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Přehledový článek | Review article

Pulmonary valvular and pulmonary arterial myxomas

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SOUHRN

Kontext: Srdeční myxomy málokdy vyrůstají z plicní chlopně nebo plicní tepny.
Materiály a metody: Při rozsáhlé rešerši literatury bylo vyhledáno 22 článků s 22 pacienty, které posloužily jako podklad pro tento komplexní přehled.
Výsledky: U většiny pacientů se projevily příznaky postihující oběhový systém. Šelest na srdci byl popsán u sedmnácti (94,4 %) pacientů. Správná diagnóza myxomu v plicních chlopních a tepnách nebyla stanovena u čtyř (22,2 %) pacientů. U pěti (22,7 %) pacientů byly myxomy plicních chlopní chybně diagnostikovány jako stenóza plicní chlopně ve dvou (40 %) případech, jako embolie plicní tepny rovněž u dvou (40 %) a jako vegetace na plicní chlopni nebo srdeční tumor u jednoho (20 %) pacienta. Ke stanovení diagnózy může pomoci zjištění pohybující se hmoty při echokardiografickém vyšetření nebo defektu plnění při vyšetření výpočetní tomografií.
Závěry: Po stanovení diagnózy je nutno kvůli možnému negativnímu ovlivnění hemodynamických poměrů a embolizaci myxom brzy chirurgicky odstranit. Prognóza pacientů po operaci je většinou příznivá. Mortalita u této pacientské podskupiny může dosahovat až 35,7 %.

Keywords:
Cardiac surgical procedures
Differential diagnosis
Myxoma
Pulmonary artery
Pulmonary valve

ABSTRACT

Background: Cardiac myxomas are rarely arising from the pulmonary valve or pulmonary artery.
Materials and methods: An extensive literature search generated 22 articles with 22 patients, which were taken as the material of this comprehensive review.
Results: Most patients manifested as circulatory system symptoms. A heart murmur was noted in 17 (94.4%) patients. Pulmonary valve and pulmonary artery myxoma was misdiagnosed in 4 (22.2%) patients. Pulmonary myxoma was misdiagnosed in 5 (22.7%) patients. It was misdiagnosed as pulmonary valve stenosis in 2 (40%), as pulmonary artery embolism in 2 (40%), and as pulmonary valve vegetation or cardiac tumor in 1 (20%) patient. A moving mass on echo or a filling defect on computed tomography can be helpful in the establishment of the diagnosis.
Conclusions: An early surgical treatment upon diagnosis is made due to the potentials of hemodynamic disturbances and predilection of embolization. Most patients have a good prognosis following surgical treatment. The mortality rate of this patient setting can be as high as 35.7%.

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Introduction

Cardiac myxoma is the most common primary cardiac neoplasm accounting for 75% of the cases [1]. It can occur in any cardiac chambers, typically in the left atrium [2]. Right ventricular myxoma is less common [3]. Myxomas rarely arise from the pulmonary valve or pulmonary artery. The myxomas located near the pulmonary valve may influence the opening and closing of the valve leading to valvular stenosis and (or) insufficiency [3]. They may also cause misdiagnosis and unnecessary investigations and treatments. Due to the rarity and particularity of this lesion, there is not enough information on pulmonary valve myxomas to establish guidelines for management. In this article, the clinical features of the pulmonary valve and pulmonary artery myxomas are described.

Materials and methods

A comprehensive retrieval was made in the MEDLINE and China Biology Medicine Disc (CBMdisc) databases, Highwire Press, Google Scholar, Yahoo! and "Baidu" search engines, LILACS and J-stage for pertinent literature published between January 1950 and June 2016. The search terms were "pulmonary artery", "pulmonary valve", "pulmonary valve annulus", "pulmonary valve commissure" and "myxoma". Myxoma inside the pulmonary artery or pulmonary valve orifice but arising from other sites, and other types of tumors of the pulmonary valve or pulmonary artery were excluded.

Results

A careful collection of full texts of pulmonary valve or pulmonary artery myxoma resulted in 22 articles in the first four databases and search engines [3–24]; whereas no related article was generated in the latter two databases. All of these articles were referring to a single patient. Of the 22 patients, there were 13 (59.1%) males and 9 (40.9%) females with a male-to-female ratio of 1.4 : 1. Patients' ages were in a normal distribution (Fig. 1) with a mean of 37.0 ± 24.0 (range, 0.17–76; median, 41.5) years (n = 22). The male patients were much younger than females (27.6 ± 25.8 years vs. 47.0 ± 17.0 years, p = 0.037). The duration of the symptoms ranged from acute onset [20] to several years [14], with a mean of 12.6 ± 19.8 (range, 0.17–60; median, 3.3) months (n = 10) [3,6,7,9,10,12,13,16,21,22].

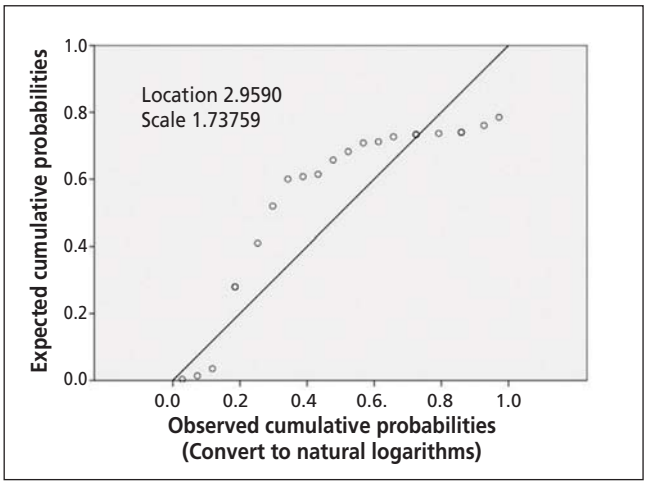

Fig. 1 – A normal distribution of patients' ages.

Of the 16 symptomatic patients, circulatory symptoms prevailed (Table 1). Four (18.2%) patients had a fever and one of them was fever of unknown origin [21].

A heart murmur was noted in 17 (77.2%) patients: a systolic murmur in 15 (88.2%), a diastolic murmur in 4 (23.5%), and a continuous murmur in 1 (5.9%) patient [16]. An abnormal heart sound was audible in 7 (31.8%) patients, including an accentuated P_2 in 3 (42.9%) patients [9,12,13], a loud A_2 in 1 (14.3%) patient [6], an accentuated S_3 (at the left sternal boarder) in 1 (14.3%) patient [7] and a P_2 split in 1 (14.3%) patient [10], and a loud and split P_2 in 1 (14.3%) patient [14], respectively. Hepatosplenomegaly was noted in 2 patients [16, 21] and hepatomegaly in 2 patients [7,13].

The associated disorders included patent ductus arteriosus (n = 1) [16], pulmonary valve insufficiency and stenosis (n = 3) [3,4,18], hypoxia (n = 2) [7,9], pulmonary artery or valve obstruction (n = 2) [10,24], pulmonary artery dilation (n = 2) [16,20], pulmonary embolism (n = 1) [9,13,20], pulmonary artery hypertension (n = 1) [13], hypertension and dyslipidemia (n = 1) [15], and complete heart block (n = 1) [9], myocardial bridging (n = 1) [14], secondary polycethemia (n = 2) [6,13], and multiple emboli with kidney infarctions (n = 1) [6].

Cytologic and microbiologic studies were done in 2 patients: gram positive cocci along with positive blood culture of *Abiotrophia streptococci* was found in a resected myxoma tissue in one patient [22], and blood culture was negative in another [21].

The electrocardiographic results were reported in 13 (59.1%) patients: normal sinus rhythm in 2 (15.4%) [3,5],

Table 1 – 50 clinical symptoms of 22 patients with pulmonary valve or pulmonary artery myxoma.

Symptom	*n* (%)	Reference
Dyspnea	10 (20)	[5,6,9,10,13,15,16,18,20,23]
Chest distress	4 (8)	[3,10,12,23]
Cough	4 (8)	[3,5,7,12]
Fatigue	4 (8)	[7,12,16,22]
Fever	4 (8)	[9,16,21,22]
Palpitation	5 (10)	[3,10,13,16,18]
Chills	2 (4)	[12,22]
Weight loss	3 (4)	[6,12,22]
Chest pain	4 (8)	[14,15,18,20]
Peripheral edema	3 (6)	[6,13,23]
Night sweats	1 (2)	[12]
Listlessness	1 (2)	[7]
Respiratory distress	1 (2)	[21]
Syncope	1 (2)	[17]
Dizziness	1 (2)	[14]
Fainting	1 (2)	[14]
Absence of radial pulse	1 (2)	[6]

atypical atrioventricular rhythm without evidence of myocardial infarction in 1 (7.7%) [6], sinus tachycardia in 1 (7.7%) [16], right ventricular hypertrophy in 3 (23.1%) [9–11], right bundle branch block with peaked P wave in 2 (15.4%) [7,21], complete atrioventricular block in 1 (7.7%) [17], pacing rhythm and ST-T changes (7.7%) [14], and atrial fibrillation in 2 (15.4%) patients [13,15].

Chest X-ray films were taken in 6 (27.3%) patients: normal in 2 (33.3%) [5,11], right heart enlargement in 2 (33.3%) [7,21], pulmonary congestion with enlarged cardiac silhouette in 1 (16.7%) [16] and decreased lung textures with prominent pulmonary artery segment in 1 (16.7%) patient [19]. A chest CT was examined in 3 patients: showing a filling defect in the main pulmonary artery and (or) right ventricular outflow tract (RVOT) in all [9,10,23]. Computed tomography angiography was done in 2 (11.1%) patients with filling defects found in both [12,15]. Magnetic resonance imaging was examined in 2 (9.1%) patients, and it showed a solid mass in the pulmonary artery trunk in both [5,18]. Perfusion scan showed absence of left lung perfusion in 1 (4.5%) patient [10]. Cardiac catheterization was performed in 6 (27.3%) patients, revealing a filling defect [20], serve pulmonary stenosis [21], serve pulmonary stenosis with filling defect in the pulmonary valve region [7], moderate aortic valve regurgitation [15], a mobile hyperlucent mass [18], and RVOT obstruction with tumor prolapse [22] in 1 (20%) patient each. Echocardiographic examinations were reported in 13 (61.1%) patients: an attenuated moving mass seen in the pulmonary artery, pulmonary valve or RVOT in 8 (63.6%) patients [3,4,8,14,17,19,22,24], a nodular mass in the RVOT [11], a space-occupying mass in the pulmonary artery [16], a moving mass in the pulmonary artery with insufficiencies and stenoses of both the mitral and aortic valves [15], and abnormal flow in the pulmonary artery [10], signs of pulmonary artery hypertension [13] in 1 (9.1%) patient each.

Table 2 – Locations of pulmonary valve and pulmonary artery myxomas.

Location of myxoma	*n* (%)	Reference
Pulmonary valve myxoma	11 (61.1)	
Pulmonary valve leaflet	5 (50)	[4,8,12,17,21]
Posterior pulmonary valve leaflet	2 (40)	[4,17]
Unspecified	5 (60)	[6, 8, 12, 14, 21]
Commissure	2 (20)	[18,24]
Pulmonary valve leaflet + conus	1 (10)	[7]
Pulmonary valve leaflet + annulus	1 (10)	[22]
Pulmonary valve leaflet + commissure	2 (10)	[11,19]
Pulmonary artery myxoma	7 (38.9)	
Main pulmonary artery	7 (66.7)	[3,5,6,9,13,15,16,20] (one extended into the left pulmonary artery [3])
Main pulmonary artery and right ventricular outflow tract	1 (16.7)	[23]
Left pulmonary artery	1 (16.7)	[10]

Pulmonary myxoma was misdiagnosed in 5 (22.7%) patients. It was misdiagnosed as pulmonary valve stenosis in 2 (40%) [7,21], as pulmonary artery embolism in 2 (40%) [9,14], and as pulmonary valve vegetation or cardiac tumor in 1 (20%) patient [17]. The diagnosis of pulmonary myxoma was missed in 1 patient [13].

The myxoma was arising from the pulmonary valve in 12 (54.5%) [4,7,8,11,12,14,17–19,21,22,24], from the pulmonary artery in 9 (40.0%) [3,5,9,10,13,15,16,20,23], and from pulmonary valve and pulmonary artery in 1 (4.5%) patient [6]. In one patient, there were two myxomas arising from the pulmonary artery [20]. The locations of the myxomas are listed in Table 2. Most pulmonary valve myxomas were arising from the valve leaflets; while most pulmonary artery myxomas were arising from the main pulmonary artery.

The diagnostic methods depended on preoperative medical imaging in most cases, while the diagnosis was made by surgical exploration in 3 (18.8%) [7,9,21], and by autopsy in 2 (9.1%) patients [6,13]. The dimension of the myxomas was 2.5 ± 1.2 (range, 1–5; median, 3) cm (n =19) [3–5,8–10,13–15,17–22,24]. There was no significant difference between the dimensions of pulmonary valve and pulmonary artery (2.4 ± 1.0 cm vs. 3.1 ± 1.2 cm, p = 0.175). Attachments of the myxomas were described in 11 (50%) patients: 7 (63.6%) were pedicled [4,8,11,14,15,18,24] and 4 (36.4%) were sessile [9,10,12,19]. The surgical approaches were reported in 10 (45.5%) patients: by a main pulmonary arteriotomy in 6 (60%) [10,14–16,18,21], by main and left pulmonary arteriotomies in 1 (10%) [9], by an RVOT incision in 2 (20%) [7,11], and by combined pulmonary arteriotomies of the main pulmonary artery, bifurcation and RVOT incision in 1 (10%) patient [3]. Cardiopulmonary bypass technique was mentioned in 13 (59.1%) reports: a conventional hypothermic cardiopulmonary bypass technique was used in 11 (84.6%) [4,7–9,11,12,14–17,19], a normothermic cardiopulmonary bypass with beating heart in 1 (7.7%) [18], and deep hypothermic circulatory arrest in 1 (7.7%) patient [21]. Apart from the two patients who had a sudden death, all remaining patients underwent a surgical operation: 19 (95%) patients had a pulmonary myxoma resection (operation unspecified in 4 [21.1%] [4,20,23,24], a sole myxoma resection in 5 (26.3%) [5,10,11,18,19], with concurrent pulmonary valve leaflet resection plus dilation of pulmonary valvular ring in 2 (10.5%) [7,21], with concurrent pulmonary valve leaflet resection in 1 (5.3%) [17], with concurrent reconstruction of the pulmonary artery trunk and RVOT in 2 (10.5%) [8,12], with concurrent pulmonary valve replacement in 1 (5.3%) [22], with concurrent aortic valve replacement and tricuspid valve repair in 1 (5.3%) patient [15] and with ductal ligation in 1 (5.3%) [16], and with one-stage myocardial bridging resection in 1 (5.3%) [14], and 1 (5%) patient underwent thromboembolectomy [9]. Diagnosis of myxoma was proved by histology in all patients. Three (15%) patients were followed up for 1, 6 and 6 months respectively [15,18,21], while follow-up information of other patients was not available. Prognosis was not given in 8 patients [3,4,8,17,19,22–24]. Of the remaining 14 (63.6%) patients, 9 (64.3%) were alive and 5 (35.7%) died. The causes of death were postoperative sustained hypothermia in 1 (20%) patient [6], conges-

tive heart failure in 2 (40%) [9,12], increasing deterioration in 1 (20%) [6], and cardiac and respiratory failure in 1 (20%) patient [13].

Discussion

Primary and secondary tumors may involve the pulmonary arteries with poorly differentiated and undifferentiated sarcomas being the most common and they tend to affect the large caliber pulmonary vessels with significant growth [25]. Valvular tumors more often seen are papillary fibroelastomas, and pulmonary valve is the least affected out of the four heart valves accounting for only 8% of tumors of valve locations [26]. Concomitant pulmonary valve and pulmonary artery tumors are even rarer. Zerkowski et al. [27] reported a female patient with a metastatic pulmonary sarcoma to the pulmonary valve involving the pulmonary artery, which warranted curative resection and a cryopreserved homograft replacement after polychemotherapy. Bloomberg et al. [28] reported a case of pulmonary valve sarcoma extending to the pulmonary artery. However, the patient died 2 weeks after surgical resection.

Primary neoplasms of the pulmonary valve and pulmonary artery are rare and lethal. The poor prognosis of the neoplasms (namely the sarcomas) is attributable to the delays in diagnosis and treatment [28].

In contrast, myxomas that arising from the pulmonary valve and pulmonary artery are very rare. Eck reported the first case of myxoma of the pulmonary valve in a premature neonate in 1935 [6], followed by the autopsied case of myxomas of the pulmonary valve and the pulmonary artery reported by Blodorn in 1955 [6]. Until present, a total of only two decades of such cases have been reported in the world. The mechanisms of these myxomas remain unknown, but it is supposed that they may arise from *in situ* or a dislodgement of myxomas from remote sites [9]. As some patients did not present with any symptoms, the myxomas were discovered by incidental findings at routine examinations [4]. Others present with circulatory or systemic symptoms. Right heart overload and right bundle branch block could be noted in electrocardiogram [21]. Pulmonary artery and pulmonary valve myxomas should be distinguished from pulmonary valve stenosis/insufficiency [3], outflow tract obstruction [8], thrombosis, pulmonary embolism [9], valvular vegetation [24], or other types of tumors of the right heart system. The misdiagnosis maybe leads to an inappropriate therapy, such as anticoagulation or thrombolysis [25]. Transthoracic or transesophageal echocardiography and cardiac computed tomography are reliable diagnostic means of pulmonary valve and artery tumors. A moving mass on echo [12,15] or a filling defect on computed tomography [5,18] can be helpful in the establishment of the diagnosis. Electron beam computed tomography clearly shows not only the location, size and mobility of the myxoma, but also the relation between myxoma and cardiac system [23]. The feature of pulmonary artery myxoma in the cardiac magnetic resonance imaging was reported to be a hypointense mass [5]. However, the final diagnosis relies on pathological investigations.

In spite of the benign nature of myxomas, it is inevitable that they not only cause valvular dysfunction and secondary pulmonary hypertension, but also have a significant propensity to embolize the pulmonary artery [9]. Pulmonary artery and pulmonary valve myxomas have the common features of right heart system, such as predilections of right ventricular obstruction and (or) right heart valve insufficiencies and pulmonary embolism, but their special character is a smaller size. Although pulmonary artery myxomas are likely to affect larger sized pulmonary arteries as pulmonary artery sarcomas do, but they usually do not behave like the malignant pulmonary artery tumors to invade adjacent structures. It demonstrated that all the lesions of the 18 patients were solitary. Nevertheless, due to the potential hazards and occasional misdiagnosis, the patients endow an early surgical treatment upon diagnosis is made [19]. Before operation, peripheral vascular embolism should be excluded by ultrasound examination even though it is a rare association [9]. During the operation, the related valve cusps can be spared by being left intact as they often are not severely destructed.

Conclusions

Pulmonary valve and pulmonary artery myxomas are rare. With modern advances of imaging technologies, the correct preoperative diagnosis of the lesions is more commonly made than before. An early surgical treatment upon diagnosis is made due to the potentials of hemodynamic disturbances and predilection of embolization. Most patients have a good prognosis following surgical treatment. The mortality rate of this patient setting can be as high as 35.7%.

Conflict of interest
None declared.

Ethical statement
Authors state that the research was conducted according to ethical standards.

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None.

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