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CASE REPORT

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Primary signet-ring cell carcinoma of the lung in an HIV-positive patient

Alberto Testori[1] | **Gianluca Perroni**[1] | **Camilla De Carlo**[2] | **Alessandro Crepaldi**[1] | **Marco Alloisio**[1] | **Ugo Cioffi**[3]

[1]Department of Thoracic Surgery, IRCCS Humanitas Research Hospital, Rozzano, Italy

[2]Department of Pathology, IRCCS Humanitas Research Hospital, Rozzano, Italy

[3]Department of Surgery, University of Milan, Milan, Italy

Correspondence
Alberto Testori, Department of Thoracic Surgery, Humanitas Clinical and Research Center – IRCCS -, via Manzoni 56, 20089 Rozzano, Mi, Italy.
Email: alberto.testori@humanitas.it

[Correction added on 26 February 2021, after first online publication: the ORCID of Ugo Cioffi has been added.]

Abstract

Primary lung signet-ring cell carcinomas are a rare entity and only a few cases of pure signet-ring cell carcinomas of the lung are reported in the English literature. They usually have an aggressive behavior and a poor prognosis because in most cases they are identified at an advanced stage. We present a unique case of primary signet-ring cell carcinoma of the lung because the patient was HIV positive, a heavy smoker, and also the tumor, discovered incidentally during chest x-ray, was a pure type of signet-ring cell carcinoma. Surgical therapy associated with chemoradiotherapy represents the gold standard in the care of these patients.

KEYWORDS

chemotherapy, lung, prognosis, signet-ring cell carcinoma, surgical therapy

INTRODUCTION

Signet-ring cell carcinoma (SRCC) is a poorly differentiated adenocarcinoma subtype characterized by abundant intracellular mucin that causes the cell nucleus to move to the end of the cell creating a crescent-shaped or signet-ring cell morphology.[1,2]

It is most commonly located within the stomach, colon, esophagus, rectum, breast, or prostate. It is rarely present as a primary neoplasm in the lung where is usually located as a metastasis of ring cell gastric cancer occurring in the lymphatics or by the hematogenous route.[3] We present a remarkable case of primary SRCC of the lung where the patient was HIV positive, a heavy smoker, and also the tumor, discovered incidentally at chest x-ray, was a pure type of SRCC.

CASE REPORT

A 60-year-old woman came to our attention after the incidental finding of a right upper lobe nodule discovered with a chest x-ray. She was a former smoker of 35 pack/years and HIV positive. A chest computed tomography (CT) scan was performed, confirming the presence of an irregular, spiculate, 15-mm lesion within the lateral segment of the middle lobe (Figure 1). The positron emission tomography (PET)/CT scan showed an intense uptake (SUV 7)

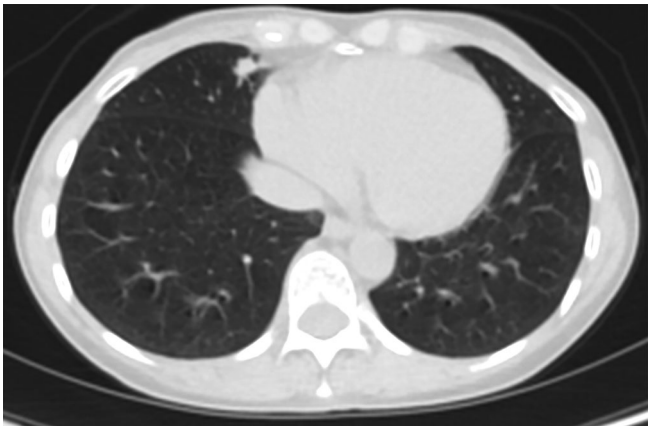

FIGURE 1 CT scan showing a 15-mm nodule located in the lateral segment of the middle lobe

(Figure 2). Because of the proximity at the right atrium, a video-assisted thoracoscopic surgery diagnostic wedge resection followed by standard lobectomy was discussed with the patient and subsequently scheduled. Her physical condition was remarkable, FEV1 was 2.69 L (103%), ppoFEV1 of 2.41 L, and a predicted death rate of 1.02% using Thoraco-score. The night before surgery, a single dose of low molecular weight heparin (nadroparin 2850 UI administered at 8 PM) and compression stockings were given to prevent an embolism. Moreover, the patient was informed about her active involvement during postoperative phase to reduce the complication rate and improve the outcome. An intraoperative frozen section revealed the presence of nonsmall cell lung cancer (NSCLC) within the specimen, and a lobectomy with lymphadenectomy was performed. Definitive histology revealed the presence of a 1.1-cm pulmonary adenocarcinoma with signet-ring features with single metastasis to mediastinal lymph node gland (4R station), configuring a pT2a N2 disease.

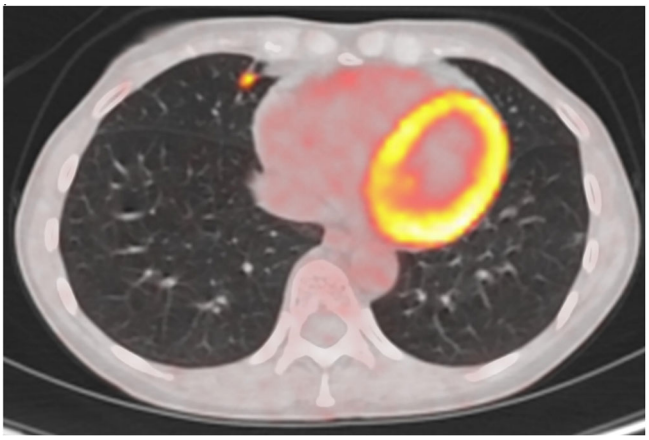

FIGURE 2 A maximum standardized uptake value (SUV max) of 7 was detected within the nodule at PET/CT scan

The lesion was an incidental finding in the middle lobe of the lung, nodular in shape, white-grayish in color, measuring 1.1 cm in diameter, located in the subpleural region, causing pleural retraction.

Microscopically, a solid growth of neoplastic signet-ring elements was evident, with focal, not transmural infiltration of visceral pleura.

To investigate the origin, a panel of immunohistochemistry was performed, including CDX2, TTF-1, CK7 and Napsin A (Figure 3). The immunophenotype of the neoplastic population demonstrated their pulmonary origin, as we found triple Napsin A, TTF-1 (Figure 3(d)) and CK7 positive (Figure 3(e)) immunostaining and CDX2 (Figure 3(c)) negative immunostaining.

After the surgery, the patient underwent three chemotherapy cycles with cisplatin (CDDP) and vinorelbine (VNB) (the fourth cycle was not performed due to intolerance).

Subsequently,a well-tolerated ilo-mediastinal radiotherapy treatment was also performed. The first check with contrast total body and brain CT scan was negative. At 1-year follow-up with total body CT scan the patient was well, free from recurrence and distant metastasis.

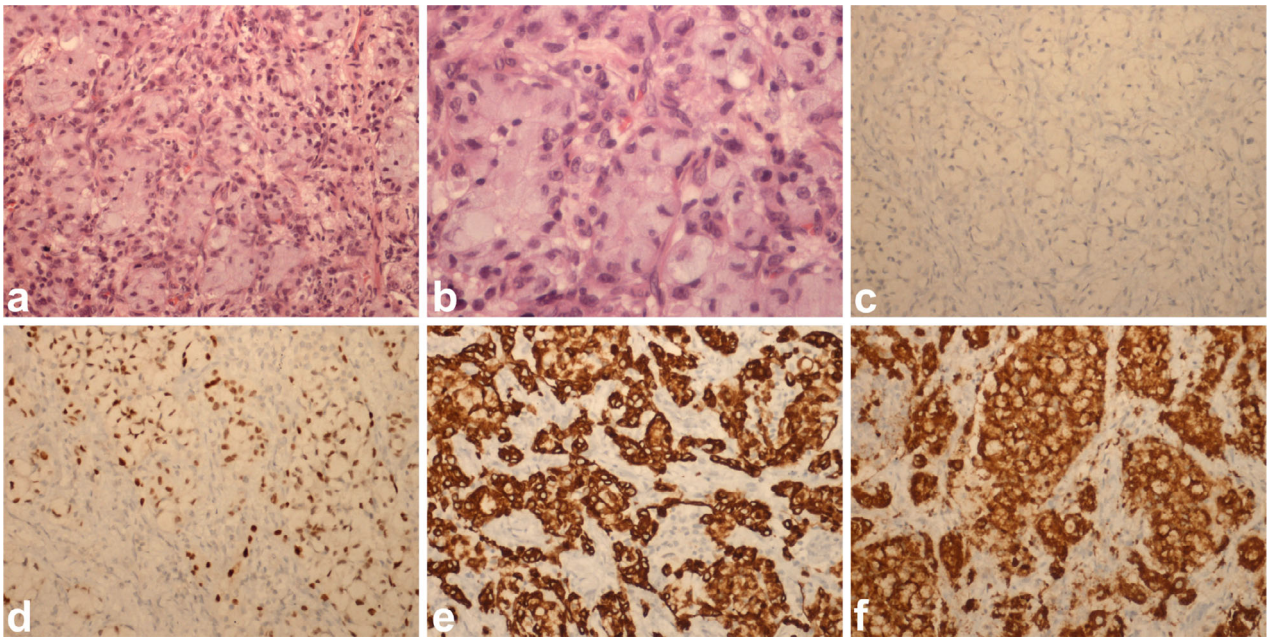

FIGURE 3 Immunohistochemistry (IHC) of a lung specimen from the considered patient. (a) and (b) H&E (20× and 40×, respectively) showing signet-ring cells with abundant intracytoplasmic mucin and peripheral nuclei. (c) Negative nuclear CDX-2 antibody of the neoplastic population. (d) TTF-1 nuclear positive staining. (e) Abundant cytoplasmic and membranous positivity for CK7. (f) Napsin a antibody presenting a diffuse membranous and cytoplasmic granular staining

DISCUSSION

SRCC is a very rare type of lung tumor, more often presenting together with other subtypes of adenocarcinoma. Usually affecting nonsmokers, it is more aggressive than lung carcinoma and carries a worse prognosis than other more common forms of lung neoplasms because in most cases it is diagnosed in stage IV disease (49.2%) compared with patients with adenocarcinoma (36.8%, $p< 0.0001$).

Because of its rarity in the lung as a primary tumor, metastatic disease of different organs is considered in the differential diagnosis. The stomach is the most frequent site of origin,[4] but SRCC has also been reported to involve the breast, urinary bladder, thyroid, and ovary. Moreover, malignant lymphomas and melanomas can sometimes exhibit signet-ring features.[5,6]

In this context, clinical data, radiologic examinations, and immunohistochemistry are essential to rule out metastasis. In our patient it was not possible to demonstrate any active neoplasm on PET study in other organs, excluding specifically a gastric origin of the cancer. This conclusion was further supported by immunohistochemistry, which mainly suggested lung carcinoma.[7] In fact, double TTF-1 and Napsin A positive immunostaining (Figure 3(d),(f), respectively) is highly specific for primary lung adenocarcinoma.[8] Moreover, primary pulmonary adenocarcinomas with signet-ring cells express TTF-1 and CK7 but are usually negative for gastrointestinal markers such as CDX2,[9] as confirmed by our results (Figure 3).

To date, the literature on primary pulmonary SRCC mainly includes case reports and small-scale retrospective analyzes, with the exception of a few publications like those of Ou et al.[3] and Tsuta et al.[10] Ou and colleagues[3] histologically identified only 262 cases of primary SRCC lung carcinoma between 1989 and 2006. Tsuta and colleagues[10] reported 39 cases (1.5%) of primary lung carcinoma with an SRCC component among 2640 resected cases for primary lung carcinomas. Patients with this lung adenocarcinoma subtype are generally younger than those with adenocarcinoma, accounting for 5% of lung cancers in individuals under 40 compared to 1.3% of all lung carcinomas within the general population.

Patients with SRCC who have not smoked cigarettes tend to be younger than those who have always been smokers and to have a slightly better prognosis, although it is statistically not significant. In 2018, another primary pulmonary SRCC study carried out by Wu et al.[11] analyzed a total of 738 cases and showed that almost all patients with primary pulmonary SRCC had distant metastases at initial diagnosis and had received less aggressive treatment. We believe that ours is the first reported case of SRCC in an HIV patient who was a heavy smoker and not associated with other diseases. The increased risk of lung cancer in HIV-infected people is likely linked to many factors, including the potential oncogenic role of HIV, recurrent lung infections, HIV-induced immunosuppression, and reduced HIV-associated immune surveillance. HIV could also mediate increased susceptibility to tobacco carcinogens.[12]

Surgical therapy should be the gold standard for patients with primary lung SRCC without distant metastasis. For primary pulmonary SRCC with distant metastasis, a multidisciplinary approach involving surgeons, radiotherapists, pulmonologists, and oncologists to improve the survival and quality of life of these patients is needed.[1,13]

CONCLUSION

We can conclude that SRCC has a more serious prognosis than primary lung adenocarcinoma since in about half of cases it is identified at stage IV. Surgical therapy associated with chemoradiotherapy remains essential even in patients with advanced disease. Further clinical and pathological studies should tell us more about these rare tumors.

CONSENT FOR PUBLICATION

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available on request.

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AUTHOR CONTRIBUTIONS

All authors carried out the concept and the design of the study and revised the manuscript.

CONFLICT OF INTEREST

None of the contributing authors have any conflict of interest, including specific financial interests or relationships and affiliations relevant to the subject matter or materials discussed in the manuscript.

ORCID

Alberto Testori https://orcid.org/0000-0002-3032-9494
Gianluca Perroni https://orcid.org/0000-0002-3007-3214
Ugo Cioffi https://orcid.org/0000-0002-5321-5828

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