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# The role of histopathological characteristics in distinguishing amalgam-associated oral lichenoid reactions and oral lichen planus

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**OBJECTIVES: To identify histological features that distinguish amalgam-associated oral lichenoid reactions (AAOLR) from oral lichen planus (OLP).**

**METHODS: Oral pathologists provided their opinion as to the possibility of distinguishing AAOLR and OLP histologically, the features important in distinguishing AAOLR from OLP and the diagnosis of 12 AAOLR and 12 OLP cases including the features that drew them to their conclusion.**

**RESULTS: There was considerable variation between pathologists in their ability to distinguish the AAOLR and OLP cases. The sensitivity and specificity for histological diagnosis were 40% and 32% respectively. There were four features that were used most commonly to discriminate between AAOLR and OLP: an inflammatory infiltrate located deep to superficial infiltrate in some or all areas; a focal perivascular infiltrate; plasma cells in the connective tissue and neutrophils in the connective tissue. Each was independently predictive of AAOLR or OLP ($P < 0.028$).**

**CONCLUSIONS: This study confirms the uncertainty of the diagnostic histological differences between AAOLR and OLP. Distinguishing these conditions should not rely on histology alone, but should be based on a synthesis of all available information including history, examination, histopathology and skin patch testing.**

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## Introduction

Oral lichen planus (OLP) is a chronic, cell-mediated autoimmune condition in which there is damage to the basal keratinocytes in the oral mucosa. These keratinocytes appear to be recognized by the immune system as antigenically foreign, triggering the release of cytokines, chemokines and other proinflammatory mediators as well as the recruitment of an inflammatory infiltrate composed predominantly of T lymphocytes that results in cell-mediated damage to basal keratinocytes (1). Classical OLP affects approximately 2% (2, 3) of the population and presents clinically as bilateral and symmetrical papular/reticular/erosive lesions of the buccal mucosa, gingiva and tongue. In such cases the trigger for autoimmune damage to the keratinocytes is not known (4).

Patients may also present with oral lesions that resemble OLP that do not fully meet this description. The lesions may be unilateral, asymmetrical or occur in uncommon sites. Some of these cases may represent reactions triggered by drugs or dental materials or be a manifestation of diseases such as graft-vs.-host disease or lupus erythematosus (5). Clinically, the term oral lichenoid reaction (OLR) is given to these. A significant proportion of OLR may be the result of a contact hypersensitivity response in areas of the oral mucosa that are in direct contact with amalgam restorations and are known as an amalgam-associated oral lichenoid reaction (AAOLR) or amalgam-associated hypersensitivity response.

In contrast, the term 'lichenoid tissue reaction' or 'interface stomatitis' has a different connotation to oral pathologists. The term lichenoid tissue reaction was first coined by Pinkus in 1973 (6) and refers to a histological pattern that is not specific to any one disease. The essential features are damage to the basal keratinocytes usually in the form of apoptosis, an infiltrate of

inflammatory cells in the connective tissue that may also extend into the epithelium and keratosis/hyperkeratosis. This pattern is seen in a number of diseases affecting the oral cavity including OLP, OLR, AAOLR, erythema multiforme, discoid lupus erythematosis (DLE) and graft-vs.-host disease. Differentiating between these conditions may be challenging for the pathologist not least because of the lack of agreed criteria and in most cases, diagnosis is made using a combination of clinical and histological features. For example, in order to make the diagnosis of graft-vs.-host disease, there must be a previous history of a bone marrow transplant. However, it has been possible to define histological criteria that distinguish oral DLE from OLP (7). Schiødt (7) found that in addition to the lichenoid tissue reaction, keratin plugging, atrophy of the rete processes, a deep inflammatory infiltrate, oedema in the lamina propria and a thick periodic acid-Schiff (PAS)-positive deposit in the basement membrane zone showed a sensitivity of 92% and a specificity of 96% against OLP. The use of similar terms with different meanings to clinician and pathologist is confusing and for this reason we have confined ourselves to the clinical use of the term OLR and narrowed it further still to amalgam-associated lichenoid reactions, as defined in the Methods section.

In 1978, the World Health Organization (WHO) Collaborating centre for oral precancerous lesions produced both clinical and histopathological criteria for the diagnosis of OLP. However, the validity of these features in the diagnosis of OLP has not been tested and there are no agreed criteria to distinguish histologically between OLP and OLR (5) or AAOLR.

The purpose of this study was to determine which histological features, if any, help to distinguish clinically diagnosed AAOLR from OLP. To do this a panel of consultant oral pathologists from different institutions in the UK were invited to provide their opinion on the following:

1 Whether it is possible to distinguish histologically between lesions diagnosed clinically as AAOLR and OLP.
2 Which histological features are important in distinguishing between AAOLR and OLP.
3 The histological diagnosis of 24 samples (12 clinically diagnosed AAOLR and 12 OLP), listing the features that drew them to their conclusion.

This information was then used to determine if the presence or absence of particular features could help to improve the accuracy of histological diagnosis in distinguishing AAOLR and OLP.

## Methods

The study had two stages.

*Stage 1*

Eight consultant oral pathologists in the United Kingdom were invited to identify histological features that help to distinguish between AAOLR and OLP. Five agreed to participate. First, the pathologists were asked 'Do you believe it is possible to distinguish OLP and lichenoid reactions to amalgam histologically'? and to indicate their response on a 4-point scale that included; never, sometimes, often and always.

Each pathologist was then given a list of histological features used by Schiødt to distinguish DLE from OLP, leukoplakia and galvanic lesions (7). They were asked to identify those features they felt were more strongly suggestive of AAOLR and those more strongly suggestive of OLP. For each selected feature they were asked to score the level of importance they attached to that feature where: 1, was low; 2, moderate and 3, the highest level of importance. If no score was given, the feature was assigned a rating of 0. The total score for each feature ranged from 0 to 15 as there were five pathologists and each could give a maximum score of 3 for any particular feature. The pathologists were also asked to provide a list of any additional diagnostic features they thought were important in distinguishing AAOLR and OLP that were not included in the list produced by Schiødt (7). The pathologists identified four new features (items 17a, 24a, 53 and 54) and the list was modified to produce a consensus list that included these additional features (Table 1).

*Stage 2*

The pathologists were given the consensus list (Table 1) as well as a set of haematoxylon and eosin (H & E)- and PAS-stained sections of lesional biopsies from a panel of 12 clinically diagnosed AAOLR and 12 OLP specimens described previously (8). Briefly, 12 specimens came from patients who had lesions that were consistent clinically with an AAOLR, i.e. lichenoid lesions confined to areas of the mucosa in direct contact with amalgam restorations. In each case, these patients were also skin patch test-positive for mercury or amalgam alloy and the oral lesions resolved on removing the restorations with which they were associated. The other 12 came from patients who clinically had classical OLP. These 12 patients were all patch test-negative for mercury and amalgam, their lesions were bilateral and symmetrically located on the oral mucosa and the lesions had no clear clinical association with amalgam restorations. None of the sections used in this study showed any evidence of the presence of *Candida*. Additionally, none of the patients had a medical history consistent with lupus erythematosus or graft-vs.-host disease.

Each pathologist was given the same set of 24 slides to examine. The slides for each of the 12 AAOLR and 12 OLP cases were randomly ordered and sequentially numbered but the order and numbering was different for each pathologist and the code was held by the study co-ordinator.

The pathologists were asked to assess the slides blind to the clinical diagnosis and decide if they were from a patient with clinically diagnosed AAOLR or OLP, or if it was not possible to say. They were also asked to list the histological features of each specimen that were influential in determining their diagnosis. No weighting was attributed to the features. In some cases patholo-

**Table 1** List of histological features modified from Schiødt (7)

| **Histological features** |
|---|
| Epithelium – keratinization |
| 1. Hyperorthokeratosis |
| 2. Hyperparakeratosis |
| 3. Keratotic plugging |
| 4. Keratotic pearls |
| 5. Chevron keratinization |
| Epithelium – thickness and configuration |
| 6. Atrophy; reduction in thickness more than 1/3 of normal area |
| 7. Acanthosis; broadening of rete ridges more than two time normal width for area |
| 8. Simple hyperplasia; thickness more than $1\frac{1}{2}$ time normal thickness for area, excluding stratum corneum |
| 9. Atrophy alternating with hyperplasia |
| 10. Pseudoepitheliomatous hyperplasia; very irregular hyperplasia which, on low magnification, has superficial resemblance to carcinoma |
| 11. Epithelial islands in connective tissue; section must not be tangentially cut or showing signs of torsion |
| 12. Finger-like rete ridges |
| 13. Drop-shaped rete ridges |
| 14. Sawtooth rete ridges |
| Epithelium – other |
| 15. Thin stratum granulosum, < 5 cell layers thick |
| 15a. Thick stratum granulosum, more than five cell layers thick |
| 16. Migration by leucocytes; easily visible small groups or heavy infiltration by leucocytes |
| 17. Microabscesses; aggregations of neutrophils in superficial part of epithelium |
| *17a. Prominent epithelial macrophages*[a] |
| 18. Liquefaction degeneration of basal layer |
| 19. Intraepithelial vesicles; subepithelial vesicles excluded |
| Epithelial – cellular changes |
| 20. Colloid bodies – civatte bodies |
| 21. Multinucleated epithelial cells; cells containing three or more nuclei |
| 22. Hyperchromatism |
| 23. Pleomorphism |
| 24. Epithelial dysplasia; slight, moderate or severe |
| *24a. Supra-basilar apoptosis*[a] |
| Connective tissue – superficial inflammatory infiltrate |
| 25. Band-shaped infiltrate, some areas |
| 25a. Band-shaped infiltrate, all areas |
| 26. Not band-shaped infiltrate, some areas |
| 26a. Not band-shaped infiltrate, all areas |
| 27. Focal/perivascular infiltrate |
| 28. Germinal follicles/dense inflammatory infiltrate |
| 29. Intensity of inflammatory infiltrate: none or slight |
| 29a. Intensity of inflammatory infiltrate: moderate or heavy |
| Connective tissue – deep inflammatory infiltrate |
| 30. Deep inflammatory infiltrate; located deep to superficial infiltrate, some or all areas |
| 31. Focal/perivascular infiltrate |
| 32. Germinal follicles |
| 33. Intensity of inflammatory infiltrate: none |
| 33a. Intensity of inflammatory infiltrate: slight |
| 33b. Intensity of inflammatory infiltrate: moderate or heavy |
| Connective tissue – cell types of inflammatory infiltrate |
| 34. Lymphocytes and histiocytes |
| 35. Plasma cells |
| 36. Neutrophils |
| 37. Eosinophils |
| Connective tissue – juxtaepithelial area |
| 38. Juxtaepithelial cell-free zone; narrow eosinophilic zone separating basal cells from inflammatory infiltrate |
| 39. Hyalinization of collagen |
| 40. Basophilia of collagen |
| 41. Melanophages |
| 42. Oedema |
| 43. Subepithelial vesicles |
| Connective tissue – PAS-positive deposits |
| 44. Thin continuous deposits ≤ height of basal cell nuclei; resembles thickening of basement membrane |
| 44a. Thick continuous deposits > height of basal cell nuclei |
| 45. Thin patchy deposits ≤ height of basal cell nuclei |
| 45a. Thick patchy deposits > height of basal cell nuclei |
| 46. Intracellular and extracellular PAS-positive granules |
| 47. PAS-positive bodies, size of plasma cell or larger |
| Connective tissue – vessels |
| 48. Dilatation of vessels |
| 49. Neutrophils in lumen of vessels |
| 50. Extravasation of erythrocytes |
| 51. PAS-positive thickening of vessel walls |
| Yeasts |
| 52. PAS-positive hyphae in epithelium |
| *53. Intact basal lamina*[a] |
| *54. Disruption of basal lamina*[a] |

[a]Additional features suggested for inclusion by the pathologists at the end of stage 1 are shown in italics.
PAS, periodic acid-Schiff.

gists used the absence of a feature to draw their conclusion and where this was the case, they were asked to list these as 'negative features'. For example, if a pathologist felt that absence of a 'deep inflammatory infiltrate, located deep to superficial infiltrate, some or all areas' (feature 30) was important in influencing their conclusion that this was a case of OLP rather than an AAOLR, then feature 30 was listed as a negative feature for OLP on that particular slide.

*Analysis*

In stage 1, the scores for each feature were summed for all five pathologists. In stage 2, the number of times each positive or negative feature was used to correctly diagnose AAOLR or OLP for all five pathologists was totalled. The results are reported separately for all AAOLR and OLP specimens. Comparisons were made by bivariate analyses using chi-squared tests and multivariate analyses were carried out using logistic regression. Significance levels were set at $P \leq 0.05$.

## Results

Table 1 is the consensus list of histological features, modified from Schiødt (7) that was used to describe the specimens. Prominent epithelial macrophages (feature 17a), supra-basal apoptosis (feature 24a), intact basal lamina (feature 53) and disruption of basal lamina (feature 54) were features added by the reviewing pathologists. When pathologists were asked 'do you believe it is possible to distinguish OLP and OLR to amalgam histologically', one responded that this could be done 'often', while the other four responded 'sometimes'.

Figure 1 is a histogram of the weighted features that the pathologists predicted would be important in distinguishing OLP and AAOLR and which they scored prior to reviewing the slide sets. Those features scoring ≥2 are also shown in Table 2. With the exception of feature 25a (band-shaped infiltrate – all areas) which

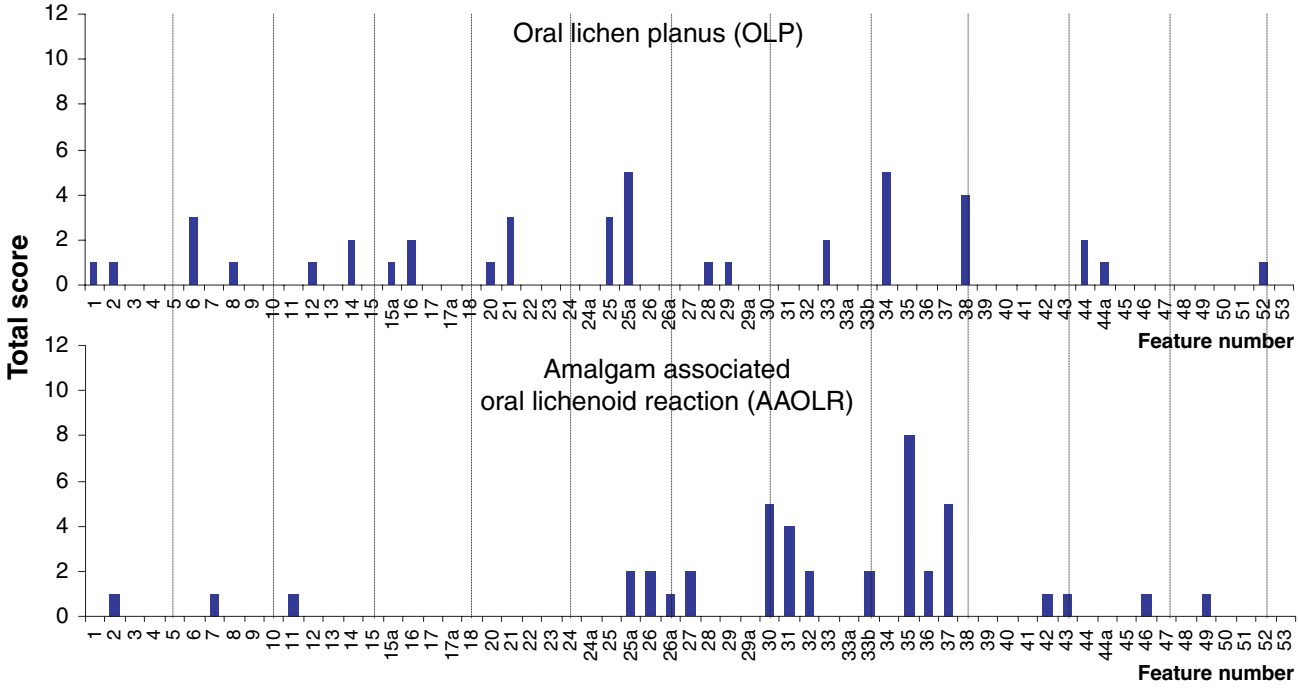


**Figure 1** From stage 1, features pathologists predicted would be helpful in distinguishing OLP (top graph) and amalgam-associated oral lichenoid reaction (AAOLR; bottom graph). Each pathologist ($n = 5$) assigned a score of 0–3 for their value in distinguishing OLP or AAOLR. Therefore, the maximum possible score per feature was 15. This graph shows the total score for each feature.

was predicted to be a feature of both (score 5 for OLP and 2 for AAOLR), those items that scored ≥2 in the predicted list for OLP did not appear in the predicted list for AAOLR and vice versa.

Figure 2 illustrates all the features that pathologists actually cited in support of their diagnosis when they correctly diagnosed OLP or AAOLR from the set of slides. Hyperorthokeratosis (feature 1), hyperparakeratosis (feature 2), liquefaction degeneration of the basal cell layer (feature 18) and lymphocytes and histiocytes in the infiltrate (feature 34) were cited more than three times as positive features for both conditions while supra-basal apoptosis (feature 24a), band-shaped infiltrate – some areas (feature 25) and lymphocytes and histiocytes in the infiltrate (feature 34) were cited as both negative and positive features of AAOLR. These features were therefore excluded from further analysis and the remaining features are listed in Table 3. Of these, the presence of a deep inflammatory infiltrate in some or all areas (feature 30), a focal/perivascular infiltrate (feature 31), the presence of plasma cells (feature 35) or eosinophils (feature 36) were discriminators of OLP and AAOLR on bivariate analysis ($P \leq 0.01$). All were identified as positive features for the diagnosis of AAOLR but negative features for OLP. These features were placed into a logistic regression analysis and each feature was found to be independently predictive of OLP or AAOLR ($P < 0.028$).

Of the 10 features predicted by pathologists to be helpful in distinguishing AAOLR (Table 2), six were actually used to correctly diagnose AAOLR when the pathologists assessed the cases. However, for OLP, only two of 10 of the predicted features were actually used to distinguish OLP (Table 3).

There was considerable individual variation between pathologists in their ability to distinguish the 12 AAOLR and 12 OLP cases using the sections provided (Table 4). The sensitivity and specificity for histological diagnosis was 40% and 32%, respectively, and when the analysis was restricted to those cases that the pathologists deemed interpretable it was 59% and 48% respectively. None of the pathologists was able to correctly distinguish seven of the 12 OLP cases or two of the 12 AAOLR cases on the basis of the specimen provided for evaluation. Overall interobserver agreement in the histological assessment of AAOLR and OLP (κ) for the five raters at three levels of responses (AAOLR, OLP and 'unable to distinguish') was 0.36 with variance of 0.0052 (9).

## Discussion

Oral lichen planus and AAOLR are common inflammatory diseases, the management of which is most often the responsibility of oral medicine specialists or general dentists. OLP is a chronic relapsing condition of unknown aetiology for which there is currently no cure. Treatment, therefore, is largely palliative and directed at suppressing disease activity and the size and occurrence of painful erosive lesions, using topical steroids and other immunosuppressants. Such treatment may need to

**Table 2** Features that the pathologists predicted would be important in distinguishing between OLP and AAOLR

| *Feature* | *Weighted score* | *Feature group* | *Feature description* |
|---|---|---|---|
| Features predicted for OLP | | | |
| *25a* | *5* | *Connective tissue – superficial inflammatory infiltrate* | *Band-shaped infiltrate, all areas* |
| 34 | 5 | Connective tissue – cell types of inflammatory infiltrate | Lymphocytes and histiocytes |
| 38 | 4 | Connective tissue – juxtaepithelial area | Narrow eosinophilic zone separating basal cells from inflammatory infiltrate |
| 6 | 3 | Epithelium – thickness and configuration | Atrophy; reduction in thickness more than 1/3 of normal area |
| 21 | 3 | Epithelial – cellular changes | Multinucleated epithelial cells: cells containing three or more nuclei |
| 25 | 3 | Connective tissue – superficial inflammatory infiltrate | Band-shaped infiltrate, some areas |
| 14 | 2 | Epithelium – thickness and configuration | Sawtooth rete ridges |
| 16 | 2 | Epithelium – other | Migration by leucocytes; easily visible small groups or heavy infiltration by leucocytes |
| 33 | 2 | Connective tissue – deep inflammatory infiltrate | Intensity of infiltrate: none |
| 44 | 2 | Connective tissue – PAS-positive deposits | Thin continuous deposits ≤ height of basal cell nuclei; resembles thickening of basement membrane |
| Features predicted for AAOLR | | | |
| 35 | 8 | Connective tissue – cell types of inflammatory infiltrate | Plasma cells |
| 30 | 5 | Connective tissue – deep inflammatory infiltrate | Located deep to superficial infiltrate some or all areas |
| 37 | 5 | Connective tissue – cell types of inflammatory infiltrate | Eosinophils |
| 31 | 4 | Connective tissue – deep inflammatory infiltrate | Focal/perivascular infiltrate |
| *25a* | *2* | *Connective tissue – superficial inflammatory infiltrate* | *Band-shaped infiltrate, all areas* |
| 26 | 2 | Connective tissue – superficial inflammatory infiltrate | Not band-shaped infiltrate, some areas |
| 27 | 2 | Connective tissue – superficial inflammatory infiltrate | Focal/perivascular infiltrate |
| 32 | 2 | Connective tissue – deep inflammatory infiltrate | Germinal follicles |
| 33b | 2 | Connective tissue – deep inflammatory infiltrate | Intensity of infiltrate: moderate or heavy |
| 36 | 2 | Connective tissue – cell types of inflammatory infiltrate | Neutrophils |

Features that received a score ≥2 are listed in rank order (score shown).
Feature 25a (shown in italics) appears in both lists.
OLP, oral lichen planus; AAOLR, amalgam-associated oral lichenoid reaction; PAS, periodic acid-Schiff.

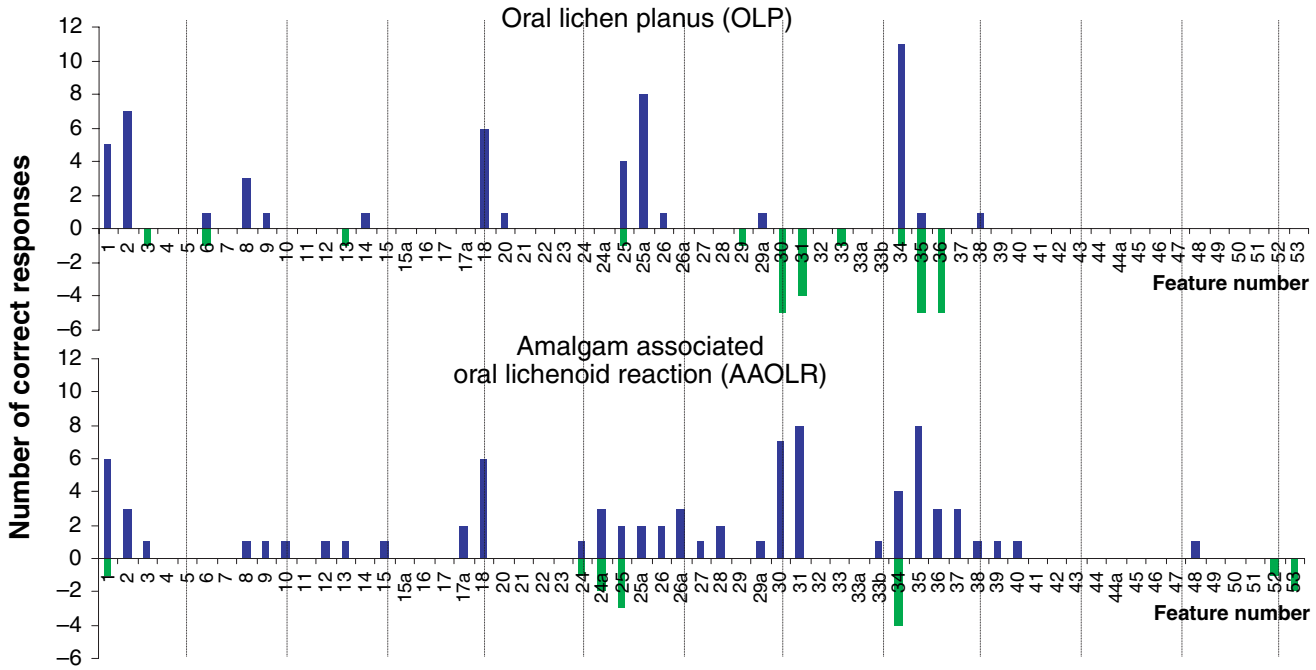


**Figure 2** The actual number of times a positive (blue bars shown above the line) or negative feature (green bars below the line) was used in making the correct diagnosis of OLP (top graph) or AAOLR (bottom graph).

**Table 3** Features most frequently used to correctly distinguish OLP and AAOLR

| *Feature* | *Usage score* | *Feature (±)* | *Feature group* | *Feature description* |
|---|---|---|---|---|
| Features used in the correct diagnosis of OLP | | | | |
| 25a | 8 | + | Connective tissue – superficial inflammatory infiltrate | Band-shaped infiltrate, all areas |
| 25 | 4 | + | Connective tissue – superficial inflammatory infiltrate | Band-shaped infiltrate, some areas |
| 30* | 5 | − | Connective tissue – deep inflammatory infiltrate | Located deep to superficial infiltrate, some or all areas |
| 35* | 5 | − | Connective tissue – cell types of inflammatory infiltrate | Plasma cells |
| 36* | 5 | − | Connective tissue – cell types of inflammatory infiltrate | Neutrophils |
| 31* | 3 | − | Connective tissue – deep inflammatory infiltrate | Focal/perivascular infiltrate |
| Features used in the correct diagnosis of AAOLR | | | | |
| 31 | 8 | + | Connective tissue – deep inflammatory infiltrate | Focal/perivascular infiltrate |
| 35 | 8 | + | Connective tissue – cell types of inflammatory infiltrate | Plasma cells |
| 30 | 7 | + | Connective tissue – deep inflammatory infiltrate | Located deep to superficial infiltrate some or all areas |
| 26a | 3 | + | Connective tissue – superficial inflammatory infiltrate | Not band-shaped infiltrate, all areas |
| 36 | 3 | + | Connective tissue – cell types of inflammatory infiltrate | Neutrophils |
| 37 | 3 | + | Connective tissue – cell types of inflammatory infiltrate | Eosinophils |

Positive (+) and negative (−) features most frequently cited in support of their diagnosis by the five pathologists when they correctly distinguished OLP or AAOLR from histological sections of 12 cases of OLP and 12 cases of AAOLR. The number of times each feature was cited is shown (usage score) and whether its presence (+) or absence (−) was used in determining the diagnosis.
*Features found to be discriminate between OLP and AAOLR on bivariate analysis ($P \leq 0.011$).
OLP, oral lichen planus; AAOLR, amalgam-associated oral lichenoid reaction.

**Table 4** Identification of cases by pathologists

| *Pathologist (No.)* | *Cases where diagnosis made, n (%)*[a] | *Correct diagnoses, n (%)* | | *Interpretable cases*[b] | | *All cases*[c] | |
|---|---|---|---|---|---|---|---|
| | | *Interpretable cases*[b] | *All cases*[c] | *Sensitivity (%)* | *Specificity (%)* | *Sensitivity (%)* | *Specificity (%)* |
| 1 | 19/24 (79) | 11/19 (58) | 11/24 (46) | 63 | 55 | 42 | 50 |
| 2 | 15/24 (63) | 5/15 (33) | 5/24 (21) | 40 | 30 | 17 | 25 |
| 3 | 11/24 (46) | 6/11 (55) | 6/24 (25) | 100 | 38 | 25 | 25 |
| 4 | 21/24 (88) | 12/21 (57) | 12/24 (50) | 67 | 50 | 50 | 50 |
| 5 | 18/24 (75) | 9/18 (50) | 9/24 (38) | 43 | 67 | 25 | 50 |
| All | 84/120 (70) | 43/84 (51) | 43/120 (36) | 59 | 48 | 32 | 40 |

[a]There were various reasons why pathologists felt they were unable to make a diagnosis (uninterpretable cases) between AAOLR and OLP including: insufficient distinguishing features; the changes were only very mild; the biopsy specimen was poorly orientated and/or the sample was too small.
[b]Correct diagnoses, sensitivity and specificity expressed as a proportion of interpretable cases only.
[c]Correct diagnoses, sensitivity and specificity expressed as a proportion of all cases.
OLP, oral lichen planus; AAOLR, amalgam-associated oral lichenoid reaction.

be continued over many years (10). In contrast, in AAOLR, the causative agent (mercury or amalgam alloy) is known, and replacement of the offending amalgam restorations with other materials or preventing mucosal contact with the restorations results in complete resolution of the lesions within 3–6 months in the majority of patients (8). Hence, it is important to distinguish these two lesions as their management and clinical outcome are completely different.

The histological features of the 'lichenoid tissue reaction' that characterize the diagnosis of OLP and OLR are well known and from a histopathological point of view it is possible to exclude malignancy and other causes of white erosive or ulcerative lesion affecting the oral mucosa with a degree of certainty. However, because of the lack of agreed criteria for distinguishing AAOLR from OLP, it is not clear how effective histopathology alone is in distinguishing between the two and pathologists differ significantly in their opinion about their ability to make the distinction. At the outset of this study, one of the five pathologists felt it was 'often' possible to distinguish AAOLR from OLP histologically, while four felt this could only be done 'sometimes'.

This study also confirmed the difficulty of making the distinction between AAOLR and OLP purely on histological grounds. Overall, the oral pathologists were able to correctly distinguish the two conditions in only one-third of the cases and even out of those cases they felt were interpretable the diagnosis was correct $<60\%$ of the time and the sensitivity and specificity for histological diagnosis was low. However, this interpretation of 'correct diagnosis' from a histopathological point of view assumes that the clinical diagnosis of AAOLR and OLP in our cases was correct. Whilst the clinical criteria in this study are well defined, difficulties in agreement between clinicians in the diagnosis of OLP have been highlighted by other studies. One study found inter-

observer agreement (κ) varied from 0.43 (moderate) to 0.77 (good) using the WHO criteria for the diagnosis of OLP (11). Our study yielded an overall κ of 0.36, indicating a poor to moderate level of agreement between pathologists in distinguishing AAOLR and OLP on histopathological information alone.

In our study no pathologist was able to correctly distinguish seven of the 12 cases of OLP presented to them. This lack of correlation between the histological and clinical diagnosis of OLP has been found in other studies. Van der Meij and Van der Waal (12) found that clinicians only agreed on the clinical diagnosis of OLP in 42% of cases and of these there was no consensus among the pathologists on the histopathological diagnosis. Similarly, in 50% of cases in which pathologists agreed a histopathological feature was diagnostic of OLP there was a lack of consensus on the clinical diagnosis. Clearly there is a need to standardize the clinical and histological diagnosis of OLP as well as to determine which criteria, if any, may be important in distinguishing AAOLR from OLP.

There were many instances in our study where the pathologists felt that it was impossible to determine the diagnosis. The reasons given included: cellular atypia (which would negate either diagnosis), insufficient specimen size, poor sample orientation, fragmented specimen, mild changes only and/or the specimen contained features which the pathologist felt was common to both AAOLR and OLP. Because some of the reasons relate to the size and orientation of the specimen, it is important that clinicians ensure they take a large enough sample from the most affected area, extend into normal tissue and if possible, orient the specimen when submitting the biopsy.

Although there are no agreed criteria, each pathologist was asked which histological features would be helpful in diagnosing AAOLR and OLP. Pathologists were better able to predict histological features for the diagnosis of AAOLR than OLP. They used six of their predicted nine features in the diagnosis of AAOLR but only two of the nine predicted features for the diagnosis of OLP. Overall the pathologists predicted that distinguishing features would be present in both the connective tissue and the epithelium in OLP but only in the connective tissue in AAOLR. In reality, the positive distinguishing features cited in both conditions involved only the connective tissue.

The essential defining features of an AAOLR should not be common to OLP and OLR and would be expected to be of value in discriminating between the two. This was indeed the case: pathologists cited hyperortho- or para-keratosis, liquefaction degeneration of the basal cell layer and lymphocytes and histiocytes in the infiltrate as features of both AAOLR and OLP. However, using bivariate analysis four features did appear to discriminate between AAOLR and OLP. The following features may be present in AAOLR: (i) an inflammatory infiltrate located deep to superficial infiltrate in some or all areas, (ii) focal perivascular infiltrate, (iii) plasma cells in the connective tissue and (iv) neutrophils in the connective tissue. Whereas, in OLP these features are absent. Thus, it appears that it is the characteristics of the infiltrate within the connective tissue rather than epithelial changes that are most important in distinguishing between AAOLR and OLP. However, when using these characteristics to distinguish between AAOLR and OLP it is important to exclude both the presence of *Candida* and areas of ulceration both of which may result in accumulations of neutrophils and plasma cells. In the present study, each pathologist was provided with a PAS-stained slide to exclude the presence of *Candida*.

Interestingly, a band-shaped infiltrate in some or all areas has been cited as one of the most important diagnostic features in the diagnosis of OLP (12). In our study although this feature was used to successfully distinguish AAOLR from OLP, it did not reach significance on bivariate analysis.

This study confirms the difficulties in distinguishing AAOLR and OLP using histological criteria only. The problem is compounded by the fact that disease activity, and hence histology, may vary over time and by the broad spectrum of histopathological appearances that may be seen in both AAOLR and OLP (13). However, four features did appear to be useful in discriminating between the two: a deep or perivascular inflammatory infiltrate in some or all areas and the presence of plasma cells and neutrophils. In clinical practice most pathologists use a combination of the histological and clinical features in order to arrive at a correct diagnosis. A good clinical description of the oral lesions, information on whether the lesions are bilateral or symmetric, the sites affected in the oral cavity, the proximity of alloy restorations to the lesions, the presence and nature of lesions elsewhere and an adequate specimen are all essential information for the pathologist.

In conclusion, this study confirms the difficulty of distinguishing AAOLR and OLP on histological features alone and indicates the importance of patient management being based on a synthesis of all available information including the history, clinical examination, histopathology and the results of special investigations such as skin patch testing.

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