

Intimal Sarcoma of the Pulmonary Artery in a Patient with Lynch Syndrome

Riccardo Gherli^{1*}, Giovanni Mariscalco², Claudio Corazzari¹, Laura Zoli³, Silvia Uccella⁴, Andrea Marcello Musazzi² and Cesare Beghi¹

¹Department of Surgical and Morphological Sciences, Cardiac Surgery Unit, Varese University Hospital, University of Insubria, Varese, Italy

²Cardiovascular Department, Cardiac Surgery Unit, Varese University Hospital, Varese, Italy

³Cardiovascular Department, Cardiac Unit I, Varese University Hospital, Varese, Italy

⁴Department of Surgical and Morphological Sciences, Unit of Pathology, Varese University Hospital, University of Insubria, Varese, Italy

Abstract

Intimal sarcomas of the Pulmonary Artery (PAS) are uncommon and highly lethal tumors. Due to their nonspecific symptoms, are often misdiagnosed with a poor prognosis due to its extreme aggressiveness. In this report, we present a case of PAS in a patient with a history of surgically treated Lynch Syndrome. Clinical and morphological findings are presented.

Keywords: Pulmonary artery; Sarcomas

Introduction

Primary intimal sarcomas are uncommon and highly lethal tumors arising in the mesenchymal tissue of great arteries [1-3]. In this setting, primary Pulmonary Artery Sarcomas (PAS) are often misdiagnosed with a poor prognosis due to their extreme aggressiveness [1-3]. Conversely, Lynch Syndrome is an inherited disorder with an increased risk of developing colorectal cancer, and a well defined spectrum of extracolonic tumors [4,5]. Even when localized in other anatomic districts, sarcomas are not included in the classic tumor spectrum of Lynch Syndrome [4,5].

We present the case of an exceptional association of PAS with the Lynch Syndrome.

Case Presentation

A 71-year-old woman was referred to the Cardiovascular Department of Varese University Hospital (Varese, Italy) for exertional dyspnoea (NYHA Class III) and fatigue. Patient's history included a previous surgically treated Lynch Syndrome (left hemicolectomy for splenic flexure adenocarcinoma, onset at age 52; right hemicolectomy with ileosigmoid anastomosis for a new primary adenocarcinoma, onset at 61; hysterectomy and bilateral annessiectomy for endometrial adenocarcinoma, onset at age 68), without evidence of relapse during the follow-up and chronic blood hypertension. At admittance, she had no signs of congestive heart failure, with normal values of blood pressure, heart rate and body temperature. However, auscultation at the lower left sternal border detected a grade III or IV systolic murmur indicative of tricuspid regurgitation. Laboratory analysis, including blood count and cardiac enzymes, revealed no abnormalities. Chest-X-ray demonstrated normal cardiac silhouette and clear lung fields; electrocardiogram normal sinus rhythm. Transthoracic Echocardiography (TTE) recognized a dilated right atrium and Right Ventricle (RV), a pulmonary artery systolic pressure of 50 mmHg accompanied with a mild pulmonary stenosis. In addition, a mass with an obstruction of the RV outflow tract was discovered. A subsequent contrast-enhanced spiral Computed Tomographic (CT) was performed, revealing massive filling defects in the main pulmonary artery, involving the proximal tract of the left pulmonary artery. and the greater part of the right pulmonary artery, mimicking pulmonary embolism; the RV outflow tract was also involved (Figure 1). Cardiac Magnetic Resonance Imaging (MRI) confirmed the dilatation of right atrium and RV, clearly demonstrating the large mobile mass attached

to the pulmonary valve, prolapsing into the RV outflow tract. The obtained data were suspicious of a cardiac tumor (Figure 1). Because of the absence, other body primary lesions or metastasis in a new enhanced total-body CT, a diagnosis of primarily pulmonary artery tumor was made. There cardiac surgery with mass removal was planned. After median sternotomy, normothermic Cardiopulmonary Bypass (CPB) was instituted with bicaval and ascending aorta cannulation. The anterior wall of the pulmonary trunk was longitudinally opened. A hard tumor was found, arising from the endothelium of the pulmonary artery, and almost completely occupying the vascular lumen, extending forward to the left pulmonary artery and backward to the pulmonary valve and the right ventricle outflow tract. The mass was accurately resected and the pulmonary valve was preserved.

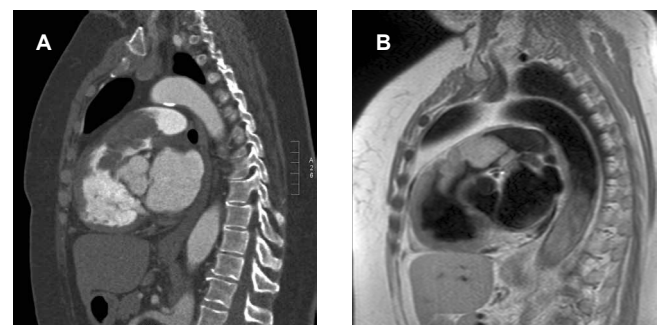


Figure 1: Contrast-enhanced spiral computed tomographic (panel A) and cardiac magnetic resonance imaging (panel B) of the thorax, showing the tumor mass attached to the pulmonary valve prolapsing into the right ventricle outflow tract.

***Corresponding author:** Riccardo Gherli, Department of Surgical and Morphological Sciences, Cardiac Surgery Unit, Varese University Hospital, University of Insubria, Via Guicciardini 7, 21100 Varese, Italy, Tel: +39.0332.278368; Fax: +39.0332.264394; E-mail: r.gherli@hotmail.com

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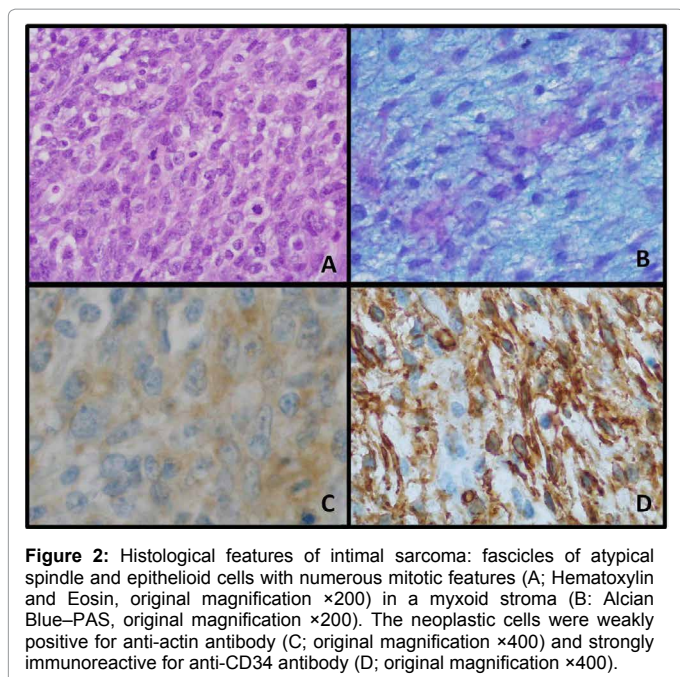


Figure 2: Histological features of intimal sarcoma: fascicles of atypical spindle and epithelioid cells with numerous mitotic features (A; Hematoxylin and Eosin, original magnification $\times 200$) in a myxoid stroma (B: Alcian Blue-PAS, original magnification $\times 200$). The neoplastic cells were weakly positive for anti-actin antibody (C; original magnification $\times 400$) and strongly immunoreactive for anti-CD34 antibody (D; original magnification $\times 400$).

Pathological Findings

The tissue consisted of multiple fragments of the neoplasm, which showed a variegated focal mucoid appearance. At light microscopy, a sarcomatous proliferation of spindle and epithelioid cells arranged in fascicles with focal storiform aspects and perivascular whorls. An alcyanophilic myxoid stroma was evident in large areas of the tumor. The proliferation was highly cellular and neoplastic cells exhibited high grade nuclear atypia, and a significant mitotic index (47 mitotic figures $\times 10$ high power fields $\times 400$). Focal tumor necrosis was also detected. No evidence of capillary-like spaces or intracytoplasmic lumina was observed, as well as any sign of muscular or other type of heterotopic differentiation. The immunohistochemical examination revealed a strong positivity in tumor cells for anti-CD34 antibody and a focal and faint immunostaining for anti-actin (HHF 35), while anti-desmin reaction was negative (Figure 2). Therefore, a histological diagnosis of high grade sarcoma with myxoid features, consistent with intimal sarcoma was made.

Follow-up and Outcome

The postoperative course was uneventful; the patient was discharged on postoperative day 8 and referred to the oncology clinic for further evaluations. She subsequently underwent 1 cycle of radiotherapy. Two months after surgery, TTE, CT scan and cardiac MRI revealed no metastasis or local recurrence of the malignancy, also showing satisfactory RV function with moderate pulmonary valvular insufficiency. However, 10 months after surgery, a new CT scan found a local recurrence of the tumor, showing a direct invasion of the lumen of the aortic arch, the left anonymous vein and the superior vena cava. A secondary lesion located in the inferior lobe of the left lung was also discovered. Conversely, at TTE examination the insufficiency of the pulmonary valve appeared stable. The patient underwent three consecutive cycles of gemcitabine, but 13 months after surgery, she reported persistent dyspnoea. The patient died of nephrotoxic complications due to the chemotherapy 5 months later.

Discussion

Lynch Syndrome is an inherited disorder in which affected individuals have an increased risk of developing colorectal cancer, and a well defined spectrum of extracolonic tumors. To our knowledge, no published cases of PAS in this population of patients have been previously described. Previous anecdotic cases report malignant association between Lynch Syndrome and sarcomas non cardiac-related [1-5]. Intimal sarcoma of the pulmonary artery is a rare and highly lethal tumor, usually presenting as vascular obstruction related to the intraluminal growth, and the associated thrombosis. No clinical picture is specifically suggestive to the diagnosis of PAS, which are often not suspected because of their nonspecific symptoms, including chest pain and dyspnoea. In addition, clinical presentation mimics pulmonary embolism, causing a significant delay of a correct diagnosis and a difficult differential diagnosis with congenital pulmonary stenosis, pulmonary hypertension, fibrosing mediastinitis and lung tumors [1-3]. Therefore, diagnosis of PAS is generally found during routine echocardiography for other reasons. CT scan and cardiac MRI are essential diagnostic tools, allowing early diagnosis in patients with symptoms of pulmonary vascular obstruction [1-3]. Histologically, PAS shows a mixture of spindle cells in a storiform pattern, with polygonal cells resembling histiocytes and malignant giant cells. The histological appearance shows a firm texture and exhibits infiltrative growth patterns [3]. As for all malignant diseases, early histopathological diagnosis is important for choice of treatment and prognosis. Aggressive surgical resection improves clinical symptoms and offers the only chance of cure [1-3].

Our case did not have detectable metastases at the time of diagnosis, but large areas with necrosis and a high mitotic activity were found, which may have worsened the prognosis. Extensive surgical resection combined with neoadjuvant chemotherapy remains the therapy of choice for PAS, although radical complete resection is rarely reported and overall prognosis remains poor, with a mean survival of less than two year from the onset of symptoms [3].

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