Common Sense Pathology

A REGULAR CASE-BASED SERIES ON PRACTICAL PATHOLOGY FOR GPs

Contents:
• Excisional, incisional and other biopsies
• Getting the most from histology tests
• Making sense of pathology reports
• Telling patients about prognosis

Sampling suspicious pigmented lesions

A JOINT INITIATIVE OF

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Introduction

It is well recognised that Australia and New Zealand have the highest incidence of skin melanoma in the world, resulting in significant morbidity, mortality and healthcare costs. Considerable effort is devoted to both reducing the onset of melanoma through safe-sun campaigns and in the early detection of melanoma. Early diagnosis and treatment (either as in situ or only superficially invasive disease) should result in an excellent prognosis.

Removal of suspicious pigmented lesions is widely practiced by GPs and dermatologists in an effort to pick up melanomas at this earliest stage. The majority of newly diagnosed invasive melanomas are localised lesions that have not metastasised. However, melanoma is a highly unpredictable disease, and a guarantee of cure cannot be made, even with thin lesions 1mm or less in depth.

Not all melanomas are pigmented (amelanotic melanomas exist) and not all pigmented skin lesions are melanocytic. Clinical diagnosis is beyond the scope of this article, which will focus on histological features concerning for melanoma. The optimum initial approach is, therefore, complete excision with a 2mm margin of normal skin and a rim of subcutis, provided that a cosmetically acceptable result can be achieved.

Clinical scenario 1

A 62-year-old fair-skinned woman presents with a pigmented lesion on her back, which she has become concerned about. It has apparently increased in size over the past year and some areas have become darker, while others have become paler. The patient indicates that the lesion bled a few weeks ago and then scabbed over. You have treated the patient previously for several basal cell carcinomas on the limbs and trunk. On examination, a 10mm diameter, variably pigmented, macular lesion is present between the shoulder blades. The margin is fairly clearly defined, with a few features concerning for melanoma. The lesion bled a few weeks ago and then scabbed over. You have treated the patient previously for several basal cell carcinomas on the limbs and trunk.

What is the best approach to this lesion?

This is a suspicious pigmented skin lesion with features concerning for melanoma. The optimum initial approach is, therefore, complete excision with a 2mm margin and a cuff of subcutis, provided that a cosmetically acceptable result can be achieved.

Orientation of the specimen by attaching a suture form. This ensures that the specimen is dissected in the laboratory so as to best demonstrate the suspicious
A 72-year-old man of South-East Asian ancestry has undergone a fruitless procedure.

The patient has presented for a skin biopsy at the request of his wife. The findings were unremarkable except for a darkly pigmented lesion on the forearm of an 80-year-old woman who has attended for a review of her diabetes medication. She has extensive solar damage and a history of multiple non-melanoma skin cancers.

The lesion is 18mm in diameter and shows scaling and erythema with telangiectasia, blonchy pigmentation and partly circumscribed margins. It is not raised and there is no induration or ulceration. Dermoscopy shows specks of brown and grey pigment, with shiny white to red areas and arborising telangiectasia. You consider that, although melanoma is a possibility, it is unlikely.

What is the best approach to this lesion?

Since the tumour is unlikely to be a melanoma, a partial biopsy is acceptable.

You decide to perform two 4mm punch biopsies. Results of histopathology identify a pigmented superficial pattern basal cell carcinoma.

It is important to remember that not every pigmented lesion is melanocytic. Pigmentation is common in a huge variety of skin lesions including basal cell carcinomas and Bowen’s disease (figure 2). Seborrhoeic keratosis, lichenoid keratosis, diabetic dermatopathy and vascular lesions such as an acquired elastotic keratosis, lichenoid keratosis, diabetic dermopathy can all be clinical considerations in this case. Incidentally, solar lentigos are now considered primarily disorders of keratinocyte pigmentation, with little or no increase in melanocytes.

When the probability of melanoma is low, a partial biopsy may be appropriate.

Clinical scenario 2

You notice a flat pigmented area on the forearm of an 80-year-old man who has attended for a review of his diabetes medication. The lesion has extensive solar damage and a history of multiple non-melanoma skin cancers.

The lesion is 18mm in diameter and shows scaling and erythema with telangiectasia, blonchy pigmentation and partly circumscribed margins. It is not raised and there is no induration or ulceration. Dermoscopy shows specks of brown and grey pigment, with shiny white to red areas and arborising telangiectasia. You consider that, although melanoma is a possibility, it is unlikely.

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Clinical scenario 3

A 72-year-old man of South-East Asian ancestry has undergone a fruitless procedure.

The patient has presented for a skin biopsy at the request of his wife. The findings were unremarkable except for a darkly pigmented lesion on the forearm of an 80-year-old man who has attended for a review of his diabetes medication. The lesion has extensive solar damage and a history of multiple non-melanoma skin cancers.

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A partial biopsy could complicate subsequent assessment of the excision sample and evaluation of prognostic data (eg, tumour thickness) may be compromised. Biopsy of a melanoma prior to excision, however, does not appear to adversely affect prognosis.

Partial biopsies are a significant cause of litigation; however, an erroneous pathology report that does not accord with clinical features does not mean that the pathologist will take all of the blame. Australian case law has determined that a negligent pathology report may not exclude the referee from negligence if symptoms and signs should have prompted action, regardless of the pathology report.

Making sense of the pathology report
Melanoma histopathology reports have become increasingly complex over the years with the addition of an array of pathological features. This can be bewildering for the non-specialist or for those who only occasionally treat patients with melanoma (figure 4). Some histological features reported are of limited proven prognostic value and their identification can be highly subjective. However, the most important prognostic features in a pathology report have become more clearly defined in recent years.

What are the most important elements?
There are five crucial features in a melanoma report that help determine stage, prognosis and appropriate treatment.

1. Breslow thickness. This is the single most important prognostic factor for melanomas that have not metastasised. It is the microscopic depth (in mm) to which the melanoma invades the skin, measured from the top of the epidermal granular layer to the most deeply invasive tumour cell (figure 5). Can be difficult to determine precisely, but the phenomenon may account for rare metastases from apparently in situ tumours. It can also lead to an underestimation of Breslow thickness.

2. Regression. Tumours may undergo partial involution, which has been associated with a worse prognosis in many studies. The reasons for this are not entirely clear, but the phenomenon may account for some metases from apparently in situ tumours. It can also lead to an underestimation of Breslow thickness.

3. Ulceration. Spontaneous loss of the epidermis over a melanoma is associated with a worse prognosis. It must be distinguished from the effects of trauma or prior treatment, so it is important to mention on the request form if the melanoma has been previously treated, biopsied or traumatised.

4. Mitotic rate. This is a measure of tumour proliferation (recorded per mm² in the dermis only). An increased mitotic rate has been shown to predict more aggressive behaviour. The presence of mitoses is now used as part of the American Joint Committee on Cancer staging system.

5. Margins of excision. Adequate clearance from the peripheral and deep margins of the sample is essential and should be clearly stated in mm for both invasive and in situ areas of tumour. Currently recommended margins are indicated in table 1 (next page).

Additional Factors. Most reports include supplementary pathological features that may be important in refining prognosis and risk of recurrence, such as tumour type and perineural or lymphovascular invasion. Lymphocytic infiltrate, cell type and growth phase are poorly reproducible and of less significant value clinically. Clark level is now largely considered to be relevant only in thin melanomas in which mitotic rate cannot be determined. Its importance is substantially outweighed by Breslow thickness.

Tumours that are histologically predominately desmoplasic may have a better prognosis. Microsatellites (spread of tumour cells to skin adjacent to the melanoma) are considered localised metastases and predict an adverse prognosis, indicating that the tumour is at least stage III. If there are any aspects of the melanoma report that are unclear, the referring clinician should be contacted for clarification. When the diagnosis is unsuspected or at odds with the clinical impression, discussion with the pathologist is essential. On occasions, it may be appropriate to request that the slides are reviewed and perhaps even sent for second opinion to another pathologist with experience in reporting melanocytic lesions. The vast majority of pathologists would be more than happy to facilitate a second opinion.

Telling patients about prognosis
Melanoma prognosis directly relates to clinical stage, namely, how far the tumour has spread. However, most melanomas excised in general practice are clinical stage I or II lesions, confined to the skin, with no metastases. In these patients, prognosis is principally determined by Breslow thickness. Thin melanomas (1mm or less in depth) have an excellent outlook, but even in this group, a cure cannot be guaranteed.

Making predictions about the behaviour of any malignancy is notoriously difficult. In addition to the pathological features outlined above, an unfavourable prognosis is seen with advanced age and in males. Tumours of the head and neck, palms, soles and nails also tend to fare somewhat worse. Pregnancy does not appear to affect prognosis.

Many prognostic models have been developed over the years, but all suffer from the problem that the predictions are more applicable to populations as a whole than to a single individual. Some patients are reluctant to consider further information about what a melanoma diagnosis means for their future, but increasingly patients are seeking guidance as to how the tumour may affect their lifestyle and lifespan.

One of the best available prognosis resources is an on-line calculator developed by the American Joint Committee on Cancer at www.melanomaprognosis.org. These predictions have been calculated from a series of 25,734 patients with localised melanoma and 2313 with metastatic melanoma from 11 large centres across the world, including Australia. However, such tools are only a rough guide and caution should be exercised when using them or recommending them to patients. An individual’s outcome may be considerably better or worse than that predicted by the model. For example, while the majority of metastases are likely to arise within five years of diagnosis, at times metastases may not become apparent until decades after the original lesion was excised.

Many Australian states have specialist melanoma...
assessment centres. Here patients, particularly those with advanced or complex melanomas, can be reviewed by a clinical team or individuals with a special interest in melanoma. Examples include the Melanoma Institute of Australia in Sydney, the Victorian Melanoma Service in Melbourne and the WA Melanoma Advisory Service in Perth.

**Sampling suspicious pigmented lesions: Key points for GPs**

1. Complete excision of a suspicious pigmented lesion with a 2mm margin is the optimal approach.
2. If this is not feasible, a deep partial biopsy may be appropriate, but a partial biopsy may yield a partial diagnosis.
3. Consider referral for initial biopsy or definitive excision.
4. Discuss all unexpected pathology results with the pathologist. Slide review, re-biopsy or full excision may be indicated.
5. Histopathology cannot be relied upon in isolation.

Every diagnosis requires clinicopathological correlation.
6. There are five key features that should be in every melanoma report that help determine prognosis and treatment: Breslow thickness, regression, ulceration, mitotic rate and margins of excision.
7. A number of prognostic tools are available, but none is totally reliable for an individual patient. Those related to the 7th edition of the American Joint Committee on Cancer Melanoma Staging System are likely to be the most dependable.

**Suitability of biopsy procedures for suspicious pigmented lesions.**

<table>
<thead>
<tr>
<th>Biopsy Type</th>
<th>Suitability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excision with 2mm margin</td>
<td>Optimal</td>
</tr>
<tr>
<td>Incisional</td>
<td>For carefully selected lesions only if primary excision is not feasible</td>
</tr>
<tr>
<td>Punch</td>
<td>Use &amp; interpret with great caution only if primary excision is not feasible</td>
</tr>
<tr>
<td>Shave</td>
<td>Generally not recommended. Deep shaves may be of value for in situ lesions in cosmetically sensitive areas</td>
</tr>
<tr>
<td>Ablation (e.g. cautery, cryotherapy, laser), Curettage</td>
<td>Unsuitable</td>
</tr>
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**Resources**
**Smartphone Apps**
Melanoma prognosis calculator (when sentinel node status is known):

Mela Stage melanoma stage and prognosis calculator:
iPhone: http://bit.ly/1ulo0ao

**Online melanoma prognosis calculator**
On this site, patient data can be entered to predict 1, 2, 5 and 10-year survival rates. The model was developed and validated from the American Joint Committee on Cancer database: www.melanomaprognosis.org

**References**