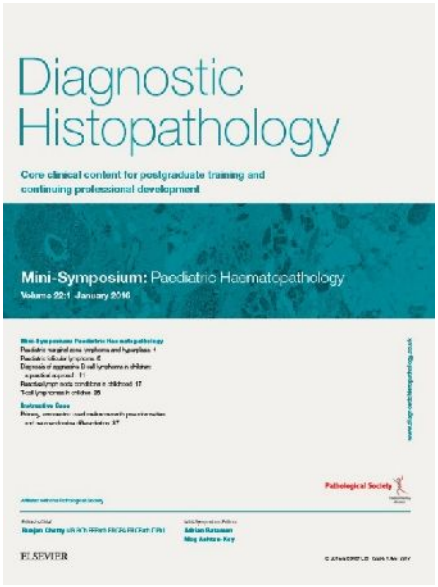
# Diagnostic Histopathology

## Instructions for authors: writing a Short Case




Elsevier's *Diagnostic Histopathology* is a continually updated resource for trainees and junior consultants. It provides a comprehensive review of the latest histopathological, cytological and related technical advances. Curated by a team of experienced experts, the journal only publishes commissioned work and every article is written to ensure accessibility and accuracy. It is affiliated with the Pathological Society of Great Britain and Ireland.

Each issue contains a mini-symposium comprising invited articles exploring one subject area in depth. Also included every month are one or more short case studies, called Short Cases. Many are written by members of the Trainees' Subcommittee of the Pathological Society of Great Britain and Ireland. Short Cases from this source are published as a *Case of the Month* on the Pathological Society website. Submissions from other sources are also encouraged.

What follows is guidance on getting your Short Case published successfully. An example of a published Short Case is shown at the end of this guidance. More are avaliable on the *Diagnostic Histopathology* website (www.diagnostichistopathology.co.uk).

### Type of case study

We are looking for Short Cases with educational value for trainee pathologists and/or that illustrate an important message that could affect readers' working practices. We are *not* specifically looking for case studies which are only notable for their esoteric nature, e.g. a rare tumour occurring at an unusual site, although such cases will not be excluded from consideration. Therefore, the entity may have already been described but your Short Case should either possess an unusual feature or represent a very good example that reinforces the original descriptions.

Such case studies could include, but not be limited to:

- pseudomalignant appearances, especially in small biopsies
- histological appearances which have been modified by pre-biopsy therapy
- a metaplasia or heterotopia which could have led to an erroneous diagnosis

- immunohistochemistry which revealed an unexpected diagnosis
- immunohistochemistry which has been misleading in the diagnostic process
- an unusual histological finding that has important implications for patient therapy
- a particularly good example of an unusual disease entity or process
- a case in which a molecular technique or analysis has been important during the diagnostic process.

## Submitting your Short Case

Please send your Short Case to the Managing Editor, Nik Prowse (edit@nikprowse.com).

If you have any questions about how to structure your case, any aspect of the publication process or suitability of a case study for inclusion, please contact Nik. For production matters he will reply directly and for medical queries he will refer you to the relevant Board member.

Subject to review, your Case Study will be published around 4–5 months after submission. Deadlines are set to allow time for checking, review, revision (if necessary), typesetting and proofreading. If you are not able to submit your Case Study by the deadline please contact Nik to discuss the matter.

## Structure of the Short Case

The Short Case should be structured as follows:

### Title page

Include, for each author:

- full name
- degrees held
- current job title
- affiliation
- email address (this will not be published)
- a conflict of interest statement (if none, this can simply state ‘none’).

### Unstructured abstract

This should provide an overview of the case and should not exceed 150 words.

### Keywords

Following your abstract add 5–10 keywords; do not include words that occur in the title as titles and keywords tend to get indexed together.

### Main text

This should not exceed 750 words in total and should include the following:

#### *a. Case report*

The demographics of the case should be given (e.g. age, gender and other details, e.g. racial origin, if pertinent to the case). Individual consent is not required *as long as the patient cannot be identified*, e.g. from their demographic details or from

submitted images. If there are any identifying features, a signed patient consent form is required when submitting the case. Note that sometimes a patient can potentially be identified solely due to the rarity of their case. Permission is not required for radiographs, ECGs or laboratory charts.

### *b. Discussion and conclusion*

The case should be discussed in the light of relevant previous literature.

### *c. Practice points*

This is a bulleted list and should include 3–5 important clinical practice points.

### *d. References*

A maximum of six references should be provided. Cite them in the text using the numbered (Vancouver) referencing system.

### *e. Self-assessment multiple-choice questions*

Three 'one best answer' questions should be provided. They need not be complex, but should provide an opportunity for the reader to test their understanding of salient aspects presented in the case report. These should be written such that the answers may be formulated by the reader solely from the question stem (i.e. they should pass the 'cover-up test'). Include the answers with the questions, in the form: 1. B, 2. A, etc.

An example of a suitable 'one best answer' question is:

*A 76-year-old male patient presents with sudden-onset bloody diarrhoea. Colonoscopy reveals mucosal inflammation and ulceration at the splenic flexure. Biopsies from this area reveal large bowel mucosa showing patchy acute inflammation and ulceration together with fibrin microthrombi and haemosiderin deposition within the lamina propria. What is the most likely diagnosis?*

*A. Crohn's disease*
*B. Ischaemic colitis*
*C. Ulcerative colitis*
*D. Diverticular disease*
*E. Campylobacter infection*

***Answer: B.***

## Images and tables

Images should clearly illustrate the salient features of the case. Up to six single images may be submitted: ideally a minimum of 300 dpi (jpeg or tiff) and no less than 8 cm in width, for single column reproduction. In addition, up to one table may be submitted. Alternatively, a table may be used in place of an image.

Figures and tables should be numbered, cited in the text and presented with a legend explaining their content. Details of primary antibodies used in immunohistochemistry should be given in the accompanying legend.

All images will become intellectual property of Elsevier.

Before you submit any image please check if it is:

- in jpeg or tiff format
- clear and readable
- in focus, not blurry or fuzzy
- not too dark.

## Grammar and presentation

Tense: there is no standard tense. It is suggested that the history is written in the past tense and the examination in the present tense. Emergency and urgent problems in case histories read well in the present tense.

Only use punctuation marks where absolutely necessary: this gives a clearer, more easily read text. Questions should follow the style of the example above.

Numbers: for numbers 1–9, give digits when numbers are followed by a unit, but not for anything else (so one patient, two biopsies, 2 days, 1 mg). For numbers 10 and above, use the digit.

Present units with an appropriate number of decimal places, e.g. baby 1.57 kg, child 32 kg.

Findings on examination need not be in full sentences and rates are given/minute, e.g. ‘On examination he appeared well. Chest clear, pulse 120/minute, respiratory rate 24/minute, blood pressure 95/60 mmHg’.

Terms and spellings should be used as commonly seen in the UK. Words spelled with a ‘z’ or an ‘s’ should be used with ‘s’, e.g. use ‘recognised’ rather than ‘recognized’. Colloquialisms should be avoided. Greek letters α and β should be spelt out in full. The following terminology should be used; GP for general practitioner, lower case for outpatient department, emergency department, social worker, health visitor, consultant paediatrician etc.

Syndromes: apostrophes are not usually added except where they are in generally accepted use e.g. ‘Crohn’s’.

Names of bacteria should be in italic and begin with an upper letter, e.g. *Pseudomonas aeruginosa, E. coli*.

Acronyms and abbreviations should be used sparingly and fully explained when first used. Abbreviations and symbols must be standard. SI units should be used throughout, except for blood pressure values which should be reported in mmHg. Commonly used abbreviations such as ALT, AST, ALP can be used without definition.

Whenever possible, drugs should be given their approved generic name. Where a proprietary (brand) name is used, it should begin with a capital letter. Standard international units should be used for all laboratory data. Drug dosages should be written as micrograms and not mcg or µg. In lab results mmol/l, µmol/l and pmol/l are used.

There follows a Short Case that was published in March 2019

# A challenging breast biopsy

Jon Griffin
David Hughes

## Abstract

Metastases to the breast are an uncommon occurrence and can mimic primary breast carcinoma clinically and morphologically. We report a case of metastatic melanoma that presented as a breast mass. We review the literature on metastases to the breast from any source and discuss the microscopic features that can help differentiate metastatic melanoma from primary breast cancer.

**Keywords** breast; melanoma; metastasis

## Case report

A 37 year old female presented to the breast clinic with a symptomatic mass in the right breast which was clinically thought to be an intra-mammary lymph node. An ultrasound guided needle core biopsy was performed. Histology showed fibrous and adipose tissue infiltrated by solid aggregates of epithelioid cells. Markedly atypical pleomorphic nuclei were present and prominent nucleoli were seen. At high power a varied degree of cytoplasmic pigmentation could be seen. This pigment was confirmed as melanin by Masson Fontana stain (Figure 1).

Review of the patient's medical history revealed a diagnosis of cutaneous malignant melanoma in 2001 with no history of recurrence or metastasis in the intervening 17 years. The clinicopathological assessment was that the breast lesion was most likely to represent a late recurrence but that a metastasis from a new, undiagnosed and possibly regressed primary tumour was also possible. Mutational testing showed a Val600Glu mutation in exon 15 of the BRAF gene, implying sensitivity to BRAF kinase inhibitor therapy.

## Discussion

Metastasis to the breast is a rare occurrence, accounting for 0.5−3% of breast malignancies. One contemporary case series identified lymphoma and melanoma as the commonest metastatic malignancies to the breast (38.3% and 23.4% of cases respectively), excluding metastasis from contralateral breast carcinoma. In a separate series that excluded haematological malignancies, Williams et al.[1] described melanoma and adenocarcinoma as the commonest breast metastases. This study also found that 11.8% of cases represented the first presentation of any malignancy and that 29.6% of cases had a history of cancer but no evidence of active disease at the time of presentation. A third study that reviewed 85 cases found that ovarian malignancies were the commonest primary site followed by melanoma. Ten cases of the cohort were initially misdiagnosed as primary breast malignancies due to morphological similarity to high grade ductal carcinoma. All of these cases were resolved when additional clinical information was provided by the treating clinician. Frequently, immunohistochemistry is required for confirmation of the diagnosis. In the present case the reporting pathologist (DH) chose to use a Masson Fontana stain for melanin as this allowed a secure diagnosis of melanoma whilst reducing the laboratory burden of immunohistochemistry and preserving tissue for molecular testing.

Metastatic malignant melanoma is a well-known mimic of other malignancies at any anatomical site. Within the breast there are many histological features that can trick the pathologist into interpreting the lesion as a high-grade adenocarcinoma particularly if limited material is available, for example with a core biopsy specimen. In their 2013 review of 20 cases, Bacchi et al. described common morphological pitfalls in this scenario[2]: Thirteen cases had well-described features of melanoma such as atypical spindled to epithelioid cells with vesicular chromatin and prominent nucleoli. In the remaining seven cases, metastatic melanoma was shown to morphologically mimic medullary carcinoma, metaplastic carcinoma, lymphoma, liposarcoma or leiomyosarcoma. Overall, pigmentation was uncommon and this finding in isolation should be interpreted with caution as ductal carcinoma can harbour melanin pigment.[3] Likewise, melanoma metastases can also contain microcalcification and the presence of this finding alone should not provide false reassurance that the lesion is a primary breast malignancy. Other morphological clues to the diagnosis of metastatic malignant melanoma include a circumscribed rather than infiltrative tumour border, absence of a desmoplastic stroma and lack of concurrent ductal carcinoma in situ. A final factor that might introduce diagnostic difficulty is the occurrence of primary breast cancer in a patient who has already had metastatic malignant melanoma at that site or vice versa. This situation has been reported to occur more often than might be expected by chance[4] and the possibility of a dual diagnosis should not be overlooked.

## Conclusion

Metastases to the breast can present a challenging scenario and may be misdiagnosed as a primary breast malignancy. Furthermore, spread to this site may be the first presentation of metastatic disease. Careful review of the patient's clinical history and judicious use of immunohistochemistry and special histochemical stains can help avoid this diagnostic pitfall. ◆

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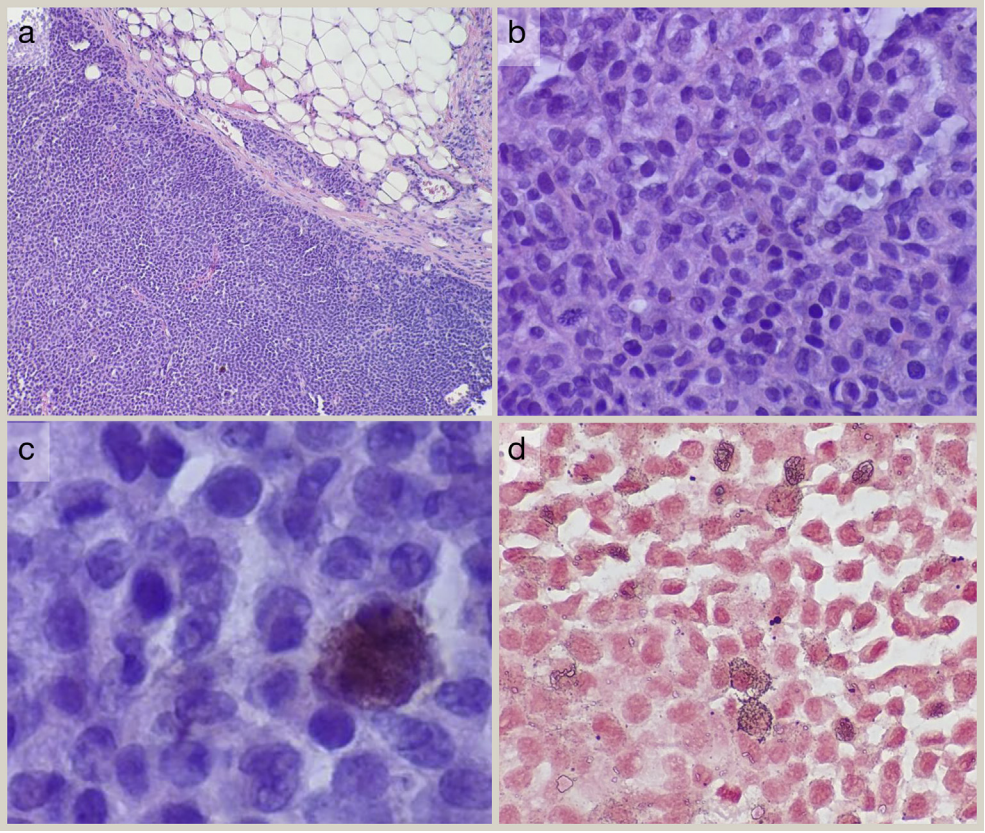


**Figure 1** (**a**) At low power the tumour is seen to have a circumscribed border. (**b**) Higher power shows nuclear pleomorphism and mitotic activity. (**c**) Brown cytoplasmic pigmentation confirmed as melanin by a Masson-Fontana stain in (**d**).

## Practice points

- Metastatic melanoma in the breast can mimic many other malignancies. In the setting of an uncommon type of breast cancer (e.g. medullary or metaplastic), metastatic melanoma should be considered.
- Pigmentation is uncommon in melanoma metastatic to the breast.
- Review of the clinical history can help avoid inappropriate use of immunohistochemistry and preserve tissue for molecular tests.

## REFERENCES

1 Williams SA, Ehlers RA, Hunt KK, et al. Metastases to the breast from nonbreast solid neoplasms: presentation and determinants of survival. *Cancer* 2007 Aug 15; **110:** 731–7.
2 Bacchi CE, Wludarski SC, Ambaye AB, Lamovec J, Salviato T, Falconieri G. Metastatic melanoma presenting as an isolated breast tumor: a study of 20 cases with emphasis on several primary mimickers. *Arch Pathol Lab Med* 2013 Jan; **137:** 41–9.
3 Zhang X, Liang Y, Wang H-Y. Invasive ductal carcinoma of the breast associated with extensive melanin melanosis: a case report and review of the literature. *Int J Clin Exp Pathol* 2014; **7:** 1218–23.
4 Koh HK, Sober AJ, Carey RA. Possible association between malignant melanoma and breast cancer. *Arch Dermatol* 1987 Jun; **123:** 712–3.

## Self-assessment

1. Metastases to the breast accounts for what percentage of breast malignancies

**A. Less than 0.1%**
**B. Up to 3%**
**C. 10–13%**
**D. 23–33%**
**E. More than 33%**

Correct answer: B, 3%

2. What is the most common morphological feature seen in metastatic malignant melanoma in the breast?

**A. Pigmentation**
**B. Infiltrative tumour front**
**C. Spindled and epithelioid cells**
**D. Background ductal carcinoma in situ**
**E. Microcalcification**

Correct answer: C, spindled and epithelioid cells