CASE REPORT

Primary signet ring cell carcinoma of the lung: a rare subtype

Speros Livieratos,¹ James K Smith,² Eduard Fatakhov,³ Christopher F Koch Jr⁴

¹Internal Medicine Section of Pulmonary and Critical Care, Georgia Regents University, Augusta, Georgia, USA

²Internal Medicine Section of Pulmonary and Critical Care, VA Specialty Care, Augusta, Georgia, USA

³Department of Internal Medicine, Georgia Regents University, Augusta, Georgia, USA

⁴Medical College of Georgia, Augusta, Georgia, USA

Correspondence to

Mr Christopher Koch, ckoch2250@gmail.com

SUMMARY

Signet ring cell carcinoma (SRCC) is a subtype of adenocarcinoma. It can arise in different organs including stomach, colon, bladder, prostate and breast. The vast majority of SRCC found in the pulmonary system is metastatic. Primary disease to the lungs is rare. The main feature of this type of malignancy is mucin-producing cells. It has been reported that out of 3500 cases of pulmonary adenocarcinoma, five cases had features of SRCC.

BACKGROUND

Adenocarcinoma of the lungs comes in many different variations ranging from bronchioloalveolar carcinoma, mucinous carcinoma, papillary carcinoma, morular papillary carcinoma and signet ring carcinoma.^{1 2} Signet ring morphology is a cytological distinction that is rare when identified in the lungs as a primary tumour. While signet-ring morphology can be observed in many other organs, including the bladder and the stomach, it is very rare indeed to be observed in a primary lung tumour. As a result after the initial diagnosis is performed a thorough examination should be conducted to make sure that the tumour is not a metastatic lesion from a different primary tumour.² The signet ring morphology that can be observed in the present case within the lung represents a poorly differentiated cell. As a result of the primitive differentiation status this tumour is a very aggressive. The 5-year survival rates are very poor as observed in a study of 15 patients with this type of cancer.³ Moreover, there are several different tumour markers that are observed in this subtype of cancer including CDX2 and thyroid transcription factor-1 (TTF-1).² Among these markers, TTF-1 is the most important one because the TTF-1 tumour marker is observed in pulmonary adenocarcinoma. Furthermore, this tumour marker is seen in both histological subtypes including acinar and diffuse. The diffuse type has a very high mortality but because of the rarity this is difficult to quantify and clearly makes this is the most aggressive mucinous type of adenocarcinoma.² Thus, when taken together this is a very rare subtype of adenocarcinoma that is a challenge to treat.

CASE PRESENTATION

The patient was a 55-year man who was seen by his primary care provider after noticing to have some enlarging lymph nodes in his neck. Owing to the rapid nature of this presentation, the primary care provider ordered a positron emission tomography

Figure 1 A large spiculated mass with lymphangitic spread to the mediastinum.

CT (PET-CT) scan. The scan showed advanced disease in the right lower neck, right supraclavicular region, subcarinal region and bilateral hilar regions (highest standard uptake value (SUV) 8.7). The chest CT scan also showed “spiculated, lymphangitic spread to the mediastinum” (figures 1–4). In addition, there was a distinct area of ground glass opacities noted in the lower lobe of the left lung (highest SUV 3.9; figures 5 and 6). A concomitant whole body CT scan noted extensive bone metastases, which included the right scapula, numerous right-sided ribs, thoracic vertebrae and lumbar vertebrae. An MRI of the brain showed lesions consistent with metastatic disease. The patient was referred for pulmonary consultation and a needle biopsy was performed of the supraclavicular nodes. Pathology showed non-small cell carcinoma. The tumour markers were positive for TTF-1 and negative for CDX2. The final pathology interpretation was reported as adenocarcinoma of the lung, signet ring

Figure 2 A more posterior view of the large spiculated mass with lymphangitic spread to the mediastinum.

To cite: Livieratos S, Smith JK, Fatakhov E, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-200111

Figure 3 A large spiculated mass with lymphangitic spread to the mediastinum and the dramatic inferior spread.

variant. He underwent three cycles of combined chemotherapy with carboplatin and paclitaxel with no success. A trial of pemetrexed chemotherapy was included and was continued for six cycles. This therapy decreased the size of the lung lesions but the bone metastasis continued to increase in size and symptomatology. In addition, he received whole brain radiation. Unfortunately, the patient became progressively weaker and he opted for a hospice care referral due to multiple admissions.

INVESTIGATIONS

There were numerous different investigations performed in the current case. The initial investigation was a combined PET-CT. This scan showed a very large tumour burden for this patient as noted above. After this was revealed the patient underwent a whole body CT scan to further elucidate the extent of the distal metastatic disease. Here again there were more lesions with multiple distal metastatic lesions which also could be demonstrated. As the patient also began to have lesions on the spinal column it was decided that the patient should also be evaluated with an MRI for metastatic lesions to the brain. After the MRI was completed it also revealed additional lesions within the cranial vault. After all of the radiological evidence was completed a biopsy was performed and immunohistochemical analysis of the factors including TTF-1 and CDX-2 were analysed.

TREATMENT

The patient was given palliative chemotherapy including pemetrexed which was continued for six cycles. This treatment

Figure 4 A lateral view of the large spiculated mass with lymphangitic spread to the mediastinum.

Figure 5 An axial view large spiculated mass with lymphangitic spread within the mediastinum.

however was not successful in relieving the tumour burden that was seen in this patient. The patient would subsequently opt for comfort care measures only.

OUTCOME AND FOLLOW-UP

The patient unfortunately succumbed to his disease comfortably after opting for hospice care.

DISCUSSION

Non-small cell lung cancers (NSCLC) are the most common type of pulmonary malignancies. Pulmonary adenocarcinoma is a subtype of NSCLC. Signet ring variant exists among the poorly differentiated types.⁴ Primary signet ring adenocarcinoma of the lung is a subtype of bronchial mucin cell carcinoma.² There are five cell types of adenocarcinomas of the lung according to Shimamoto and co-workers: cells that resemble bronchial goblet cells, bronchial gland cells, bronchial epithelial cells, type 2 pneumocytes and non-ciliated bronchiole cells. According to Ou *et al*, patients with SRCC of the lung tended to be non-smokers, younger and had a worse prognosis compared to their counterparts.³⁻⁵ In addition, the patients with SRCC variant usually present with more advanced cancer (stage 4). This study found that primary SRCC was rare; out of 50 351 patients, 262 had primary SRCC of the lung.³⁻⁵ When SRCC is observed in the pulmonary system, it is assumed to be a metastatic focus from the gastrointestinal system.² Various immunohistochemical tumour markers exist to confirm or deny that; mainly TTF-1 and also CK7, CDX2.¹⁻⁴ SRCC lung primary

Figure 6 A more inferior axial view large spiculated mass with lymphangitic spread within the mediastinum.

tumours will be positive only for CK7 and TTF-1. Secondary tumours from a gastrointestinal primary will be positive for CK20 and CDX2.

In conclusion, we presented a case of a rare subtype of adenocarcinoma of the lung with associated images.

Learning points

- ▶ Adenocarcinoma of the lung is one of the most common types of lung cancer.
- ▶ Among the variants of adenocarcinoma, signet ring cell carcinoma (SRCC) is extremely rare.
- ▶ The patient with SRCC tends to be non-smoker, younger and have a much lower 5-year survival rate compared to the patient with other types of adenocarcinoma of the lung.

Contributors SL and JKS observed, treated and helped in writing the manuscript. EF was instrumental in the editing of the case. CK would complete the final aspects of editing and writing of the case report.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Hayashi H, Hajime K, Yukio N, *et al*. Primary signet-ring cell carcinoma of the lung: histochemical and immunohistochemical characterization*1. *Hum Pathol* 1999;30:378–83.
- 2 Moran CA. Pulmonary adenocarcinoma: the expanding spectrum of histologic variants. *Arch Pathol Lab Med* 2006;130:958–62.
- 3 Castro Y, Moran CA, Flieder DG, *et al*. Primary signet ring cell adenocarcinoma of the lung: a clinicopathological study of 15 cases. *Histopathology* 2001;39:397–401.
- 4 Maemondo M, Yasuo S, Masahito E, *et al*. Rapidly progressive primary adenocarcinoma of the lung with signet-ring cells responding to 5-fluorouracil and leucovorin: a case report. *Int J Clin Oncol* 1997;2:47–50.
- 5 Ou S-HI, Argyrios Z, Jason AZ. Primary signet-ring carcinoma (SRC) of the lung. *J Thorac Oncol* 2010;5:20–7.

Copyright 2013 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow