Case report

Primary pulmonary valve sarcoma involving pulmonary artery and right ventricular outflow tract

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A R T I C L E   I N F O

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A B S T R A C T

The group of pulmonary valve and pulmonary artery primary tumors is the most frequently represented by schwannomas, myxomas, papillary fibroelastomas, primary choriocarcinomas and sarcomas. These tumors are very rare. The most common clinical manifestation of pulmonary artery tumor is dyspnea, followed by chest pain, cough, and haemoptysis.

A case of 44-year-old male with history of progressive dyspnea, fever, cough, and weight loss is presented. Imaging methods showed large saddle embolus in the right ventricle outflow tract, pulmonary valve and pulmonary artery trunk. He was admitted to a hospital for anticoagulation therapy. Since there was no clinical improvement, the patient had to undergo surgery. Nearly full artery caliber filling tumor in pulmonary artery was found with its origin in pulmonary valve. Next exploration showed several little tumors in right ventricular outflow tract and also in pulmonary artery. The final outcome of histological examination showed the presence of leiomyosarcoma high grade 3.

Presented case highlights that pulmonary artery tumor should always be included in the differential diagnosis of pulmonary embolism, especially if the symptoms progress while on adequate anticoagulation, and if any risk factor for deep vein thrombosis is not present. Unfortunately, prognosis of pulmonary artery sarcomas is usually dismal, secondary to late diagnosis.

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Introduction

Primary tumors of the pulmonary artery and pulmonary valve are rare and may pose a difficult clinical diagnosis. The group of these tumors includes schwannomas, myxomas, papillary fibroelastomas, primary choriocarcinomas and sarcomas [1–4]. Pulmonary artery sarcomas (PASs) are the most common primary tumors of the pulmonary artery, but the incidence of this diagnosis is extremely rare. PASs was first described in autopsy by Mandelstamm in 1923 [5]. There have been reported around 200 cases of PASs in the literature up to date [6].

PASs is predominantly presented among patients from their third to seventh decade, with an average age of 49 years [7,8]. PASs are always highly malignant, women are involved twice as often as men [9]. The most common clinical
manifestation of PASs is dyspnea (72%) followed by chest pain (45%), cough (42%), and haemoptysis (24%) [6,10]. The presence of these symptoms often causes misdiagnosis of pulmonary embolism [7]. Systematic symptoms of PASs are less rare and they include weight loss (21%), syncope (9%), and fever (8%) [6]. PASs more frequently affect segments of the pulmonary artery with large diameter, predominantly the trunk (85%), right (71%) and left (65%) arteries. The pulmonary valve (32%) and right ventricular outflow tract (10%) are involved less frequently [6,11–14].

There are two major categories of PASs known: intimal and mural. The intimal PASs show an intraluminal polypoid growth pattern and histological evidence of fibroblastic and myofibroblastic differentiation. These subtypes are typically positive for vimentin and osteopontin and negative for endothelial markers. The mural PASs show characteristics related to the soft tissue sarcomas [8,15]. There have been many histopathological subtypes of PASs reported, including undifferentiated sarcomas, leiomyosarcomas, rhabdomyosarcomas, fibrosarcomas, chondrosarcomas and osteosarcomas [6]. Table 1 shows the incidence of PASs subtypes described by several authors (Table 1) [8,16,17].

### Table 1 – Incidence of PASs subtypes described by several authors [8,16,17].

<table>
<thead>
<tr>
<th>Author</th>
<th>Cox et al.</th>
<th>Nonomura et al.</th>
<th>Gaumann et al.</th>
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</thead>
<tbody>
<tr>
<td>Year</td>
<td>1997</td>
<td>1988</td>
<td>2008</td>
</tr>
<tr>
<td>Number of patients</td>
<td>138</td>
<td>110</td>
<td>18</td>
</tr>
<tr>
<td>Subtype of PASs and incidence in groups</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Undifferentiated sarcoma</td>
<td>31%</td>
<td>31%</td>
<td></td>
</tr>
<tr>
<td>Leiomyosarcoma</td>
<td>16%</td>
<td>21%</td>
<td></td>
</tr>
<tr>
<td>Spindle-cell sarcoma</td>
<td>14%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malignant fibrous histiocytoma</td>
<td>7%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibrosarcoma</td>
<td>5%</td>
<td>6.4%</td>
<td></td>
</tr>
<tr>
<td>Rhabdomyosarcoma</td>
<td></td>
<td>6.4%</td>
<td></td>
</tr>
<tr>
<td>Myxofibrosarcoma</td>
<td></td>
<td></td>
<td>22%</td>
</tr>
<tr>
<td>Epitheloid</td>
<td></td>
<td></td>
<td>22%</td>
</tr>
</tbody>
</table>

Case report

A 44-year-old male with medical history of appendectomy and hepatitis was accepted to the emergency room with several week history of progressive dyspnea, fever, cough, and weight lost of 4 kg. He denied chest pain. Initial transthoracic echocardiography showed right ventricle dilatation and pulmonary hypertension. Contrast CT scan of chest was performed and revealed what appeared to be a large saddle embolus in the right ventricle outflow tract, pulmonary valve and pulmonary artery trunk (Figs. 1–4). According to these findings the patient was admitted to a hospital for anticoagulation therapy using low molecular weight heparin and warfarin. Since there was no clinical improvement recorded, the patient was transported to the cardiology institute.

Repeated transthoracic echocardiography was performed with suspicion of pulmonary valve and right ventricle outflow tract tumor. Ventilation/perfusion scan recorded moderate asymmetry with declining of signal in right lung without evident segmental defects. Coronarography did not reveal any coronary artery stenosis. The patient was indicated for cardiac surgery.
Standard midline sternotomy was performed. Afterwards, a cardiopulmonary bypass was established and the heart was arrested using an anterograde intermittent cold blood cardioplegic solution. Pulmonary artery was opened and nearly full artery caliber filling tumor was found (Fig. 5). The tumor had its origin in pulmonary valve. Tumor including pulmonary valve was excised and subsequent histological examination revealed sarcoma (Fig. 6). Next exploration showed several little tumors in right ventricle outflow tract and also in pulmonary artery. Such finding was determined as surgically unresectable. Pulmonary valve was replaced by a biological prosthesis St. Jude Medical Epic. Pulmonary artery and right ventricle outflow tract was sutured using pericardial patch (Fig. 7). The early post-operative period was without complications. The final outcome of histological examination documented the presence of leiomyosarcoma high grade 3 positive for actin, desmin, and vimentin and negative for caldesmon. Resection margins were positive for tumor cells. The patient was discharged and adjuvant chemotherapy initiated.

Discussion

Even though sarcoma is the most common pulmonary artery tumor, it is very rare in this location. Diagnosis is usually delayed because of late symptoms. In fact, symptoms mimic chronic pulmonary embolism, as in described case report. Systemic symptoms of PASs are useful to determine a right diagnosis, however, these symptoms are not frequent [18]. One of the diagnostic methods is computer tomography (CT), with some specific imaging features to distinguish PAS from pulmonary embolism: (1) pulmonary embolism is more frequently peripheral (75%) and bilateral (83%), whereas PAS is presented as unilateral and central polyloid filling defect (80%); (2) in contrast to the abrupt narrowing and cut-off often recorded in pulmonary embolism, PASs form a contiguous soft smooth tapering tissue, extending from the pulmonary trunk to the peripheral arteries; (3) PASs cause complete unilateral filling of the vascular lumen at CT and complete unilateral defect at ventilation/perfusion scan (90%), while this phenomenon is not observed in pulmonary embolism; (4) transmural invasion is presented only in PASs; and (5) parenchymal abnormalities observed in PASs rarely touch the pleura (Table 2) [8,18-20]. In presented case report, only the first three differences were recorded. Despite magnetic resonance imaging (MRI) was not performed in presented patient, MRI is also useful diagnostic method for distinguishing PAS and pulmonary embolism. Low-intensity heterogeneous features on T1-weighted images and peripheral enhancement of the thickened pulmonary artery
wall on T2-weighted images and after gadolinium application have classically been thought to support a diagnosis of PASs or other pulmonary artery tumor on MRI [18,21]. Fluorodeoxyglucose (FDG)/positron emission tomography can also distinguish tumor and thrombus, as the maximum standardized uptake value of pulmonary artery sarcomas (7.63 ± 2.21) is higher than that of pulmonary emboli (2.31 ± 0.41) [6,22-24]. Other characteristics, such as the absence of risk factors for deep vein thrombosis and high erythrocytes sedimentation rate should raise the suspicion of a process other than pulmonary embolism. Lack of response to anticoagulation therapy and thrombolysis leads toward diagnosis of pulmonary artery tumor, as mentioned in our case report and some other publications [7,18]. The only method to definitely differentiate diagnosis between PASs and pulmonary embolism is histopathology; tissue pattern can be obtained either by angioscopy or by surgery [9].

Surgery is the most effective treatment of intimal sarcoma and is successful if total resection is performed [25]. Cardiosurgery can be extended by concomitant lung surgery, if combined surgical approach is needed [26]. Some authors complete the operation by pneumonectomy with no clear proof for survival benefit [9]. In presented case, only incomplete resection was executable because of the size and location of the tumor. Palliative surgical procedure and pulmonary valve replacement was performed. The optimal adjuvant treatment is still unclear. Chemotherapy or radiation therapy after surgery can improve survival and/or progression-free interval [15]. Chemotherapy is palliative for most of the patients with unresectable or metastatic disease. Ifosfamide and doxorubicin are standard drugs, single agent doxorubicin being considered the drug of choice. For younger patients with aggressive tumor, high doses of ifosfamide with doxorubicin are used. Response rate to this therapy is 50–60% [15]. Trabectedin, a selective inhibitor of DNA transcription, has shown activity in phase I/II clinical trials in advanced disease refractory to conventional treatment with a low rate of objective remission, but with high rate of interruption of disease progression [27,28]. The use of targeted molecular therapies against the proto-oncogene c-Kit, epidermal growth factor receptor (EGFR), and vascular endothelial growth factor receptor (VEGFR) is being investigated [15,29].
Table 2 - Characteristics of pulmonary artery sarcoma compared to pulmonary embolism [17,19].

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Pulmonary artery sarcoma</th>
<th>Pulmonary embolism</th>
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<tr>
<td>Localization of filling defect</td>
<td>Unilateral/central</td>
<td>Peripheral, bilateral</td>
</tr>
<tr>
<td>Character of filling defect</td>
<td>Continuous from pulmonary trunk</td>
<td>Abrupt narrowing</td>
</tr>
<tr>
<td>Complete unilateral ventilation/perfusion defect</td>
<td>Typically</td>
<td>Very rarely</td>
</tr>
<tr>
<td>Transmural invasion</td>
<td>Typically</td>
<td>Never</td>
</tr>
<tr>
<td>Pleura invasion</td>
<td>Typically</td>
<td>Never</td>
</tr>
</tbody>
</table>

Prognosis of PASs is usually unfavorable, secondary to late diagnosis. Direct extension to lung, heart, pleura, and mediastinum is more common than extrathoracic metastasis. Pulmonary and mediastinal metastasis are present in 50% of patients at the time of diagnosis [6]. Patients undergoing curative resection have median survival of 36.5 months compared to 11 months survival for those undergoing incomplete resection. Multimodality treatment leads to longer patient survival compared to single-modality treatment [30]. Survival of patients also varies according to a histologic subtype, with better prognosis for leiomyosarcoma than for undifferentiated sarcoma, or rhabdomyosarcoma as the least favorable type [31]. Patients who are not treated by surgical means, or those that do not respond to chemotherapy have very poor prognosis [32].

There is one case of spontaneous regression of primary pulmonary artery sarcoma published in the literature. Uematsu et al. presented case of 76 years old man with unresectable PAS with invasion into the left atrium and to the left lung. During 22 months patient observation there was a complete regression of primary tumor recorded. On the other hand patient died because of the tumor metastasis complications. Primary tumor regression was explained by insufficient blood support due to enormous fast tumor growth [33].

Conclusion

Our case report emphasizes that PAS should always be included in the differential diagnosis of pulmonary embolism especially if symptoms progress despite adequate anticoagulation therapy, and if any risk factor for deep vein thrombosis is not present. Prognosis of pulmonary artery sarcomas is usually dismal, secondary to late diagnosis. Patients not treated by surgery and no respond to chemotherapy have very poor outcome.

Conflict of interests

The authors declare no conflict of interest.

Funding body

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Ethical statement

The case report was performed according to ethical standards.

Informed consent

Medical management of the patient was not influenced by case report processing. Patient did not refuse medical records processing for publication.

REFERENCES


