

# A very rare case of synchronous primary lung cancer lymph node metastasis

Kate Marks

Radhika Ramnath

## Abstract

A 76 year old patient presented with two synchronous primary lung tumours. One was identified as an adenocarcinoma and the second as an atypical carcinoid tumour. When reviewing the lymph node slides it was seen that one lymph node contained metastatic deposits from both primary tumours. Synchronous lung tumours are fairly rare occurrences, but even rarer is the finding of synchronous metastases to the same lymph node. The atypical carcinoid deposit was very subtle in appearance and could easily have been overlooked. This case demonstrates a useful learning point to not miss these rare and subtle findings as the resulting tumour staging was affected and may have implications for further patient management.

**Keywords** synchronous lymph node metastases; synchronous tumours

## Case report

A 76 year old lady was referred for a plain chest radiograph following a possible exposure to TB from a family member. She also presented with ongoing productive cough with clear sputum and occasional sweating at night. She was an ex-smoker with a 40 pack year history and an exercise tolerance of over half a mile or 3 flights of stairs.

The chest radiograph revealed an opacity in the right upper lobe and so a CT scan was performed. This confirmed a spiculate right upper lobe nodule measuring 19mm and a satellite lesion within the same lobe, measuring 8mm that was 35mm from the first nodule. A CT guided lung biopsy was undertaken and histological examination revealed a primary adenocarcinoma with a predominantly lepidic growth pattern as well areas of acinar pattern.

A right upper lobe lobectomy was performed. A 25mm tumour was identified deep to the hilum as well as a separate firm white nodule measuring 10mm. The main tumour was an adenocarcinoma with acinar, lepidic and focal solid patterns,

**Kate Marks PhD MBChB** Histopathology Clinical Research Fellow, Pathology and Data Analytics, University of Leeds, UK. Conflicts of interest: none declared.

**Radhika Ramnath MBBS FRCPath** Consultant Histopathologist, Department of Histopathology, St James's University Hospital, Leeds, UK. Conflicts of interest: none declared.

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which showed positive staining with CK7, TTF1 and Napsin A and that was negative for CK20 (Figure 1). Of the 13 lymph nodes submitted, three were involved, all of which were N1 nodes and final staging for this tumour was pT1c pN1.

The separate 10mm nodule was composed of small to medium cells with stippled chromatin and small amounts of cytoplasm (Figure 2). The mitotic count was 2 per 2 mm<sup>2</sup>; however, there was no necrosis present. The cells were positive for MNF116, CD56, synaptophysin and showed weak TTF1 positivity. They were negative for CK7, CK20, CD45 and Napsin A. The appearances were of an atypical carcinoid tumour.

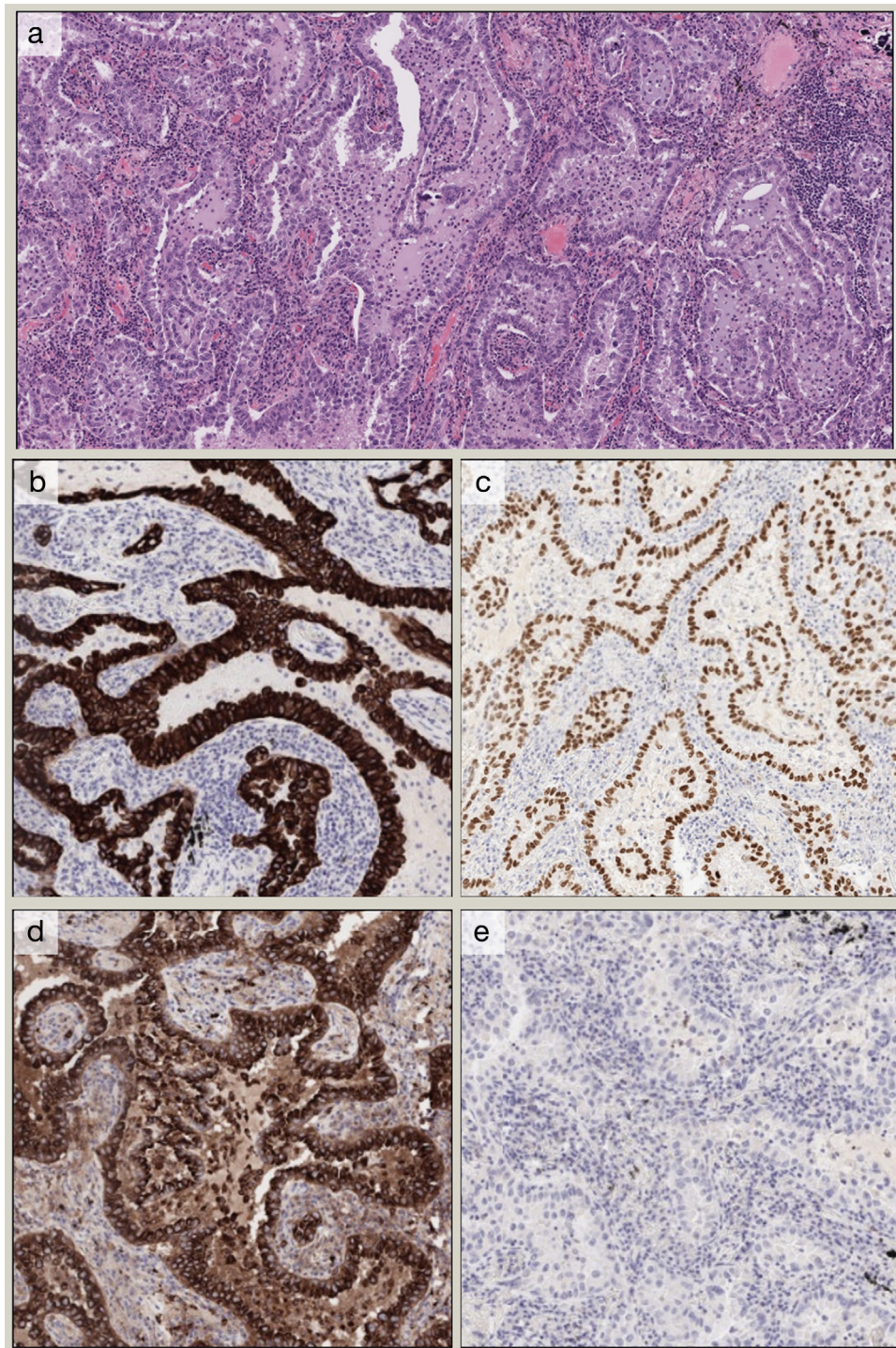
One of the hilar lymph nodes which contained a metastatic deposit from the adenocarcinoma, also contained a second focus of metastasis; however, this had spread from the carcinoid tumour and was confirmed by immunohistochemistry (Figure 3). Therefore, final staging for the second synchronous tumour was pT1a pN1.

The patient recovered well from surgery and regained her mobility and exercise tolerance well. Unfortunately a follow up CT scan revealed a new possible lymph node metastasis and the patient is planned for palliative chemotherapy and tissue samples are undergoing EGFR mutation testing.

## Discussion and conclusion

Synchronous primary lung tumours, defined as being diagnosed either simultaneously or within 6 months of each other, are rare with an average incidence of 0.2–8% of all lung tumour diagnoses<sup>1</sup> although the true incidence is thought to be higher. The diagnosis of synchronous tumours has increased over recent years due to improved imaging and earlier detection. However, the presentation of adenocarcinoma and carcinoid simultaneously is reported very infrequently.<sup>2</sup> Even rarer is the presentation of both primary tumours metastasising to the same lymph node as seen in this case.

Carcinoid tumours comprise of <1% of primary lung malignancies and more commonly present in patients under 60 years of age.<sup>3</sup> Atypical carcinoid tumours account for 10–30% of carcinoid tumours, usually show faster growth compared to typical carcinoid tumours and more often metastasise to lymph nodes. They are also more commonly seen in Caucasian and female patients. Atypical carcinoid tumours are differentiated from typical carcinoid by the presence of either necrosis and/or 2–10 mitoses per 2 mm<sup>3</sup>. Although not required for diagnostic



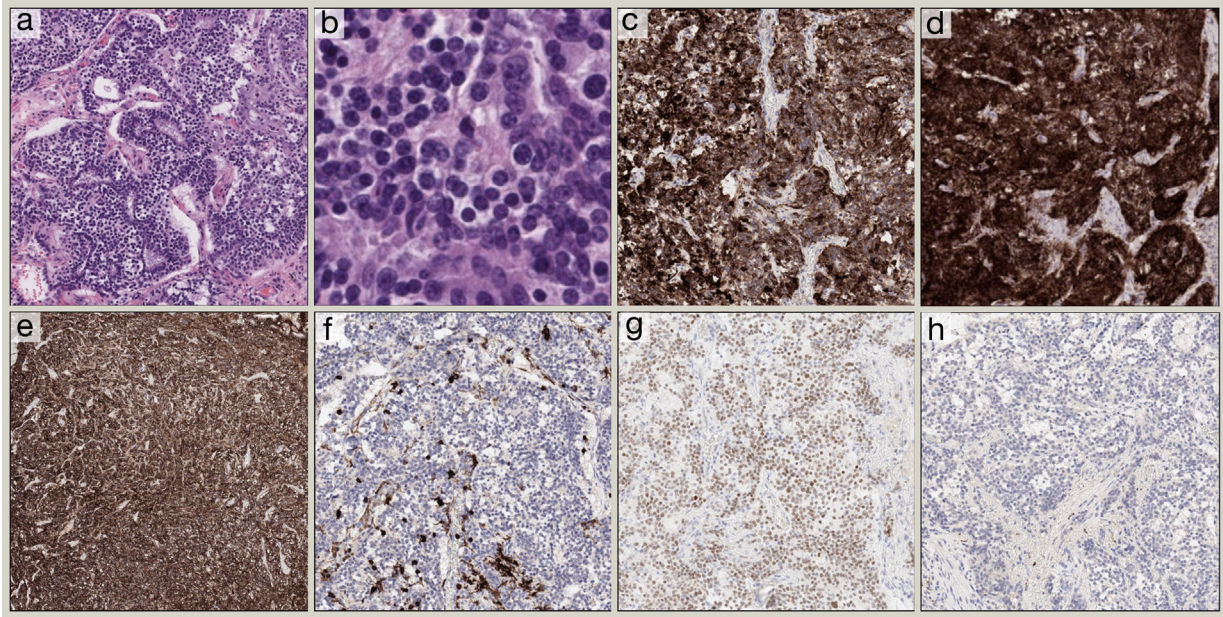
**Figure 1** Main tumour low power magnification. (a) H&E, (b) CK7, (c) TTF1, (d) Napsin A, (e) CK20.

purposes according to the WHO classification, Ki67 is often performed to confirm the diagnosis.<sup>3</sup> Ki67 may be a useful stain to perform in the context of assessing small primary biopsies which have been subject to crush artefact. In this scenario it can be difficult to differentiate between a neuroendocrine tumour or a small cell lung tumour on morphology alone and a high Ki67 would indicate a small cell tumour rather than neuroendocrine.

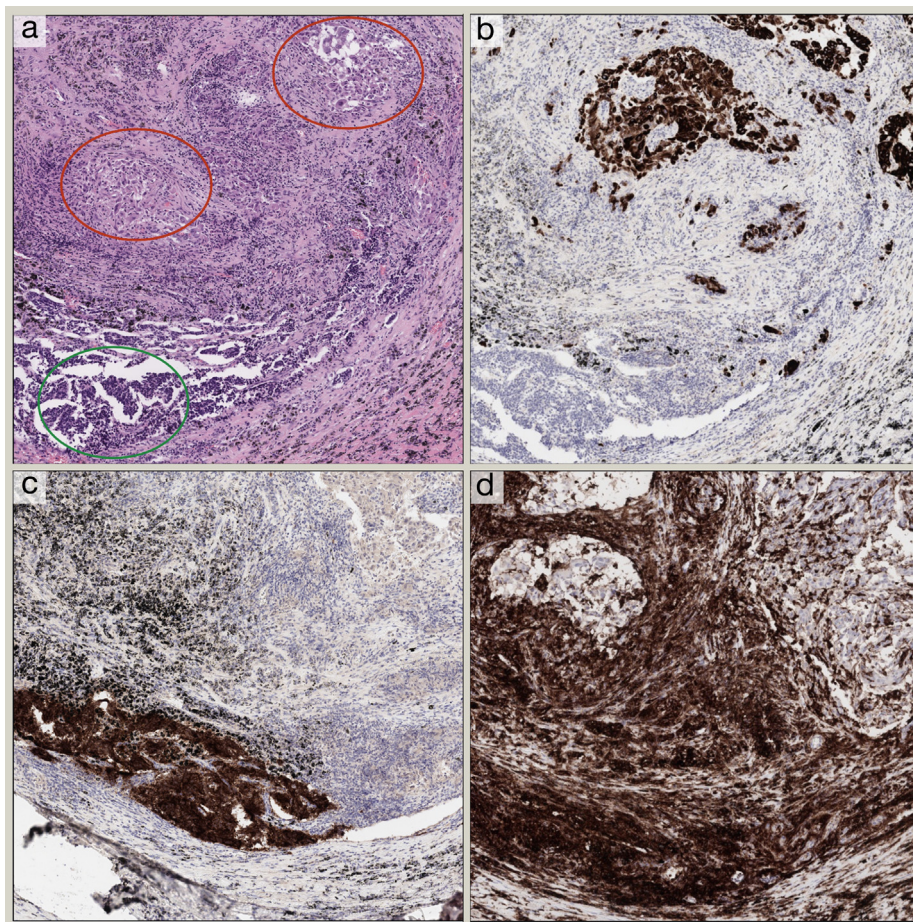
Studies have indicated that smoking may be a contributing factor to the development of synchronous tumours of differing

types, due to multiple cellular insults from the carcinogens resulting in simultaneous tumour development from different cell types.<sup>4</sup> It is important to differentiate synchronous but differing primary lung tumours from advanced disease as the prognosis and treatment can differ. It has been demonstrated that surgery for these patients can result in outcomes similar to those without synchronous differing tumours.<sup>5</sup>

Not only are synchronous differing tumours very unusual, but the finding of metastasis from both tumours to the same lymph



**Figure 2** Second separate tumour Nodule. (a) H&E low power magnification, (b) H&E high power magnification, (c) MNF, (d) synaptophysin, (e) CD56, (f) CD45, (g) TTF1, (h) Napsin A.



**Figure 3** Lymph node with tumour deposits. (a) Low power H&E showing area of adenocarcinoma metastasis (red circles) and carcinoid metastasis (green circle), (b) CK7 highlighting adenocarcinoma metastasis. (c) Synaptophysin highlighting carcinoid metastasis, (d) CD45 demonstrating background lymph node positivity.

node is an extremely rare phenomenon. The true incidence of this finding is difficult to know with certainty and to our knowledge has not been previously reported in the literature. A tiny carcinoid deposit may be easily missed and hard to distinguish from background lymphoid tissue on first glance in a haematoxylin and eosin stained slide, especially if an adenocarcinoma deposit has already been identified.

A small focus of lymph node metastasis from a carcinoid tumour may be especially subtle to spot, as seen in this case. However this very rare occurrence is still important to identify as it could be clinically relevant for subsequent management and outcomes for the patient. ◆

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## Practice points

- Where synchronous primary tumours are identified with different morphology it is important to check lymph nodes for metastatic deposits from both primary tumours
- The diagnosis of synchronous tumours is increasing due to improved imaging and earlier detection
- The combination of adenocarcinoma and atypical carcinoid as two synchronous lung tumours is a very rare finding. Even rarer is for both tumours to metastasise and metastasis of both tumours to the same lymph node has not been previously reported in the literature.

## Self-Assessment Questions

- 1 Which of the following is the IARC definition for a synchronous tumour?**
- A. Two or more tumours diagnosed within 3 months
  - B. Two or more tumours diagnosed within 6 months
  - C. Two or more tumours diagnosed after 6 months
  - D. A tumour occurring after the surgical resection of an initial tumour
  - E. Two or more tumours with different histological subtypes

Answer B

- 2 In what demographic do carcinoid tumours most commonly present?**

- A. Patients under 60 years of age
- B. Patients over 60 years of age
- C. Male patients
- D. Non-Caucasian patients

Answer A

- 3 Which of the following is a diagnostic criteria for an atypical carcinoid tumour?**

- A. No presence of necrosis
- B. Positive TTF1 immunohistochemistry
- C. Monotonous morphology
- D. 2–10 mitoses per 2mm<sup>3</sup>

Answer D