

Cutaneous biopsies

Introduction

Cutaneous disorders are among the most common conditions presented to primary care doctors. Many are easily identifiable and may be dealt with effectively without the need for cutaneous biopsy. Nevertheless, in many instances the diagnosis is not obvious on clinical grounds. The rash may display atypical features or may not respond to therapy as predicted. In these cases, and when dealing with cutaneous tumours or worrying pigmented lesions, cutaneous biopsy with histological assessment becomes necessary. The art of cutaneous biopsy is to derive the maximum amount of information from the minimum amount of tissue, causing least discomfort to the patient. This will be achieved if due regard is given to the advantages and shortcomings of the various techniques available for biopsying cutaneous tissue, and if the pathologist is supplied with a good clinical history.

Clinical History

For several reasons, clinical history assists greatly in the interpretation of skin biopsies. Clinicopathological correlation is particularly important in many inflammatory cutaneous disorders. As the histological features can be very similar, clinical notes may help us to arrange a list of provisional diagnoses in order of likelihood.

The key features to discuss with regard to cutaneous rashes include:

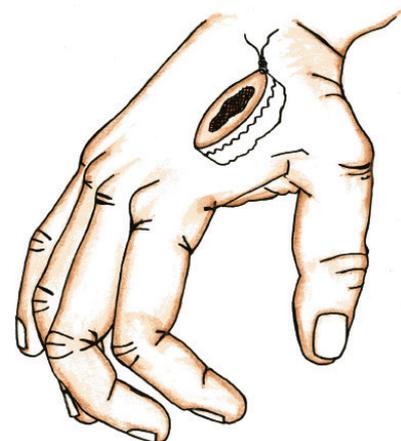
- duration
- distribution
- description (macular, papular, vasculitic or vesicular)
- drugs or other possible aetiological agents
- provisional clinical diagnosis.

As there is wide variation in the normal microscopic picture from different sites, the area biopsied should also be stated. For biopsies performed to distinguish between squamous cell carcinoma and keratoacanthoma, the rate of growth of the lesion is important. When sending specimens of pigmented

lesions, the degree of clinical suspicion should be stated, together with any history of melanoma within the individual or within the individual's family. Any condition associated with cutaneous disorders, such as systemic lupus erythematosus, pregnancy or bone marrow transplant, should be mentioned in the clinical notes. The clinical history should also include the type of biopsy procedure used (see below) as this determines the way we handle the specimen in the laboratory. For example, the whole of an incisional biopsy will be blocked in order to gain the maximum amount of information, whereas an excisional biopsy will be transversely sectioned in order to fully assess the lateral excision margins in the case of a tumour biopsy.

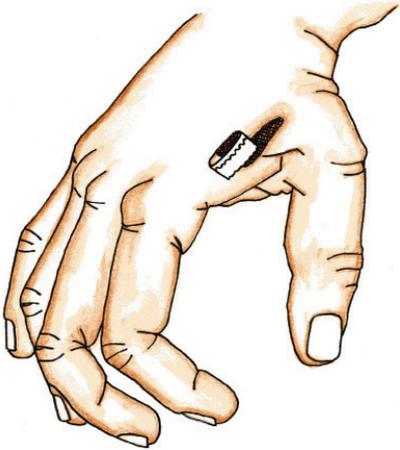
Excision Biopsy

This is the best technique to use for pigmented lesions and cutaneous tumours. It allows for histological assessment and diagnosis of the lesion, and assessment of surgical excision margins. If appropriate, an orientation suture can be placed at one end of the excision, e.g. the superior end of the specimen, so that if the excision is inadequate, the margin involved can be indicated on an accompanying diagram. Occasionally, excision biopsy is appropriate for inflammatory cutaneous disorders where the condition is characterised by the formation of vesicles. The best chance of removing an intact vesicle (which greatly aids diagnosis) may be through excision.



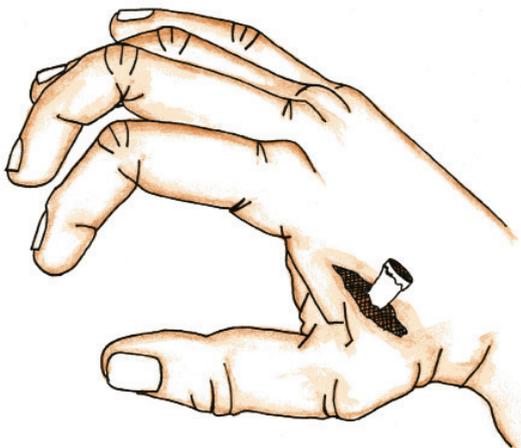
Incision Biopsy

With incision biopsy, a thin elliptical biopsy is taken radially through the edge of the tumour or through the edge of a macular or annular rash. Incision biopsy is superior to punch biopsy for diagnosing rashes, more tissue is displayed on histological section and scarring is often reduced. A typical incision biopsy is 5 to 6 mm in length and about 2 mm in width. It should be deep enough to extend into the subcutaneous adipose tissue. The biopsy should run radially from the centre or central areas of the lesion to include approximately 1 mm of normal cutaneous tissue surrounding the lesion.



Punch Biopsy

Punch biopsies are easier to perform and, in general, are more convenient. Nevertheless, they nearly always yield less information than an incision biopsy. For tumours, the biopsy should be taken centrally. For cutaneous eruptions, the biopsy should be taken from an area typical of the rash. In some cases, multiple biopsies may increase the amount of information. In this procedure, it is best not to include normal skin. Punch biopsies come in various sizes. As 2 mm punches often yield inadequate information for diagnosis, a 3 mm punch biopsy is the smallest that should be used.



Shave Biopsy/Curettage

This technique is suitable for superficially-located lesions with plaque-like clinical features, e.g. seborrhoeic keratoses. It is not an appropriate technique for nodular lesions, cutaneous rashes or melanocytic lesions.

Ancillary Investigations

Microbiological culture: In some instances, an inflammatory cutaneous disorder may be due to an infective process and microbiological culture should be considered. For example, there may have been a history of penetrating trauma or an associated discharge in the area. If culture is considered to be warranted, it is best for a second specimen to be taken. Dividing a cutaneous biopsy often results in considerable crush artefact in that part of the specimen received for histological examination. This artefact can seriously hamper interpretation. Providing it will reach the laboratory within approximately 4 hours, the biopsy for culture should be submitted fresh in a sterile container. If there is likely to be a delay, a small amount of sterile normal saline can be added to the biopsy portion.

Immunofluorescent microscopy: The diagnosis of vesiculobullous eruptions and cutaneous lupus erythematosus is greatly aided by the submission of tissue for immunofluorescent microscopy. As with culture, it is best to take a separate specimen rather than divide one specimen. Tissue for immunofluorescent microscopy should be placed in special transport medium, available from all Sullivan Nicolaides Pathology laboratories. Tissue stored in formalin is not suitable for this technique. When preparing the cutaneous surface, allow the alcohol to dry before biopsying. Any alcohol included with the specimen and transferred to the transport medium acts as an antifreeze, which inhibits the preparation of the frozen section integral to this technique. In cutaneous lupus, a biopsy taken centrally is best. With vesiculobullous disorders, perilesional skin is often best as the immune deposits frequently break down in the base of a formed vesicle, resulting in a false negative result.

General comments concerning cutaneous biopsies

Preparation of the skin surface: Be gentle when cleaning the skin surface prior to biopsy; try not to disturb any overlying scale as the keratin layers sometimes contain diagnostic information (e.g. this is where dermatophytic fungi may be seen). Let any alcohol preparation dry before collecting specimens for immunofluorescence.

Local anaesthesia: Only a small amount of local anaesthetic is required for punch biopsy procedures (0.5 mL maximum). Too much local anaesthetic within the tissues can distort the histological appearances and simulate dermal oedema.

Marking the lesion: It is often prudent to mark the target area for biopsy with an ink marker, as some lesions can blanch following introduction of local anaesthetic. The erythema in many lesions is due to vascular dilatation occurring as part of the inflammatory disorder. Local anaesthetic can cause vasoconstriction and diminish the erythema clinically. This may result in a poorly targeted biopsy yielding subdiagnostic histology.

Depth of biopsy: It is best to continue into the subcutaneous adipose tissue so that the entire dermis is represented on histological section. This helps greatly with the categorisation of many inflammatory skin disorders and also demonstrates the deep border of any cutaneous tumour. When performing a punch biopsy, the biopsy instrument appears to 'give' when it penetrates the dermal connective tissue into subcutaneous adipose tissue. A similar sensation will be noticed when dissecting free an incision biopsy.

Care with biopsy tissue: All too often, after biopsy tissue has been retrieved from the patient, crush artefact occurs during its transfer into formalin. Crush artefact greatly distorts the histological appearance and repeat biopsy may become necessary. Rather than grasping the biopsy tissue with non-tooth forceps, it should be transferred to the specimen container using needle tips, a skin hook or fine forceps, delicately grasping one edge of the biopsy.

Fixative: Ordinary blue, 10% buffered formalin supplied with the specimen jars is suitable for nearly all cutaneous biopsies, except those submitted for microbiological culture or immunofluorescent examination.

Labelling: Please label all specimen containers with the patient's name and details, which should match those stated on the request slip. Unlabelled specimens can still be processed and interpreted if they arrive with labelled paperwork; however the medico-legal status of any generated report is doubtful. The report will usually be generated with a 'specimen received unlabelled' comment attached.

Specific clinical settings and appropriate biopsy procedures

1) Pigmented skin lesions: These are best biopsied by excision. The reasons for this are two-fold. Firstly, morphological features vary within a given pigmented lesion, so that some areas may show features of a naevus (sometimes of a so-called dysplastic naevus), while other areas may show melanomatous features. Secondly, some areas within a melanoma may have undergone regression which also results in morphological heterogeneity. Punch biopsy, or another form of limited biopsy, taken from a regressed area, or an area with naevus morphology, may lead to a false negative result. When a pigmented lesion is excised following a previous biopsy, it often demonstrates so-called pseudomelanomatous change with architectural and cytological disturbance. This makes interpretation very difficult and may result in an over diagnosis of melanoma. For these reasons, suspicious pigmented lesions are best completely excised in the first instance.

2) Squamous cell carcinoma vs keratoacanthoma: Distinguishing between these two can be difficult. The importance of clinical history has already been stated. Any biopsy technique used to separate these two entities should include the base of the lesion. We see many squamous cell carcinomas arising within keratoacanthomas, often in the base of the lesion. For this reason, superficial biopsies are not appropriate. The best way to distinguish between keratoacanthoma and squamous cell carcinoma is through excision biopsy so the entire base of the lesion can be seen and assessed.

3) Crusted plaques—probable skin cancer or seborrhoeic keratosis: With relatively flat lesions, a shave biopsy or curettage specimen is usually perfectly adequate for demonstrating the histology of the lesion. Typical lesions in this group include seborrhoeic keratoses, intra-epidermal carcinomas and basal cell carcinomas of superficial multifocal type. Often curettage / shave biopsy is also curative.

4) **Annular rash:** A radial incision biopsy through the edge of the annular rash is the gold standard for demonstrating the pathology in this setting. A punch biopsy can be used but often yields less information. Consideration should be given to sending scrapings for fungal culture.

5) **Macular rash:** A radial incision biopsy can be taken to include 1 mm of normal skin, or a punch biopsy can be taken from the central area of the rash for histological examination. If the lesions are developing in 'crops', then consider biopsying both an early and a fully-formed lesion. If cutaneous lupus is in the list of differential diagnoses, then consider submitting a specimen for immunofluorescent microscopy.

6) **Papular rash:** An incision biopsy can be used to include two or more papules in the one biopsy specimen. Alternatively, a punch biopsy, centred on a papule, will also help in most cases.

7) **A vesiculobullous rash:** Vesicles yield most information when biopsied early. Try to retrieve an intact vesicle with either a punch biopsy or a limited excision biopsy if this is possible. Failing this, a radial incision biopsy through the edge of a vesicle may yield sufficient information. A separate biopsy of perilesional skin for immunofluorescent examination becomes important when subclassifying the group of vesiculobullous cutaneous disorders (bullous pemphigoid vs pemphigus and its variants, etc.).

8) **Petechial rash, ? vasculitis:** Like vesiculobullous lesions, vasculitic lesions should be biopsied early in the course of their evolution.

9) **Nodular or indurated cutaneous eruptions:** Make sure the biopsy includes components of the subcutaneous adipose tissue as the patient may have a panniculitis (an inflammatory disorder centred upon the subcutaneous adipose tissue) such as erythema nodosum. Diagnosis of these conditions is not possible in biopsies which include only epidermis and dermis.

Conclusion

Diagnosing cutaneous conditions can be challenging. The chances of success are improved when the clinician, is armed with a variety of biopsy techniques for use in the correct clinical setting, and when the pathologist is supplied with an adequate clinical history.



Dr Kevin Whitehead FRCPA

Dr Kevin Whitehead joined Sullivan Nicolaides Pathology in 1992 and honed his skills in New York under the renowned dermatopathologist A Bernard Ackerman. Based at Taringa, Kevin works closely with dermatologists, plastic surgeons, and oculoplastic surgeons, and has an ongoing role lecturing.

Dr Whitehead is available for consultation.

T: (07) 3377 8655

E: kevin_whitehead@snp.com.au

SULLIVAN NICOLAIDES PTY LTD • ABN 38 078 202 196 • A subsidiary of Sonic Healthcare Limited • ABN 24 004 196 909
134 WHITMORE STREET • TARINGA • QLD 4068 • AUSTRALIA
TEL (07) 3377 8666 • FAX (07) 3870 0549
PO BOX 344 • INDOOROOPIILLY • QLD 4068 • AUSTRALIA