time and with experience.[21,22] It should be noted that the accuracy of FNAB depends on the experience of the clinician performing the procedure as well as the experience of the cytopathologist interpreting the specimen.[23] Previous concerns regarding pseudocapsule rupture and risk of tumour seeding in the management of salivary gland tumours have been largely discounted and replaced by

concerns as to whether the test is useful and whether it actually affects treatment decisions.[10,11,24–26] Tumour seeding is not known to occur with the use of narrow bore needles currently used for aspiration,[12] and serially sectioning the needle track has not revealed any evidence of tumour seeding.[13] The use of FNAB elsewhere in the body is also not associated with increased risk of recurrence.[27] Though open incisional biopsy is not commonly used to diagnose salivary gland tumours, its use is recommended when FNAB fails to provide the diagnosis.[14] Intraoperative frozen section analysis is also not commonly used as it may be associated with a significant false-positive rate.[28]

It is also interesting to look at the incidence of tumour recurrence and risk of malignant transformation in SGPAs. Using modern surgical techniques, the risk of recurrence is 0–2%, even when prior FNAB has been performed.[24,29] A number of studies have found that pseudocapsule disruption and tumour spill do not increase recurrence of pleomorphic adenomas in salivary glands.[24–26] As one would expect, an inadequate initial resection has been found to be the most important indicator in determining recurrence.[30]

On the issue of malignant transformation in SGPA, while it is generally accepted that there is a progression of benign to malignant change in pleomorphic adenoma, there is no evidence that recurrent tumours have a greater malignant potential.[31] In cases where recurrent tumours have shown malignant transformation, postoperative radiotherapy has been implicated as a risk factor.[32] The absence of a clear correlation between tumour recurrence and malignant transformation supports the view that some SGPA may possess inherent malignant potential.[33,34] It should be noted here that most of the data on SGPA has been obtained from studies on parotid gland pleomorphic adenoma. We agree that there are problems in extrapolating data from one group of tumours to another, but in this case we believe that LGPA and SGPA share sufficient similarities in histology, biological behaviour, and cytogenetic alterations,[35,36] so that data from the more common and more extensively studied SGPA will be of benefit in improving our understanding of LGPA.

From the foregoing review of the literature, it is clear that the apparent potential for tumour recurrence and malignant transformation (largely a result of inadequate excision owing to varying surgical technique) have been instrumental in entrenching the 'no-biopsy' policy for LGPA. It is, therefore, surprising that there is no evidence in the literature to show that incisional biopsy/FNAB, in themselves, leads to a greater risk of recurrence or malignant transformation of LGPA. It appears that this belief is a result of equating incomplete resection with biopsy. While there is no doubt that incomplete resection

has significant adverse long-term consequences, there is no reason to believe that biopsy followed by definitive management carries the same risks. Certainly there is no basis for the belief that performing FNAB or incisional biopsy increases the risk of malignant transformation that is more probably a feature of the natural history of this tumour.

Hence, in summary, the published literature does not provide strong evidence against the use of preoperative biopsy in LGPA. Nevertheless, some caution is merited in the assessment of the evidence as it is acknowledged that recurrence of incompletely excised tumours can take decades and the average follow-up of the available studies is less than 10 years.

Conclusion

On the basis of the review of the available literature on LGPA and with the supporting evidence from the literature on SGPA, we believe that it is no longer tenable to continue a strict 'no-biopsy' policy for suspected LGPA. Lacrimal gland tumours are uncommon lesions and optimal management depends to a great extent on a definite preoperative diagnosis. Preoperative or intraoperative biopsy should, therefore, be considered in all suspected lacrimal gland neoplasia and management should be tailored to the biopsy findings. If surgical resection is then required, it may be prudent to excise the biopsy tract to ensure complete removal of the tumour.

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