

Pulmonary Sarcomatoid Giant Cell Carcinoma with Paraneoplastic Hypertrophic Osteoarthropathy: A Case Report

Osagie Igiebor, Rishard Abdul, Natalie Sun, Leen Khoury, Gil Hevroni, Samy I. McFarlane*

Department of Internal Medicine, SUNY- Downstate Health Science University, 450 Clarkson Avenue, Box 50, Brooklyn, NY 11203

*Corresponding author: smcfarlane@downstate.edu

Received February 19, 2020; Revised March 29, 2020; Accepted April 12, 2020

Abstract Giant-cell carcinoma of the lung (GCCL) is a rare histological form of poorly differentiated non-small-cell lung cancer, which is classified as a subtype of pulmonary sarcomatoid carcinomas. In this case report, we describe the case of a 57 year old female with a past medical history of HIV on HAART (CD4 count at the time was 621 cell/ μ l). She presented to the hospital with a two months history of productive cough with yellowish sputum containing streaks of blood, twelve pound weight loss, bilateral hand swelling, and knee pain with noticeable finger clubbing on physical examination. Chest computed tomography scan and subsequent bronchoscopy was performed and revealed a protruding endobronchial lesion in the right upper lobe (RUL) bronchus. Definitive diagnosis established by way of pathologic analysis of the resected specimen obtained from RUL lobectomy revealed sarcomatoid giant cell carcinoma, with tumor size 9.5 cm and invasion of the visceral pleura and 1/13 hilar lymph node involvement. The pathological stage was determined as pT3N1Mx based on the tumor node metastasis (TNM) staging system. The patient was started on adjuvant combination cisplatin and docetaxel therapy with supplemental G-CSF four months after surgery and followed as an outpatient. The significance of this case is that it highlights a very rare lung cancer, unveiling a possible paraneoplastic syndrome associated with this malignancy and the impact of HIV HAART therapy in carcinogenesis.

Keywords: *giant cell carcinoma, paraneoplastic, hypertrophic osteoarthropathy*

Cite This Article: Osagie Igiebor, Rishard Abdul, Natalie Sun, Leen Khoury, Gil Hevroni, and Samy I. McFarlane, "Pulmonary Sarcomatoid Giant Cell Carcinoma with Paraneoplastic Hypertrophic Osteoarthropathy: A Case Report." *American Journal of Medical Case Reports*, vol. 8, no. 7 (2020): 162-165. doi: 10.12691/ajmcr-8-7-1.

1. Introduction

Sarcomatoid carcinoma (SC) is a rare primary malignant tumor. It can occur in many different organ systems such as the skin, thyroid gland, bone, urinary tract, breast, pancreas, liver and other systems. Its incidence is estimated at 0.3-1.3 % of all primary lung malignancies. [1-6] It is more common in males particularly with a heavy smoking history, and the average age at diagnosis is at 60 years. [3]

According to the 2015 WHO classification of lung tumors, pulmonary sarcomatoid carcinoma is a general term that encompasses pleomorphic carcinoma, pulmonary blastoma, spindle cell and giant cell carcinomas. Giant cell carcinoma consists almost entirely of tumor giant cells (including multinucleated cells), with no differentiated carcinomatous elements. The definitive diagnosis may only be made on a resected tumor with specific histological components mentioned in the diagnosis. [5]

Most lung malignancies are notorious for producing paraneoplastic syndromes. Paraneoplastic syndromes are a group of clinical disorders that are associated with

malignant diseases and are not directly related to the physical effects of the primary or metastatic tumors. [7] Hypertrophic pulmonary osteoarthropathy (HPO) is a paraneoplastic syndrome defined as the presence of hypertrophic osteoarthropathy (HOA) in a patient with lung cancer. HOA is a constellation of symptoms due to abnormal proliferation of the cutaneous and osseous tissues at the distal regions of the extremities. The triad of clinical signs and symptoms include finger clubbing, symmetric polyarthritis, and periostitis of the long tubular bones. [8] In this text, we report a case of SC giant cell carcinoma with hypertrophic osteoarthropathy encountered in a HIV positive patient.

2. Case Report

A 57-year-old Latina woman with a past medical history of HIV on anti-retroviral therapy (ART) presented with complaints of a 2 month history of cough productive of yellow sputum with associated streaks of blood, 12 pound weight loss, bilateral hand swelling, finger clubbing and knee pain. Chest CT revealed a prominent, slightly rounded consolidation of the inferior right upper lobe with

adjacent ground glass and interstitial opacities likely representing pneumonia (Figure 1A). The patient was admitted and initially treated for community acquired pneumonia. However, an interval chest radiograph done one month later revealed a persistent and enlarging right upper lobe infiltrate (Figure 1 B & C). The patient subsequently underwent bronchoscopy, which revealed a protruding endobronchial lesion almost completely obstructing the right upper lobe bronchus limiting any further visualization of the RUL segments. Initial pathologic analysis of specimens biopsied during bronchoscopy revealed non-small cell lung carcinoma (NSCLC). Subsequently, a positron emission tomography (PET) scan was performed and showed a hypermetabolic RUL pulmonary mass with obstruction of RUL bronchus compatible with malignancy in addition to low level uptakes in the adrenal and thyroid glands. A MRI of the

abdomen was done to better examine the adrenal gland, however, no masses were observed, only mild thickening. It was determined by the tumor board that the patient would best benefit from tumor excision and adjuvant chemotherapy. Subsequently, a definitive diagnosis was established by way of a RUL lobectomy. The resected specimen consisted of multiple fragments of tan/black soft tissue measuring 0.3 x 0.3 x 0.2 cm in aggregate. Pathologic analysis of the resected specimen showed sarcomatoid giant cell carcinoma, tumor size 9.5 cm with invasion of the visceral pleura and 1/13 hilar lymph node involvement. The pathological stage was pT3N1Mx based on the tumor node metastasis (TNM) staging system. By immunohistochemistry, the tumor cells were diffusely positive for CK7 while negative for CK20, TTF-1 and p40. The patient was started on adjuvant chemotherapy (do you know the chemo meds?) and followed as an outpatient.

A.



B.



C.



Figure 1. Imaging findings (A) Computed tomography (CT) of the chest showing inferior right upper lobe consolidation with adjacent ground glass and interstitial opacities. (B) Baseline plain chest radiography showing inferior right upper lobe mass. (C) One month follow up plain chest radiography showing inferior right upper lobe mass with significantly expanded infiltrates

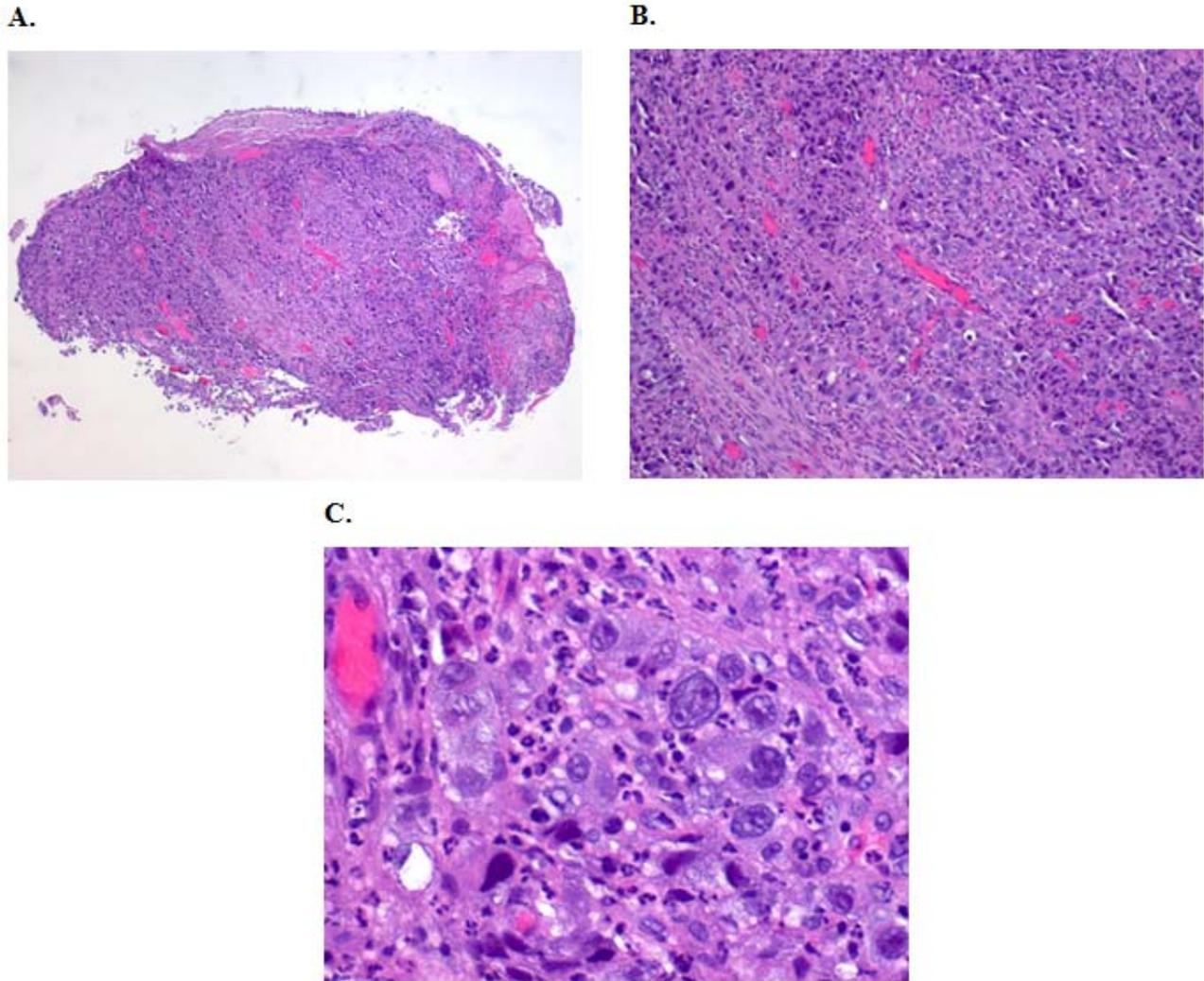


Figure 2. Histological findings (Hematoxylin and eosin). The tumor was roughly round with fragmented margins (A, original magnification). The tumor exhibited typical features of sarcomatoid carcinomas such as areas of carcinomatous and sarcomatous elements (B, x100). Very large, multinucleated, bizarre cells were observed (C, x400)

3. Discussion

This case reveals a possible paraneoplastic syndrome associated with pulmonary SC, the impact of HIV HAART on carcinogenesis and the prognosis of HIV patients with SC. Paraneoplastic syndromes are a group of clinical disorders that are associated with malignant diseases and are not directly related to the physical effects of the primary or metastatic tumors. [9] Hypertrophic osteoarthropathy is a paraneoplastic syndrome consisting of a triad of symptoms including clubbed fingers, symmetric polyarthrititis, and periostitis of the long tubular bones. [9,10] The above patient presented with signs and symptoms suggestive of this paraneoplastic syndrome which has not yet been reported to be associated with this type of cancer in the literature.

SC is a rare malignancy accounting for less than 1% of all lung cancers. [9,10] It is characterized by components of sarcoma or sarcoma like structures (spindle cell or giant cells) and it includes five histological variants.⁹ Immunohistochemical studies play an important role in determining the histological type of non-small lung carcinoma. In general, CK5/6 and p63 are markers of squamous cell carcinoma. SP-A and TTF-1 are markers of

adenocarcinoma. CK7 and CK20 are important in discriminating primary lung carcinoma and metastatic lung carcinoma [3]. In our patient, the immunohistochemistry was positive for CK7, but negative for TTF-1, p40 and CK20. The CD7/CK20 pattern suggested a primary lung carcinoma.

Due to the heterogeneity in histopathology, surgical biopsy is required for definitive diagnosis. Treatment principle is the same as NSCLC, however, compared to NSCLC, patients with SC have a worse prognosis, higher recurrence after tumor resection and a lower survival rate. [8,11] The prognosis of these patients depend on tumor size and presence or absence of metastases. [13] Fishback et al. in 1994 concluded that tumor size > 5 cm, a clinical stage > stage I, and lymph node involvement was associated with a significantly shorter patient survival. The median survival of patients with sarcomatoid carcinoma is 10 months, which is significantly lower when compared to that of more common lung carcinomas (20 months for adenocarcinoma, 18.5 months for squamous cell carcinoma, and 12.6 months for large cell carcinoma). [15]

Although uncertain, the effects of factors such as a history of HIV may alter the prognostic variables of SC in the present case. A substantive number of patients have

died despite non-detectable HIV viral loads and well preserved immunity measured by CD4 cell counts. It is also unclear if HIV directly increases the risk of this malignancy in this patient population. However, HIV/AIDS is well known to increase the risk of certain malignancies including Kaposi sarcoma and non-Hodgkin's lymphoma, both of which are classified as AIDS-defining cancers (ADC). In the post - HAART era, the non-ADCs including anal cancer, lung cancer, liver cancer and head/neck cancer constitute an increasing proportion of documented malignancies in HIV patients. Therefore the role of HAART therapy and its carcinogenic properties in relation to the increased incidence of non - ADC needs to be explored as there has been only one reported case of giant cell carcinoma of the lung not associated with HAART therapy. For example, azidothymidine approved for HAART therapy of HIV-1 integrates into DNA, resulting in mutations of the hypoxanthine-guanine phosphoribosyl-transferase and thymidine kinase genes and other genotoxic effects in cultured cells. [11] Such mutations may contribute to cellular carcinogenesis.

There are currently no standard effective chemotherapeutic regimens for pulmonary sarcomatoid giant cell carcinoma. However, traditionally platinum-based chemotherapy is used if the patient is not a surgical candidate or if adjuvant chemotherapy is indicated. Adjuvant chemotherapy is indicated for nodal or chest wall involvement because they are associated with worse prognosis. [12,14] SC are more resistant to first line platinum based chemotherapy in comparison of other subtypes of NSCLC. [12] The role of targeted treatment like EGFR inhibitors is still not completely understood in SC as compared to NSCLC. Our patient continues to follow up at the oncology clinic and completed 4 cycles of combination cisplatin and docetaxel therapy with supplemental G-CSF four months after surgery.

Acknowledgements

This work is supported, in part, by the efforts of Dr. Moro O. Salifu M.D., M.P.H., M.B.A., M.A.C.P., Professor and Chairman of Medicine through NIH Grant number S21MD012474.

References

- [1] N.F. Fishback, W.D. Travis, C.A. Moran, D.G. Guinee Jr., W.F. McCarthy, C.A. Koss Pleomorphic (spindle/giant cell) carcinoma of the lung: a clinicopathologic correlation of 78 cases *Cancer*, 73 (1994), pp. 2936-2945.
- [2] M. Nakajima, T. Kasai, H. Hashimoto, Y. Iwata, H. Manabe. Sarcomatoid carcinoma of the lung: a clinicopathologic study of 37 cases *Cancer*, 86 (1999), pp. 608-616.
- [3] G. Rossi, A. Cavazza, N. Sturm, M. Migaldi, N. Facciolo, L. Longo, et al. Pulmonary carcinomas with pleomorphic, sarcomatoid or sarcomatous elements: a clinicopathologic and immunohistochemical study of 75 cases. *Am J Surg Pathol*, 27 (2003), pp. 311-324.
- [4] W.D. Travis, L.B. Travis, S.S. Devesa; Lung cancer. *Cancer*, 75 (1995), pp. 191-202.
- [5] D. Travis, E. Brambillia, K. Muller-Hermelink, C.C. Harris (Eds.), WHO classification of tumours. Pathology and genetics. Tumor of the lung, pleura, thymus and heart, IARC Press, Lyon (2004), pp. 53-58.
- [6] Spiro SG, Gould MK, Colice GL. Initial evaluation of the patient with lung cancer: symptoms, signs, laboratory tests, and paraneoplastic syndromes: ACCP evidenced-based clinical practice guidelines (2nd edition) *Chest*. 2007; 132: 149S-160S.
- [7] Nobuhiro Kanaji, Naoki Watanabe, Nobuyuki Kita, Shuji Bandoh, Akira Tadokoro, Tomoya Ishii, Hiroaki Dobashi, and Takuya Matsunaga; Paraneoplastic syndromes associated with lung cancer. *World J Clin Oncol*. 2014 Aug 10; 5(3): 197-223.
- [8] Martin, Linda W. et al. Sarcomatoid Carcinoma of the Lung: A Predictor of Poor Prognosis. *The Annals of Thoracic Surgery*, Volume 84, Issue 3, 973-980.
- [9] Beasley, Mary Beth et al. The 2004 World Health Organization classification of lung tumors, *Seminars in Roentgenology*, Volume 40, Issue 2, 90-97.
- [10] Travis, William D. et al, The 2015 World Health Organization Classification of Lung Tumors, *Journal of Thoracic Oncology*, Volume 10, Issue 9, 1243-1260.
- [11] Yendamuri S, Caty L, Pine M, et al. Outcomes of sarcomatoid carcinoma of the lung: a Surveillance, Epidemiology, and End Results Database analysis. *Surgery* 2012; 152 (3): 397-402.
- [12] Vieira, Thibault et al, Efficacy of First-Line Chemotherapy in Patients with Advanced Lung Sarcomatoid Carcinoma *Journal of Thoracic Oncology*, Volume 8, Issue 12, 1574-1577.
- [13] Huang S-Y, Shen S-J, Li X-Y. Pulmonary sarcomatoid carcinoma: a clinicopathologic study and prognostic analysis of 51 cases. *World Journal of Surgical Oncology*. 2013; 11: 252.
- [14] Raveglia, Federico et al, Personal Experience in Surgical Management of Pulmonary Pleomorphic Carcinoma, *The Annals of Thoracic Surgery*, Volume 78, Issue 5, 1742-1747.
- [15] Panagiotis Hountis, Sotirios Moraitis, Panagiotis Dedeilias, Polychronis Ikonomidis and Mattheos Douzinas, Sarcomatoid lung carcinomas: a case series. *Cases Journal* 2009, 2: 7900.

