DOI: 10.15825/1995-1191-2021-4-143-150

SURGICAL TREATMENT OF BIATRIAL MYXOMA

A.S. Ivanov, N.P. Mozheiko, G.A. Akopov, M.K. Lugovskiy, O.O. Shelest

Shumakov National Medical Research Center of Transplantology and Artificial Organs, Moscow, Russian Federation

Cardiac myxoma is a primary tumor histologically formed by multipotent subendocardial mesenchymal cells. Myxomas account for approximately 50% of all cardiac tumors in adults. Myxomas are most commonly located in the left atrium. Very rarely, myxomas can be located in several heart chambers. Only about 100 cases of patients with myxomatous lesions of both atria have been described in the literature. In this paper, we present a successful clinical case of a young patient with biatrial myxomas.

Keywords: cardiac myxoma, cardiac neoplasm, cardiac tumor, biatrial myxoma, atrial myxoma, familial myxoma, Carney complex, myxoma diagnosis, history of heart tumor surgery.

The first description of cardiac tumors was made by Italian Renaissance anatomist and surgeon Matteo Realdo Colombo. In his book "De re anatomica", published in 1559 by his pupils after his death, the following description is given: "In Cardinali Gambaro Brixiano tumorem praedurum, et ad ovi magnitudinem in sinistro cordis ventricolo Romae vidi, ubi illum in affinium gratiam dissecarem". The literal translation of the quotation reads, "In Rome I saw a solid tumor, large like an egg, in the left ventricle of Cardinal Gambaro of whom I was committed by the Pope to make autopsy.") [1].

For centuries, cardiac tumors have been incidental findings in autopsies of deceased patients. In a 1951 article reviewing 150 cases of cardiac tumors detected at autopsy, Richard Prichard wrote that the most common tumor, the myxoma, has never been diagnosed in a living patient [2].

In the same year, Goldberg and colleagues were the first to diagnose left atrial myxoma in vivo. The patient was a 3.5-year-old boy with residual weakness in the right side of the body after incoming hemiparesis. By the time of angioventriculography and tumor imaging, the patient had already undergone 4 hospitalizations. In addition to weakness in the limbs, physical examination of the patient revealed a distinct systolic murmur at the apex of the heart. Surgical treatment of the child was postponed due to high risk and waiting for completion of the tweaking of the heart-lung machine. Nevertheless, 7 months later, the child with clinical signs of pulmonary edema was operated on for emergency indications. The operation was unsuccessful, histological picture of the resected tumor was consistent with cardiac myxoma [3]. Angiocardiography was not the technique of choice for diagnosing cardiac tumors because of a number of significant drawbacks. This diagnostic procedure was performed only in large medical centers, was highly invasive, painful and inaccessible to the general population. In 1959, the first echocardiographic imaging of an intracardiac tumor was obtained, which was certainly a breakthrough in treatment, greatly simplifying the diagnosis of this disease [4]. The first successful operations to resect heart and pericardial tumors were performed on a working heart. In 1936, S. Beck resected an intrapericardial teratoma [5]. In 1951, E. Maeur reported a successful resection of an epicardial lipoma [6]. All attempts to resect tumors localized inside the heart chambers ended in the death of the patient. The most successful attempt was made in 1952 by Bahnson. The operation was performed under hypothermic conditions. The surgeon performed a right atriotomy, isolating the blood flow of the vena cava from the right atrium, which allowed to remove a large right atrial myxoma. Unfortunately, the patient died 24 days later from transfusion complications [7]. The use of a heart-lung machine was a clear breakthrough. It allowed to obtain the necessary tumor resection time under direct visual control. One of the pioneers of world cardiac surgery, Clarence Crafoord, performed the first successful tumor resection under artificial circulation. In 1954, a woman with atypical mitral stenosis was referred to him. She complained of dizziness and transient ischemic attacks, but she had preserved sinus rhythm, which surprised the professor. The patient underwent transthoracic puncture of the left atrial posterior wall with an 18-cm needle. Dr. Bjork describes his memories of the diagnostic procedure as follows: "*We got a very clear image of the myxoma fixed to the interatrial septum. During diastole, it fell downward, blocking the mitral valve opening. This case taught us how to conduct differential diagnosis of myxoma in the presence of mitral stenosis and preserved sinus rhythm*." The operation to remove

Corresponding author: Maksim Lugovskiy. Address: 1, Shchukinskaya str., Moscow, 123182, Russian Federation. Phone: (926) 590-62-05. E-mail: livertranspl@mail.ru

this myxoma was the first case of the use of a heart-lung machine in Sweden. It was performed when the patient was cooled to 28 °C, on a fibrillating heart through a left lateral thoracotomy access. After performing atriotomy, the tumor was divided into three parts and removed. The patient remained on the operating table until the next morning. Thirty-eight years later, she described her condition as excellent [8]. For a long time, surgical procedures under artificial circulation, hypothermia, on a fibrillating heart were the gold standard of cardiac surgery. Sometime after this operation, many publications on successful resections of intracardiac tumors began to appear. In the Soviet Union, the first operation to remove a right atrial myxoma under artificial circulation was performed by Soviet surgeon Ivan Kolesnikov in 1962 [9]. A little later, Yipintsoi et al. described the first case of successful removal of a biatrial myxoma, in 1967 [10].

Myxomas are the most common primary cardiac tumor in the adult patient population with about 0.0017% prevalence in the general population. Among all cardiac tumors, myxomas account for 50% in the older age group and 15% in the younger age group [11]. The peak diagnostic incidence is in the 30–40 year age group [12]. The formation usually attaches to the interatrial septum on the left atrial side (60–88%). Right atrial myxomas are 3–4 times less common (4–28%). Myxomas of several anatomical localizations account for 5% of all observations, and bi-atrial localization is only 2.5% [13]. Biatrial myxomas are usually attached by a stalk in the area of the oval fossa of the interatrial septum and grow towards the cavities of both atria [14]. Cases of localization of myxomas on the inner wall of the pulmonary artery, ventricles, vena cava, and atrio-ventricular valves have also been described in the literature [15, 16]. About 5% of patients have a familial form of the disease – multifocal tumor complex with autosomal dominant mode of inheritance. Patients in this group have an abnormal chromosomal DNA genotype. They are usually young [17]. In the familial form, there is no correlation between male and female gender. Myxomatous lesions of several chambers of the heart are significantly more common in these patients than in the sporadic form. Despite the identical histology, the recurrence rate after surgical resection in the familial form is higher, and is seen in 21 to 67% of cases. There is a familial syndrome inherited in an autosomal X-linked mode of inheritance, named after Irish physician J Aiden Carney. This complex includes recurrent myxoma of the heart, proliferative pathology of endocrine organs, skin lesions: nevi, pigmented spots, or skin myxomas. Endocrine disorders are variable, usually represented by one of the following proliferative disorders: adrenal cortical tumor, breast fibroadenoma, pituitary adenoma, thyroid tumors, Sertoli cells of the testes in men, or a combination of these [18, 19]. The diagnosis of Carney disease is most likely reliable when there are two or more diagnostic findings. Biatrial myxoma may be part of Carney disease, so a patient with this diagnosis needs consultation with an endocrinologist and a dermatologist [20].

The size of myxoma, on average, varies from 1 to 12 cm in diameter, and the mass ranges from 0.6 to 80 g. The average mass often varies between 50–60 g. The macroscopic picture of myxomas is varied. Zuckerman et al. (1999) distinguish three types of myxomas depending on the tumor shape: 1) ovoid dense formations (oval, ovoid, spherical); 2) lobular formations consisting of several large lobes; 3) villous formations (aciniform) resembling a bunch of grapes in appearance. According to the literature, myxomas are more often oval in shape with a lobular or smooth structure. The color of a tumor varies from white, yellowish to dark brown. The outside of a tumor is often covered with thrombotic masses. Tumor mobility depends on the place and area of its attachment, as well as the amount of intercellular matrix collagen in the body and stalk of the mass. Most tumors have a short, wide stalk; myxomas on a wide base are less common [21]. Histologically, myxomas are represented by mesenchymal multipotent subendocardial progenitor cells of various shapes located in isolation in the intercellular matrix containing reticular and collagen fibers, mucopolysaccharides [11]. In addition to myxoma cells, smooth muscle cells, reticulocytes and blood cells can also be found in the neoplasia. In 10% of cases, calcium deposits and glandular structures can be found in myxoma [22]. At the base of myxoma, there are vessels that connect the tumor to cardiac subendocardium [23]. Myxomas usually exhibit exophytic growth [24].

Early diagnosis of intracardiac tumors is very difficult due to the frequent absence of symptoms, or their nonspecificity [25, 26].

Findings on clinical examination of a patient with myxoma depend on the size, location, and mobility of the tumor. In biatrial myxoma, episodes of embolism by tumor fragments or by thrombotic masses layered on its surface may occur in both circulatory circuits. Small circle embolization can be accompanied by lung infarction with cough, hemoptysis and other characteristic symptoms. Patients with embolization of the large circulatory circle have neurological symptoms or may complain of muscle or joint pain in the limbs, usually of ischemic etiology. On auscultation of patients with a mobile tumor, a third heart tone may be heard, caused by the tumor striking or sliding against the atrio-ventricular valve leaflets. Large masses obstructing the lumen of the right heart can mimic the clinical picture of superior vena cava syndrome. Left atrioventricular orifice tumor obstruction is usually accompanied by the clinical picture of transient ischemic attacks, acute pulmonary edema, and can also lead to sudden cardiac death [27]. Some patients present with immunoconstitutional symptoms: fever, weight loss, obesity, weakness, myalgia and arthralgia. These symptoms are accompanied by changes

in the general blood count: erythrocytosis, leukocytosis or, conversely, hemolytic anemia, thrombocytopenia, as well as increased erythrocyte sedimentation rate, hypergammaglobulinemia. IL-6 production by tumor cells or its metastases can be the cause [28–30].

The most widespread method of detecting cardiac tumors is echocardiography, which has 100% sensitivity in diagnosing a myxoma in heart chambers. Transesophageal echocardiography provides the most accurate information on tumor size, location of tumor attachment, and mobility. Transesophageal cardiography can detect tumors that were not detected during transthoracic examination, the smallest tumors with a diameter of 1 to 3 mm [31]. Computed tomography and magnetic resonance imaging should be performed in all patients with detected cardiac tumors if possible. The data obtained helped to estimate the structure of a tumor, its density and the degree of invasion into surrounding tissues, which is important for differential diagnostics of myxoma with other cardiac tumors. Despite the fact that echocardiography has now supplanted contrast-enhanced cardiac X-ray, it is mandatory for all patients over 40 years of age to diagnose coronary lesions.

CLINICAL CASE

After a routine check-up at her place of residence, the 33-year-old patient was referred to Shumakov National Medical Research Center of Transplantology and Artificial Organs in Moscow. She led an active lifestyle, worked as a senior nurse, and had no complaints about her well-being. Physical examination and auscultation did not reveal any diagnostic findings. After echocardiography, two intracardiac tumors attached to the interatrial septum were detected. Both tumors were mobile, prolapsed into the ventricles through locally appropriate atrio-ventricular valves during cardiac diastole. Computed tomography of the chest and abdomen was performed to exclude secondary tumor genesis and to detect metastases. It showed negative results. Taking into account the mobility of the detected tumor and probability of embolization by fragments, the patient underwent urgent surgery. Before the operation, transesophageal echocardiography was performed to establish a clear localization, clarify the information on the tumor attachment site and its size (Fig. 1a and b). In this case, the tumor was localized biatrically, attached to the interatrial septum in the oval fossa. The size of the part located in the right atrium was 63 × 49 mm. The left part of the tumor was 35 × 24 mm in size. Complete median sternotomy was chosen as the surgical access to the heart. After connecting the CPB pump according to the vena cava-aorta scheme, infusion of one portion of blood cardioplegia into the aortic root according to Calafiori protocol, right atriotomy in the tumor projection was performed (Fig. 2). Part of the tumor located in the right atrium was a multilobular dark brown mass of gelatinous consistency, covered with thrombotic masses, which was attached by a 1 cm^2 stalk to the interatrial septum in the oval fossa. Due to the large size of the tumor and its consistency, we decided to resect the tumor in two stages. The first stage was a precision resection of the right tumor component with thrombotic masses. Then the interatrial septum was dissected with an arched incision 5 mm away from the stalk. Together with its part, the left tumor component was dissected (Fig. 3). After the tumor was removed, the chambers were thoroughly inspected for the remaining fragments and other foci of tumor localization. Atria and ventricles were repeatedly flushed with cold saline to prevent embolism. The main stage of the operation was completed by interatrial septum plasty with a xenogeneic pericardium patch. After removal of the clamp from the aorta, the heart restored sinus rhythm on its own. Transesophageal echocardiographic examination performed after disconnection of the CPB pump showed the absence of regurgitation on the atrio-ventricular valves and blood discharge at the level of interatrial septum. Circulatory time was 42 minutes, myocardial ischemia lasted for 28 minutes. The resected tumor masses were sent for histological study. The result corresponded to the histopathological structure of cardiac myxoma (Fig. 4). The main mass of the tumor consisted of myxoma satellite cells, inflammatory cells, and a large amount of surrounding myxomatous stroma. In the area of myxoma base, native vessels feeding the tumor were detected (Fig. 5). The right atrial myxoma was covered by thrombotic masses (Fig. 6).

The results obtained during transthoracic echocardiography corresponded to the control transesophageal study. The postoperative period was uneventful. The patient was discharged from the hospital on day 7 after operation.

Myxoma of both atria is a very rare clinical case. Currently, about 100 cases are available in the literature. The purpose of this paper is to describe our own experience with surgical treatment of a patient with myxoma of such localization. It should be noted that the frequency of embolization by tumor fragments or thrombotic masses in myxomatous lesions of the heart chambers according to the literature reaches 40% [30]. For this reason, patients with an established diagnosis should be examined as soon as possible and operated on urgently.

Multiple myxomas of the heart chambers are more often an inherited condition. If it is detected, the patient needs to consult an endocrinologist and a dermatologist. Examination of the patient's immediate family may be required to rule out any suspicion of familial myxoma.

Despite precision removal of tumor masses, recurrence rates reported for cardiac myxomas are 4% to 7% for sporadic cases and 10% to 21% for familial cases [32]. The recurrence rate is significantly higher in younger patients. Typically, tumor recurrence occurs

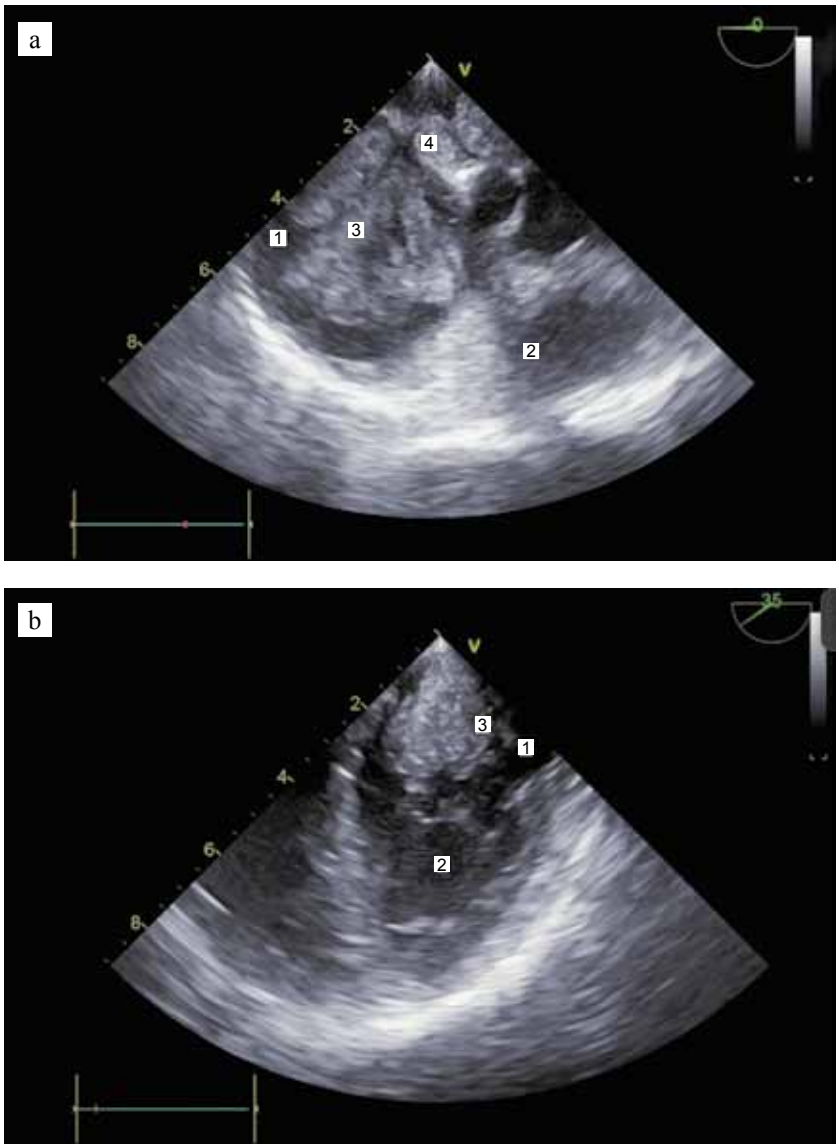

Fig. 1. Transesophageal echocardiography: a, right heart chambers (1, right atrial cavity; 2, right ventricular cavity; 3, tumor masses; 4, tumor stalk); b, left heart chambers (1, left atrial cavity; 2, left ventricular cavity; 3, tumor masses)

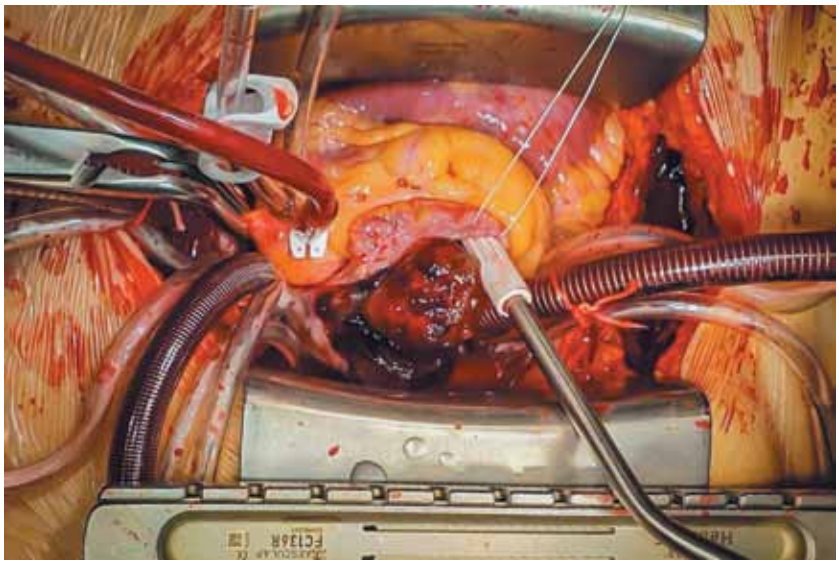

Fig. 2. Intraoperative photograph of myxomatous masses with thrombotic overlays, taken during right atriotomy

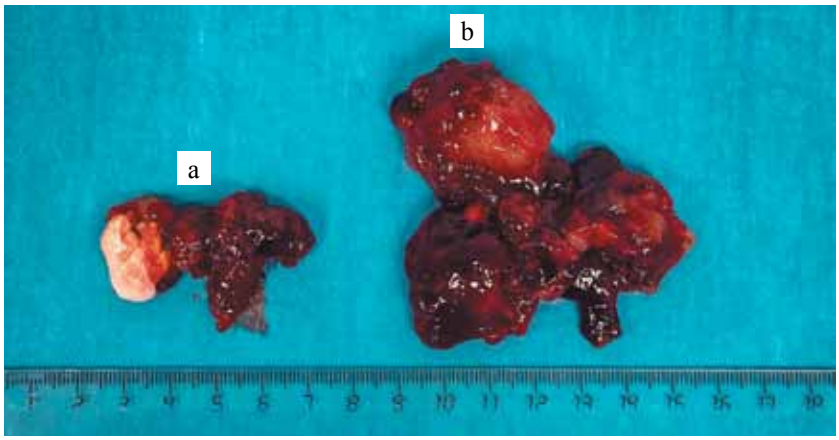

Fig. 3. Intraoperative photograph of excised fragments of the biatrial myxoma: a: left atrial fragment with pedicle; b: right atrial fragment with thrombotic masses

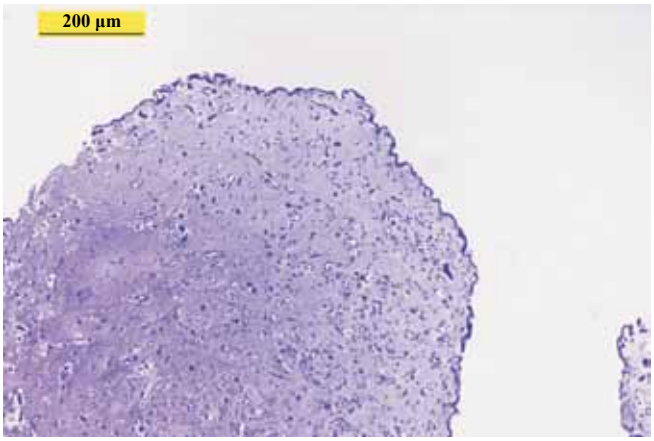

Fig. 4. Myxoma parenchyma. A papillary-type formation consisting of elongated spinous cells with large oval and spindle-shaped, fusiform hyperchromatic nuclei, as well as the surrounding myxoid matrix. Masson's trichrome stain, 200 µm scale, 20× magnification

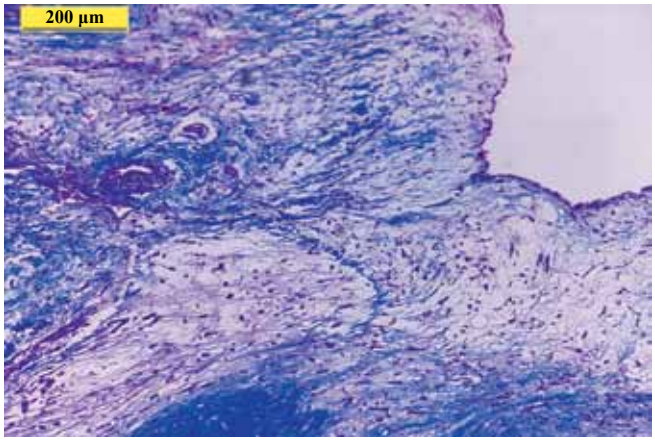

Fig. 5. Base of myxoma. Vessels surrounded by solid structures and unilayer complexes consisting of rounded, stellate, and spindle-shaped cells with weakly basophilic nuclei are seen at the base of the stalk. Scattered mononuclear cells, large focal clusters of erythrocytes, fibrin filaments with admixture of hemosiderin grains were visualized in all fields. Masson's trichrome stain, 200 µm scale, 20× magnification

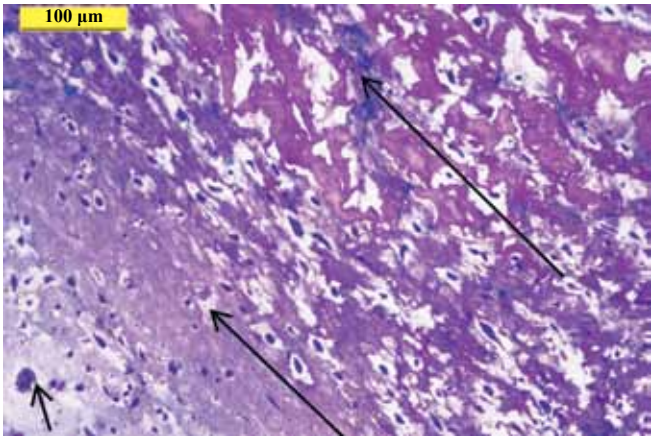

Fig. 6. Boundary of thrombus adherence to myxoma. The border of adhering thrombotic masses consisting of fibrin, unchanged and lysed red blood cells, leukocytes is traced between the arrows. Masson's trichrome stain, 100 µm scale, 40× magnification

within 5 years after the first resection surgery [33]. For these reasons, patients with cardiac myxoma of any localization should undergo periodic examination with echocardiography at least once a year in the long-term postoperative period.

The authors declare no conflict of interest.

REFERENCES

1. *Columbus M.R.* De Re Anatomica, Libri XV. Venice: N Bevilacque, 1559: 269.
2. *Prichard RW.* Tumors of the heart: review of the subject and report of 150 cases. *AMA Arch Pathol.* United States, 1951; 51 (1): 98–128 PMID 14789340.
3. *Goldberg BHP, Glenn F, Dotter CT.* Myxoma of the Left Atrium Diagnosis Made during Life with Operative and Post-mortem Findings. 2015; VI: 762–767. PMID: 12988355. doi: 10.1161/01.cir.6.5.762.

4. *Effert S, Domanig E*. Diagnosis of intra-auricular tumors & large thrombi with the aid of ultrasonic echography. *Dtsch Med Wochenschr.* Germany, 1959; 84 (1): 6–8. PMID: 13619382. doi: 10.1055/s-0028-1113531.
5. *Beck CS*. An Intrapericardial Teratoma and a Tumor of the Heart: Both Removed Operatively. *Ann Surg*. 1942; 116 (2): 161–174. PMID: 17858078. doi: 10.1097/00000658-194208000-00001.
6. *Maurer ER*. Successful removal of tumor of the heart. *J Thorac Surg.* United States, 1952; 23 (5): 479–485. PMID: 14928267.
7. *Bahnson HT, Newman EV*. Diagnosis and surgical removal of intracavitary myxoma of the right atrium. *Bull Johns Hopkins Hosp.* United States, 1953; 93 (3): 150–163. PMID: 13094264.
8. *Chitwood WR*. Clarence Crafoord and the first successful resection of a cardiac myxoma. *Ann Thorac Surg*. 1992; 54 (5): 997–998. PMID: 1417305. doi: 10.1016/0003-4975(92)90676-u.
9. *Pryhodko VP, Nyjdin MD*. Primary cardiac tumors: history of development and methods of surgical treatment. *Patologiya krovoobrashcheniya i kardiokhirurgiya*. 2011; 4: 65–70. URL: https://cyberleninka.ru/article/n/pervichnye-opuholi-serdtsa-istoriya-razvitiya-sovremennye-printsipy-i-metody-hirurgicheskogo-lecheniya.
10. *Yipintsoi T et al*. Bilateral atrial myxoma with successful removal. Report of a case. *Dis Chest*. 1967; 52 (6): 828–834. PMID: 6064988. doi: 10.1378/chest.52.6.828.
11. *Reynen K*. Cardiac myxomas. *N Engl J Med*. United States, 1995; 333 (24): 1610–1617. PMID: 7477198. doi: 10.1056/NEJM199512143332407.
12. *Carney JA*. Differences between nonfamilial and familial cardiac myxoma. *American Journal of Surgical Pathology*. 1985; 9 (1): 53–55. PMID: 3970298. doi: 10.1097/00000478-198501000-00009.
13. *Peachell JL et al*. Biatrial myxoma: A rare cardiac tumor. *Ann Thorac Surg*. 1998; 65 (6): 1768–1769. PMID: 9647099. doi: 10.1016/s0003-4975(98)00206-9.
14. *Imperio J et al*. The Distribution Patterns of Biatrial Myxomas. *Ann Thorac Surg*. The Society of Thoracic Surgeons, 1980; 29 (5): 469–473. PMID: 7377889. doi: 10.1016/s0003-4975(10)61682-7.
15. *Bortolotti U et al*. Right atrial myxoma originating from the inferior vena cava. *Ann Thorac Surg*. The Society of Thoracic Surgeons, 1990; 49 (6): 1000–1002. PMID: 2196010. doi: 10.1016/0003-4975(90)90889-e.
16. *Croti UA et al*. Right ventricle and tricuspid valve myxoma. *Brazilian J Cardiovasc Surg*. 2008; 23 (1): 142–144. PMID: 18719845. doi: 10.1590/s0102-76382008000100026.
17. *Van Gelder HM et al*. Familial cardiac myxoma. *Ann Thorac Surg*. The Society of Thoracic Surgeons, 1992; 53 (3): 419–424. PMID: 1540058. doi: 10.1016/0003-4975(92)90261-2.
18. *Havrankova E et al*. Carney complex with biatrial cardiac myxoma. *Ann Thorac Cardiovasc Surg*. 2014; 20: 890–892. PMID: 24088910. doi: 10.5761/atcs.cr.13-00121.
19. *Stratakis CA, Kirschner LS, Carney JA*. Clinical and Molecular Features of the Carney Complex: Diagnostic Criteria and Recommendations for Patient Evaluation. *J Clin Endocrinol Metab*. 2001; 86 (9): 4041–4046. PMID: 11549623. doi: 10.1210/jcem.86.9.7903.
20. *Bennett WS, Skelton TN, Lehan PH*. The complex of myxomas, pigmentation and endocrine overactivity. *Am J Cardiol*. 1990; 65 (5): 399–400. PMID: 4010501. doi: 10.1097/00005792-198507000-00007.
21. *Lygovskiy MK*. Myxomas of the heart: surgical treatment results and clinical and morphological characteristics. Federal Research Center of Tranplantology and Artificial Organs, Ministry of health of the RF. 2017: 23–24.
22. *McAllister HA Jr.* Primary tumors and cysts of the heart and pericardium. *Curr Probl Cardiol*. 1979 May; 4 (2): 1–51. PMID: 230012. doi: 10.1016/0146-2806(79)90008-2.
23. *Ferrans VJ, Pk D, Roberts WC*. Structural features of cardiac myxomas: Histology, Histochemistry, and Electron Microscopy. *Hum Pathol*. 1973 Mar; 4 (1): 111–146. PMID: 4713680. doi: 10.1016/s0046-8177(73)80051-6.
24. *Krikler DM et al*. Atrial myxoma: a tumour in search of its origins isra. *Br Heart J*. 1992; 5: 89–91. PMID: 1531423. doi: 10.1136/hrt.67.1.89.
25. *Xiao Z et al*. A Typical Bilateral Atrial Myxoma: A Case Report. *Case Reports Cardiol*. 2012; 2012 (Figure 3): 1–3. PMID: 24826252. doi: 10.1155/2012/460268.
26. *Kuon E et al.* The challenge presented by right atrial myxoma. *Herz*. 2004; 29 (7): 702–709. PMID: 15580325. doi: 10.1007/s00059-004-2571-7.
27. *Vijan V, Vupputuri A, Chandrasekharan Nair R*. An Unusual Case of Biatrial Myxoma in a Young Female. *Case Reports Cardiol*. 2016; 2016: 1–3. PMID: 26881142. doi: 10.1155/2016/3545480.
28. *Saji T et al.* Increased serum interleukin-6 in cardiac myxoma. *Am Heart J*. United States, 1991; 122 (2): 579–580. PMID: 1858647. doi: 10.1016/0002-8703(91)91022-f.
29. *Kuroki MK et al*. Increased interleukin-6 activity in cardiac myxoma with serum interleukin-6 in cardiac myxoma with mediastinal lymphadenopathy. 2010; 34 (1): 31–38. PMID: 1286228. doi: 10.2169/internalmedicine.31.1207.
30. *Guhathakurta S, Riordan JP.* Surgical treatment of right atrial myxoma. *Texas Hear Inst J*. 2000; 27 (1): 61–63. PMID: 10830633.
31. *Samdarshi TE et al*. Transesophageal echocardiographic diagnosis of multicentric left ventricular myxomas mimicking a left atrial tumor. *J Thorac Cardiovasc Surg*. American Association for Thoracic Surgery, 1992; 103 (3): 471–474. PMID: 1545546.
32. *Turhan S et al*. Second recurrence of familial cardiac myxomas in atypical locations. *Can J Cardiol*. Elsevier, 2008; 24 (9): 715–716. PMID: 18787723. doi: 10.1016/s0828-282x(08)70671-8.
33. *Perek B et al*. Early and long-term outcome of surgery for cardiac myxoma: Experience of a single cardiac surgical centre. *Kardiol Pol*. 2011; 69 (6): 558–564. PMID: 21678290.

The article was submitted to the journal on 2.08.2021