Right ventricular cardiac myxoma. Histopathology diagnosis in forensic autopsy case

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Abstract: Primary cardiac neoplasms are very rare as compared to metastatic tumors. Myxomas are the most common of the primary cardiac tumors. Myxomas represent almost 50% of cardiac masses with an incidence reported at one in 10000 autopsies. A greater percentage (75%) are located in the left atrium, of these, 90% originate from an area in the atrial septum near the fossa ovalis. Right atrial myxoma are uncommon being three to four time less frequent than those located in the left atrium. The incidence of those arising in the left and right ventricles is 2.5-4%. We report on case of right ventricular cardiac myxoma, confirmation with histopathological examination, what is first case in forensic medicine practice.

Key Words: right ventricular cardiac myxoma, histopathology diagnosis

Primary tumors of the heart are rare [1], however, among them cardiac myxoma is the most common tumor accounting for half of the primary cardiac neoplasms [2,3]. Cardiac tumor incidence is between 0.0017 and 0.19 percent in unselected patients at autopsy [4,5]. Myxomas represent almost 50% of cardiac masses with an incidence reported at one in 10,000 autopsies [6]. A greater percentage (75%) are located in the left atrium [7,8]. Of these, 90% originate from an area in the atrial septum near the fossa ovalis [9]. Right atrial myxomas are uncommon, being three to four times less frequent than those located in the left atrium [6,10]. The incidence of those arising in the left and right ventricles is 2.5-4% [2,11]. Biatrial tumors are present in approximately 2.5% of all cases [12].

Myxomas occur in all age groups but are particularly frequent between the third and sixth decades of life [4,7]. The youngest known patient was a stillborn infant [13], and the oldest a 95-year-old woman [2]. Women predominate in most series [7]. Myxomas usually occur sporadically, but familial myxomas have been reported [14].

Myxomas are neoplasms of endocardial origin [2]. The tumor usually projects from the endocardium into the cardiac chamber. The cells giving rise to the tumor are considered to be multipotential mesenchymal cells that persist as embryonal residues during septation of the heart and differentiate into endothelial cells, smooth-muscle cells, angioblasts, cartilage cells, and myoblasts [16]. The prevalence of myxomas in the atrial septum is therefore understandable [2]. The rate of growth of myxomas is unknown, but they generally appear to grow rather quickly [17]. There is one report, however, of a left atrial myxoma that did not change in its appearance during a period of 28 months [18].

Cardiac myxomas produce IL-6 (interleukin-6) constitutively, which is a possible explanation for the inflammatory and immune features observed in patients with this tumor [19]. Interleukin-6 is a multifactorial cytokine that produces differentiation and proliferation of normal and malignant cells, induction of the acute-phase response and fever. Exist an correlation of IL-6 serum levels with preoperative constitutional symptoms and
immunologic abnormalities, and the possible role played by this cytokine in tumor recurrence [20]. They measured IL-6 serum levels by enzyme-linked immunosorbent assay method preoperatively, and one and six months after surgery in eight consecutive patients with nonfamilial myxoma. Two of the cases involved recurrent tumor; one patient had undergone his first surgery at a different institution and died during the second procedure, so his data were incomplete. Although patients with a first occurrence of tumor demonstrated a positive correlation between IL-6 serum level and tumor size, the two patients with recurrent tumors appeared to have higher IL-6 levels regardless of tumor size [20]. Once the tumor was surgically removed, IL-6 levels returned to normal values, and this was associated with regression of clinical manifestations and immunologic features. According to this study [21], the overproduction of IL-6 by cardiac myxomas is responsible for the constitutional symptoms and immunologic abnormalities observed in patients with such tumors, and might also play a role as a marker of recurrence. This study also suggests that recurrent cardiac myxomas form a subgroup of cardiac myxomas with a highly intrinsic aggressiveness, as implied by their greater IL-6 production despite their smaller size [21].

We report a case of right ventricular myxomas, what is first case in forensic medicine practice.

**Case Report**

A 43-year-old women was found deceased on the railway on February 9, 2011. The forensic autopsy (nr.399-77/2011, IML Tg.Mureș) established at the external examination numerous signs of violence, cephalic extremity and left upper limb trauma. The internal examination found a right parietal and occipital comminutive skull depressed fracture, diffuse meningeal bleeding, right tempo-parietal and left parietal cortical contusion and cerebral oedema. Status after old hysterectomy and bilateral oophorectomy. The heart weight was 300 gr. In the right ventricular cavity there was a tumor of size 1.5x1 cm, with soft consistency and a haemorrhagic surface (fig.1, fig.2).

The diagnostic established by histopathology (nr.27291/2011, IML Tg.Mureș) is right ventricular myxoma (fig.3,4,5,6). The deceased had no cardiac symptoms during life.

**Discussion**

Primary cardiac neoplasms are very rare as compared to metastatic tumors; 70% to 80% of the them are benign myxomas [22]. Myxomas are the most common of the primary cardiac tumors [23]. Left atrial myxoma presenting with myocardial infarction is a rare but recognized phenomenon, however, presentation with ventricular fibrillation arrest has only been reported once before [24]. Sudden cardiac death due to myxoma is extremely rare and
usually associated with asystolic or pulseless electrical activity (PEA) arrest secondary to mechanical obstruction of the mitral valve [25]. Right atrial and ventricular myxomas are sometimes asymptomatic, however, they can manifest with a variety of signs and symptoms, including fever, weight loss, and arthralgias [26].

In search for candidate cells or tissues as precursor cells of cardiac myxoma, in 1951 Prichard [27] described a kind of microscopic endocardial structure of the atrial septum, which was suggested to be related to cardiac myxomas. The confirm the existence of Prichard’s structures and to clarify their role in the genesis of cardiac myxoma, Acebo et al. [28] examined histologically the fossa ovalis and performed an immunohistochemical study of the endocardial abnormalities. Histological study of 100 atrial septa and am immunohistochemical study of three out of the 12 endocardial abnormalities that were used to detect vimentin, CD31, CD34, alpha-smooth muscle actin, S100 protein, thrombomodulin, calretinin and c-kit (CD117), and a tyrosine kinase growth factor receptor for stem cell factor usually expressed by embryonic/fetal endothelium. They found structures similar to the them in the left side of the fossa ovalis. The hearts with these structures were from patients 10 years older that the ones without them (72±10 versus 62±16 years, P=0.006). Immunohistochemically the cells comparing Prichard’s structures were positive for vimentin, CD31, CD34 and thrombomodulin, and negative for alpha-smooth muscle actin, S100 protein, calretinin, and c-kit. Therefore, these cells seem to be mature endothelial cells, but not primitive multipotent mesenchymal cells. Furthermore, these cells were not found in the atrial tissue from the bases of any of cardiac myxomas. From these results, they concluded that there is no apparent relation between Prichard’s structures and cardiac myxomas, and that Prichard’s minute endocardial deformities are age-related phenomena. Even from this meticulous study, the presence of nests of pluripotent primitive mesenchymal cells in the interatrial septum are still mysterious, and a search for primitive cell differentiating myxoma cell should be continued [21].

The clinical features of myxomas are determined by their location, and mobility [2]. Most patients present with one or more of the triad of embolism, intracardiac obstruction, and constitutional symptoms [29,30,31]. Occasionally, there are no symptoms, particularly with small tumors [4,31].

Emboli occur in 30 to 40 percent of patients with myxoma [32,33]. Since most myxomas are located in the left atrium, systemic embolism is particularly frequent [2]. In cases of right atrial myxomas, clinically evident embolic events are uncommon [34]. Nevertheless, there have been reports not only of embolization of thrombi or tumor fragments into the pulmonary vessels, with subsequent pulmonary hypertension [35,36] but also of lethal fulminant pulmonary embolism in cases of right atrial [37] or right ventricular [34] myxoma.

The combination of left atrial myxoma and mitral stenosis has been reported only in single cases [33,38]. Right atrial myxomas may mimic constrictive pericarditis by producing functional stenosis of the tricuspid valve, with increased right atrial pressure [35,36,39]. Ventricular myxomas may mimic stenosis of the aortic or pulmonic valve because of the narrowing of the left or right ventricular outflow tract, respectively and may also cause syncope; embolism is common [31,40,41].

Constitutional disturbances, such as fatigue, fever, erythematous rash, arthralgia, myalgia, and weight loss, and laboratory abnormalities, such as anemia and elevation in the erythrocyte sedimentation rate and the serum C-reactive protein and globulin levels, have been observed in many patients, irrespective of the site and size of tumor, suggesting an infection, immunologic disorder or malignant disease [29,31,42,43]. Recent finding suggest that the production and release of the cytokine IL-6 (interleukin-6) by the tumor itself may be responsible for the inflammatory and autoimmune manifestations [44,45]. In any case, the systemic signs disappear after the tumor has been removed [30,45].

Occasionally, myxomas are infected [46,47]; in this circumstance, there is great danger of systemic embolization. In one case, a vegetation on a myxoma was detected by echocardiography, and the finding verified at surgery [48].

References


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