

Case Report

A very rare and aggressive lung tumor

Claudia Cordoba-Carrillo^{1*}, José Nieves-Nieves¹, Viridiana Salinas-González¹, María Christina Betancourt-Quiles¹, Rosángela Fernández-Medero¹, Ricardo Fernández-González¹, José Lozada-Costas², Melissa Sepúlveda-Ramos³, Román Vélez-Rosario³

¹Pulmonary Medicine Department, San Juan City Hospital, P. M. B. 463 P. O. Box 70344 San Juan, PR 00936 San Juan, Puerto Rico.

²Hematology and Oncology Department, San Juan City Hospital, San Juan, Puerto Rico.

³Pathology Department, University of Puerto Rico School of Medicine, San Juan, Puerto Rico.

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Rhabdoid phenotype is an uncommon histopathologic malignancy found in <1% of pulmonary large cell carcinomas and is associated with an extremely poor prognosis. To our knowledge, merely forty-six cases have been reported in the literature with reasonable immunohistochemical discoveries allowing differentiation from other rhabdoid-like neoplasms though none acknowledged effective treatment of this exceedingly aggressive tumor. At this moment, there is no specific treatment for large cell cancer with rhabdoid phenotype for this subpopulation and most cases have been treated as non-small cell lung cancer. Herein presented is a case of a 63 year-old male non-smoker diagnosed with this aggressive tumor phenotype which had an aggressive behavior and unfortunate prognosis. The main characteristics of the tumor and the most recent treatment options are discussed.

Key words: Pleural effusion, large cell lung carcinoma, rhabdoid phenotype, immunohistochemical stains, lung cancer.

INTRODUCTION

Large Cell Carcinoma with Rhabdoid Phenotype (LCCRP) is a rare histological variant of lung tumors. Approximately 10% of its cells contain distinctive eosinophilic whorled perinuclear inclusions composed of intermediate filaments, giving the cells a resemblance of a rhabdomyosarcoma (Travis et al., 2004). This variant was first reported in 1995 and recognized by the World Health Organization in 1999 (Tamboli et al., 2004; Brambilla et al., 2001). To our knowledge there have been only 46 reported cases worldwide. Saini et al. (2009) published a literature review of this malignant process and reported 38 cases in the English literature until 2009. Since then, Izquierdo-Garcia et al. (2010) reported 7 new cases of infrequent histological types, and Dettmer et al. (2012) described the first case of an exon 19 deletion in epidermal growth factor receptor (EGFR) in a

LCCRP associated with a poorly differentiated pulmonary adenocarcinoma.

Tobacco smoking and male gender have been the most common risk factors identified for the development of this rare condition. We report a case where interestingly, our patient had no significant risks factors for this uncommon variant.

The objective of this article is to provide relative medical literature concerning therapeutic management options available today for this aggressive tumor.

CASE

A 63 year-old man that worked as a gardener and who had a history of arterial hypertension and bronchial asthma

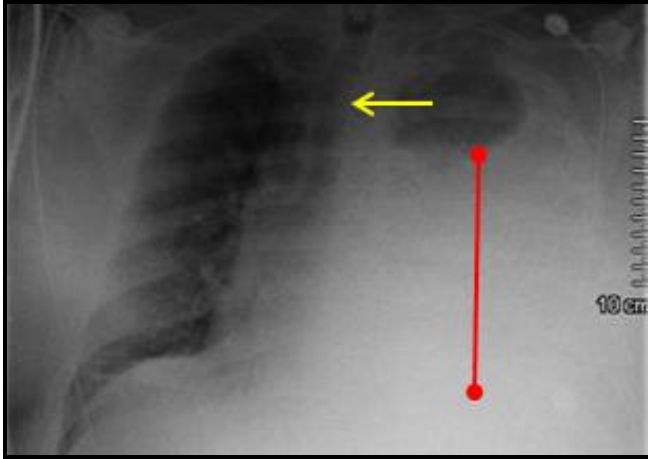


Figure 1. Chest XRAY demonstrating opacity of the left lung (red bar) and deviation of the trachea to the right (yellow arrow).



Figure 2. Chest computed tomography representing left lung tumor (red arrow).

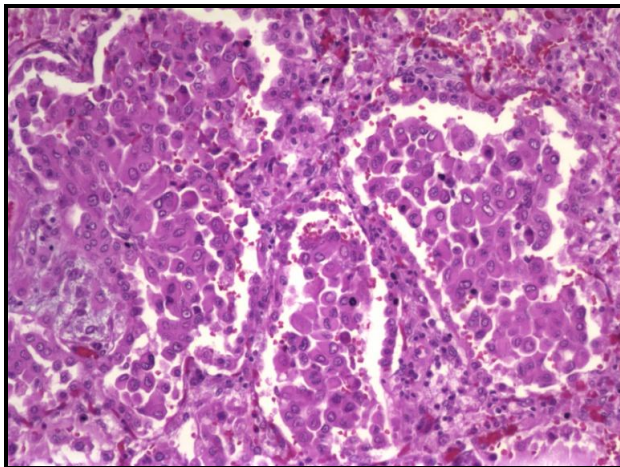


Figure 3. Lung involved by rhabdoid carcinoma showing large cells with eosinophilic cytoplasmic inclusions. (H&E, 200x).

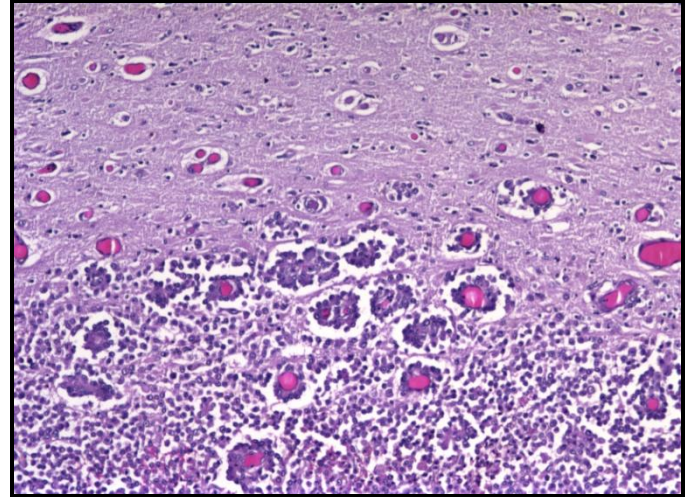


Figure 4. Rhabdoid carcinoma of lung metastatic to brain; tumor in lower half and uninvolved brain in upper half. (H&E, 100x).

asthma was evaluated after presenting a non productive cough and shortness of breath associated with a left sided pleuritic chest pain of one week evolution. He had neither history of tobacco smoking nor any other identifiable environmental exposures. Pertinent clinical findings included tachypnea, decreased breath sounds, dullness to percussion and tactile fremitus on his left hemithorax. The laboratories were unremarkable except for respiratory alkalosis and hypoxemia on the arterial blood gases. Chest images demonstrated a complete opacification of his left lung due to a large pleural effusion (Figures 1 and 2). A diagnostic as well as therapeutic thoracentesis was performed showing an exudative fluid with impression remarkable for atypical reactive mesothelial cells with inflammatory infiltrates. Partial symptomatic relief was obtained until the reaccumulation of the pleural effusion leading to a chest tube placement for fluid drainage. However, the patient's condition deteriorated rapidly, consequently requiring mechanical ventilator support and eventually died from complications of septic shock and multi-organ failure. An autopsy gave the diagnosis of LCCRP features, along with alveolar hemorrhage and metastatic lesions to the heart, liver, pancreas, adrenals, kidneys, thyroid, lymph nodes, and brain (Figures 3 and 4). The lung tissue immunohistochemical staining was positive for cytokeratin, vimentin and pankeratin lastly providing the diagnosis of metastatic rhabdoid carcinoma of the lung (Figures 5 and 6). Due to the nature of the advanced disease and diagnosis made post mortem, no treatment protocols of chemotherapy or radiotherapy were initiated.

DISCUSSION

As in our case, LCCRP has been found to be very

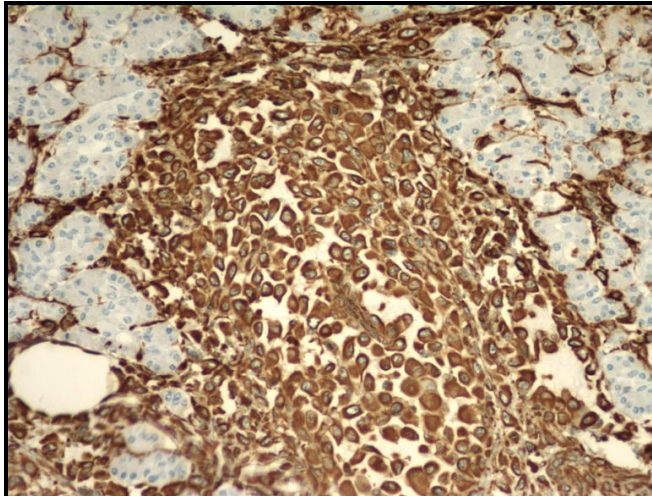


Figure 5. Vimentin positive (brown) rhabdoid carcinoma metastatic to pancreas (light blue) (200x).

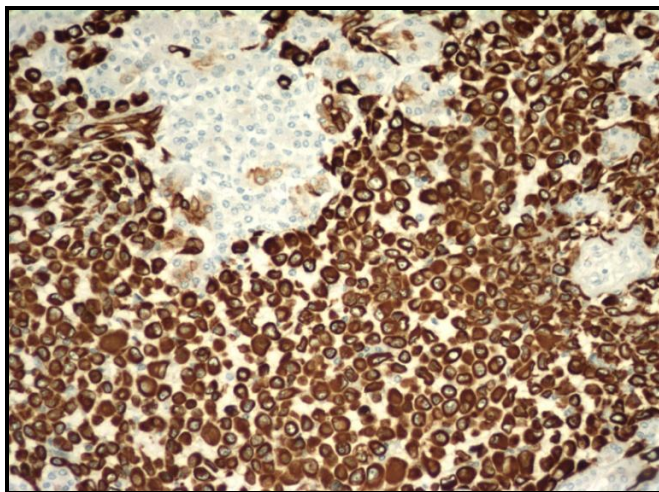


Figure 6. Cytokeratin positive (brown) rhabdoid carcinoma metastatic to pancreas (light blue) (200x).

aggressive. Although the cases reported in the literature have been related to heavy cigarette smoking our patient had no recognizable risk factors for this rare tumor. This entity generally when diagnosed is at an advanced stage, with an expected mortality within months of diagnosis. There have been reports suggesting that the presence of rhabdoid cells is a marker of poorer prognosis. Specific immunohistochemical stains are required for the diagnosis, such as vimentin, which is ubiquitously expressed and is often intermingled with cytokeratins. Other markers including neuron-specific enolase, epithelial membrane antigen, chromogranin, and synaptophysin, are frequently mentioned to some degree in a significant proportion of rhabdoid cells (Saini et al., 2009; Shimazaki

et al., 2001). The expression of thyroid transcription factor-1 (TTF-1), a commonly used marker for primary lung cancers, appears to be less common in this variant (Tamboli et al., 2004).

No clinical trials have been conducted specifically for treatment for LCCRP since most cases have been treated as non small cell lung cancer (NSCLC) following existent guidelines. As in NSCLC, patients with LCCRP treated with surgery at early stages of diagnosis have better survival outcomes. In selected cases, surgical resection of metastatic disease can also have a positive effect on survival (Saini et al., 2009; National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology, 2012; Kaneko et al., 2002; Otera et al., 2010).

The management of advanced disease NSCLC is based on histologic, molecular characteristic and patient performance. The initial therapy should be the one with the highest benefit and less toxicity. Most protocols are platinum-based but when adequate response is not achieved or the diagnosis is made at advanced stages, combination therapy has been mentioned as well.

Bevacizumab, a humanized monoclonal antibody that inhibits vascular endothelial growth factor (VEGF) inhibiting the process of angiogenesis and/or chemotherapy alone has been given to patients who have good performance status and advanced or recurrent NSCLC. Bevacizumab has been reserved for disease progression.

Another agent, Erlotinib, which specifically targets the epidermal growth factor receptor (EGFR) tyrosine kinase, which is highly expressed and occasionally mutated in various forms of cancer, is indicated as first-line therapy in patients with EGFR mutation. Other tyrosine kinase inhibitors include Crizotinib - the preferred therapy in anaplastic lymphoma kinase (ALK) positive patients.

If the disease progresses, the single-agent docetaxel with its well-established anti-mitotic chemotherapy properties, which interferes with cell division, is well recognized as a second-line agent. Erlotinib is also used as a second-line agent. Erlotinib is furthermore indicated as a third line agent; in reported cases it has been superior to supportive care (National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology, 2012).

Conclusion

Although the available information has been limited due to few reported cases, chest physicians should be aware of this very aggressive and uncommon malignancy. LCCRP may be considered in male patients without significant risk factors and an unusual hemithorax opacification. This rare tumor usually has catastrophic outcome however early intervention for tissue diagnosis is essential since therapies such as pneumonectomy and adjuvant chemotherapy may improve survival.

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ABBREVIATIONS

LCCRP, Large cell carcinoma with rhabdoid phenotype; **NSCLC**, non-small cell lung cancer; **TTF-1**, thyroid transcription factor-1; **VEGF**, vascular endothelial growth factor; **EGFR**, epidermal growth factor receptor, **ALK**, anaplastic lymphoma kinase.

REFERENCES

- Travis WD, Brambilla E, Muller-Hermelink HK, Harris CC (2004). World Health Organization Classification of Tumours. Pathology and Genetics of Tumors of the Lung, Pleura, Thymus and Heart. IARC Press, Lyon. pp. 45-50.
- Tamboli P, Toprani TH, Amin MB, Ro JS, Ordóñez NG, Ayala AG, Ro JY (2004). Carcinoma of lung with rhabdoid features. *Hum. Pathol.* 35(1):8-13.
- Brambilla E, Travis WD, Colby TV, Corrin B, Shimosato Y (2001). The new World Health Organization classification of lung tumors. *Eur. Respir. J.* 18(6):1059-68.
- Saini G, Kumar M, Julka PK, Puri T, Sharma M, Rath GK (2009). Rhabdoid variant of lung cancer: clinicopathological details of a case and a review of literature. *J. Cancer Res. Ther.* 5(1):54-7.
- Izquierdo-Garcia FM, Moreno-Mata N, Herranz-Aladro ML, Cañizares MA, Alvarez-Fernandez E (2010). Lung carcinoma with rhabdoid component. A series of seven cases associated with uncommon types of non-small cell lung carcinomas and alveolar entrapment. *Histol. Histopathol.* 25(10):1287-95.
- Dettmer M, Hench J, Pang B, Willi N, Cathomas G (2012). Rhabdoid large cell carcinoma of lung, with illustrative immunohistochemical and molecular findings. *Appl. Immunohistochem. Mol. Morphol.* 20(3):208-13.
- Shimazaki H, Aida S, Sato M, Deguchi H, Ozeki Y, Tamai S (2001). Lung carcinoma with rhabdoid cells: a clinicopathological study and survival analysis of 14 cases. *Histopathology* 38(5):425-34.
- National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology (2012). National Comprehensive Cancer Network. Available at www.nccn.com. Accessed January, 2012.
- Kaneko T, Honda T, Fukushima M, Haniuda M, Komatsu H, Kodama T (2002). Large cell lung carcinoma of the lung with a rhabdoid phenotype. *Pathol. Int.* 52:643-7.
- Otera H, Ikeda F, Nakawaga S, Kono Y, Sakurai T, Tada K, Hashimoto K, Ikeda A (2010). Intussusception of small intestine due to metastasis of large cell carcinoma of the lung with a rhabdoid phenotype. *Eur. Respir. Rev.* 19(117):248-252.