Hemoptysis in a patient with pulmonary angiosarcoma

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Abstract

Pulmonary Artery Angiosarcoma (PAS) is a rare malignant vascular tumor with an aggressive clinical course and poor prognosis. The first line therapy is the surgical resection, but an early diagnosis is difficult due to the nonspecific clinical and radiological manifestations. The purpose of this case report is to analyze the difficulties in PAS diagnosis. A 32 years-old man, with a history of hemoptysis in the last two months, undergoes total body CT, which revealed multiple nodules in his left lung, surrounded by areas of ground glass opacity, without any extra-lung lesion. Fiberoptic bronchoscopy and bronchial washing were negative for neoplastic cells and open lung biopsy was necessary for diagnosis of PAS. A surgical resection was not allowed because the left lung was hepatized, so the surgeon couldn't reach the hilum; furthermore, the subclavian vessels were infiltrated by cancer. After a month of supportive therapy, the patient died as a consequence of multiple organ failure. Our case report underlines that PAS should be considered as a possible diagnosis for patients with hemoptysis and lung nodules surrounded by ground glass opacity.

Introduction

Pulmonary Artery Angiosarcoma (PAS) is a rare tumor that originates from the endothelium of the pulmonary arteries. It has an incidence ranging from 0.001% to 0.03% of all malignancies, with a slight prevalence in men and between 50 and 55 years.[1] The risk factors are associated with radiation, polyvinyl chloride, and pesticides. The clinical manifestations are similar to those of lung carcinomas: dyspnea, dry cough, chest pain, hemoptysis, while on the radiological aspect the appearance is of a single or multiple bilateral lung nodules with areas of parenchymal thickening with ground glass. The average duration of the disease is approximately 3 months after diagnosis, but early radical surgery increases survival to approximately 1 year.[2]

Case Report

A 32 years-old man, a trader, with a history of smoking and drug addiction (marijuana and hashish), is hospitalized in our operating unit complaining for about two months of hemoptysis, dyspnea, fever, asthenia and weight loss. On auscultation of the chest there are crackles in the left upper lobe (Figure 1). Blood tests show severe iron deficiency anemia with the need for transfusions of concentrated red blood cells, an increase in inflammation indexes (ESR, PCR) and negativity of neoplastic markers and autoantibodies.

Hemogasanalysis shows severe hypoxemic respiratory failure (PAO_2/FIO_2 <250) treated with High-flow Nasal Oxygen Therapy (HFNC). The Full Body CT scan with contrast describes at the level of the apico-dorsal segment of the upper left lobe a nodule with blurred edges (3.5 x 2.1 cm) with slight enhancements after contrast without aerial broncogram, surrounded by areas of parenchymal thickening with frosted glass extended to almost the whole lobe, as by alveolar blood suffusion (Figure 2).

The fiberoptic bronchoscopy confirms the presence of clots in the left upper lobar bronchus without showing an endobronchial tumor or a source of bleeding (Figures 3 and 4). Cytological and microbiological tests on bronchoaspirate were negative for the presence of neoplastic cells, bacteria and fungi.

At Full Body PET-TC scan with fluorodeoxyglucose the metabolic evaluation is highly positive (SUV max 6) at the level of the left pulmonary nodule while it is not significant at the level of perinodular parenchymal thickening of the left upper lobe (SUV max 1.12) probably from alveolar hemorrhage. Cardiac catheterization is performed, but does not reveal pulmonary arteriovenous malformations and bleeding sites from the bronchial, intercostal and pulmonary arteries. The patient starts broad-spectrum cortisone and antibiotic therapy (piperacillin-tazobactam) without benefits.

For the worsening of dyspnea and hemophtoe it is considered appropriate to repeat the Full Body CT with contrast, that highlights the progression of the disease with an increase in the size of the left pulmonary nodule (10 cm), the display of lung thickenings with ground glass at the lung lobe left lower, upper and middle lobes of the right lung, hilar adenomegalias and a 0.4 cm right adrenal lesion as per hemorrhagic infarction (Figure 5). The Full Body PET-TC is also repeated, which overlaps the previous one without showing a further metabolic absorption. The patient is treated by the multidisciplinary team (oncologist, pulmonologist, radiologist and thoracic surgeon) who decides on the surgery for the diagnosis and control of the hemoptysis. Left radical pneumonectomy cannot be per-

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formed because the tumor infiltrates the apex of the thorax and subclavian vessels and the fully hepatized lung does not provide access to all channels for removal. Multiple biopsies of the left lung parenchyma are performed, the histological examination documents it to be poorly differentiated pulmonary angiosarcoma with clusters of epithelial-like cells, with atypia of hyperchromic nuclei and eosinophilic cytoplasm surrounding irregular blood-filled vascular spaces. Immunohistochemistry shows that these atypical cells are positive for antibodies to factor VIII, CD31 and CD34, which are specific markers of endothelial tumors.

After a month of supportive therapy, the patient died of severe cardiorespiratory failure and anemia.

Discussion

Angiosarcoma is a rare malignant vascular tumor (1-2% of all sarcomas) that affects the skin of the head and neck, the soft tissue, the breast, the liver, the spleen, the bones, the heart, the lung. The lung is rarely the site of a primary lesion, therefore it is always necessary to exclude with careful clinical and radiological examination that the pulmonary manifestation is not secondary to an angiosarcoma of another organ, given the high incidence with the presence of these metastasized forms the lung.[2,3] Early diagnosis is difficult because the symptoms and signs are not specific to the disease. The hemoptysis, cough, dyspnoea, chest pain, fever, malaise and weight loss that these patients complain about, with crackles while listening to the chest, are also present in other diseases (pneumonia, malignant tumors, autoimmune disorders).[3] The most frequent radiographic images are a single or multiple bilateral lung nodules, an expression of the perivascular growth of the tumor, associated with ground glass images, an expression of alveolar hemorrhage.[2] Patients with multiple lung lesions have a worse prognosis than those with a single lung node due to the impossibility of radical surgery, the rapid progression of the disease and the lesser response to therapies.[2,4] PET TC helps differentiate sarcomas from benign tumors and assess the aggressiveness of angiosarcoma based on the value of the SUV max. If the SUV max is high, the tumor will be more aggressive. In our case, the SUV max 6 corresponds to poorly differentiated and aggressive angiosarcoma.

The second PET-CT scan does not confirm the extent of the evident disease to total body CT because it is probably haemorrhagic lesions that do not capture radioactive glucose.[5] Faced with the need for the histopathological and immunohistochemical definition of the lesion, biopsy sampling in the course of videothoracoscopy or thoracotomy must be used because the bronchoaspirate and pulmonary needle aspiration under CT guidance do not provide enough material for diagnosis.[6,7] Histopathological examination shows the presence of numerous irregular vascular spaces, anastomosed, filled with blood, delimited by endothelial cells with variable degrees of atypia. The poorly differentiated forms consist of clusters of epithelial-like cells with high atypia, frequent mitosis that surround lumens reduced to thin cracks. At immunohistochemistry these atypical cells are positive for specific markers for endothelial tumors: factor VIII, CD31, CD34, which have also been highlighted in our case.[2,3] Radical surgery represents the only therapeutic modality capable of increasing survival to one year. Chemotherapy with doxabucine, ifos-

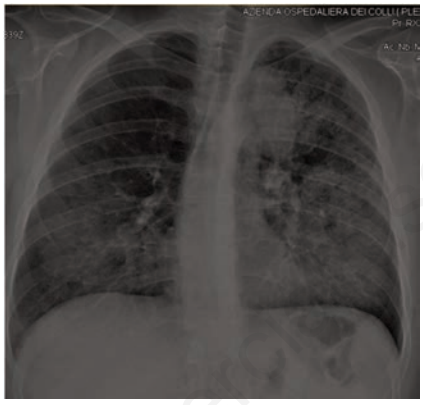

Figure 1. Chest X-ray (anteroposterior): in the correspondence of the left pulmonary lobe a coarse round opacity can be seen.

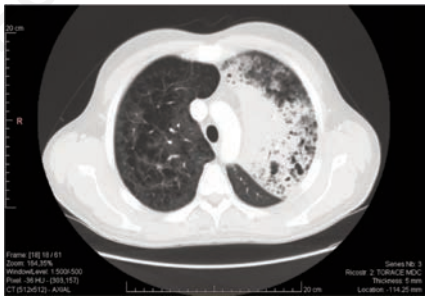

Figure 2. Solid formation with irregular margins, without air bronchogram, of about 10 cm in diameter, in the anteroposterior segment of the left upper lobe, surrounded by additional areas of parenchymal thickening that are barely delimitable from it, separated from each other and from the air spaces emphysematic cyst. The unconsolidated part of the left upper lobe has a "crazy pavement" appearance, partly in congruence with the breath of the alveolar blood. The upper right lobe and central lobe also have a "crazy pavement" appearance.

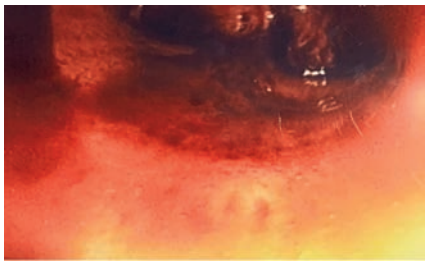

Figure 3. The left main bronchus is completely blocked by live blood clots. With aspiration and continuous washing, the main bronchus and the lower lobar bronchus are unclogged and the presence of a large clot is confirmed which occludes the orifice of the upper lobar bronchus which is not removed to avoid further bleeding.

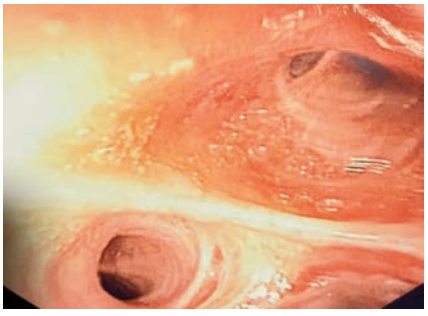

Figure 4. The entire right bronchial hemisystem is occupied by clots and live blood. The bronchial aspiration and the toilet are performed, restoring the complete canalization at all levels up to the limit of the visualization.

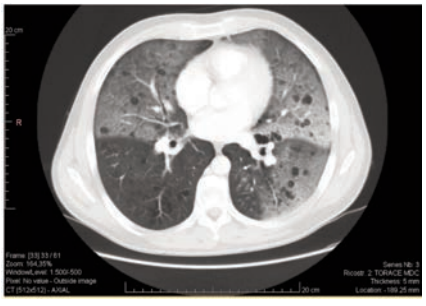

Figure 5. Significant increase in the size and density of the left upper lobe and the appearance of centrolobular nodules of ground glass in the right lower lobe. Significant increase in the extent and density of left lower lobe consolidation.

famide, docetaxol, gemcitabine, radiation therapy and immunotherapy with interleukin-2 do not improve survival.[5]

In our case, it was not possible to perform the left pneumonectomy due to the lack of access to the hilum for the hepatized lung and for the infiltration of the apex of the lung and the subclavian vessels. It was not possible to start chemotherapy, radiotherapy and immunotherapy for the serious clinical conditions of the patient.

Conclusions

PAS is an aggressive disease, with a rapid evolution, underdiagnosed and misunderstood. PAS should be considered as a possible diagnosis for patients with hemoptysis and lung nodules surrounded by ground glass opacity. Both fiberoptic broncoscophy and transbronchial biopsy often fails to deliver adequate tissue samples. Lung biopsy during videothoracoscopy or thoracotomy is essential for histopathological and immunohistochemical diagnosis. Early radical surgery is the only therapy that improves prognosis, but most patients are not candidates for surgery either because they have a bilateral lung injury or because of serious clinical conditions. Radiotherapy, immunotherapy, chemotherapy or a combination of those, hasn't shown to be effective.[5]

Discussion in multidisciplinary team must be the method for diagnostic and therapeutic decisions of the patient with angiosarcoma. Furthermore, given the rarity of the disease, it is appropriate to send patients to the centers of reference for rare diseases for better patient management.

References

1. Todaro M, Orlassino R, Forlengo C, et al. Un caso di angiosarcoma polmonare e revisione della letteratura. G Ital Cardiol 2017;18:792-5.
2. Piechuta A, Przybytowski T, Szolkowska M, et al. Hemoptysis in a patient with multifocal primary pulmonary angiosarcoma. Pneumonol Alergol Pol 2016;84:283-9.
3. Shimabukuro I, Yatera K, Noguchi S, et al. Primary pulmonary Angiosarcoma presenting with hemoptysis and ground-glass opacity-a case report and literature review. Tohoku J Exp Med 2015;237:273-5.
4. Piciucchi S, Dubini A, Tomassetti S, et al. Angiosarcoma in the chest: radiologic-pathologic correlaction. Case Report Med (Baltimore) 2016;95: e5348.
5. Kim EY, Lee HY, Han J, Choi JY. Primary pulmonary low-grade angiosarcoma characterized by Mismatch between F-FDG-PET and dynamic contrast –enhanced CT. Korean J Radiol 2015;16:1166-70.
6. Ren Y, Zhu M, Liu Y, et al. Three case reports and literature review. Thorac Cancer 2016;7:607-3.
7. Lim R, Harper L, Swiston J. Clinical manifestations and diagnostic methods in pulmonary angiosarcoma: protocol for a scoping revew. Syst Rev 2017; 6:136