

## The cardiac tumors – some exceptional heart conditions

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### Abstract

Cardiac tumors are exceptional cardiac conditions, since they have a minimal occurrence, according to statistics. The cardiac myxoma cases are the most dominant for the representative examples for these clinical situations. Those tumors being benign, the patients enjoy a reasonable life expectancy provided they receive an early diagnosis. In the absence of potential complications, the symptoms can vary very much and they may often be non-specific, a fact which makes it more difficult to establish a proper diagnosis and to quickly tailor the optimal therapeutic solutions. Surgery is, in the most cases, a comfortable solution, allowing the cases to be permanently healed. Nowadays, cardiac surgery provides all the needed facilities to diagnose cases at an early stage, when diagnosis is quick and accurate. This paper illustrates, by the means of two suggestive cases, how difficult it is to establish a quick positive diagnosis, which is vital for healing this condition with an evolutionary risk frequently worsen by major complications.

**Keywords:** cardiac tumors, myxoma, cardiovascular surgery, valvular apparatus.

### ✉ Introduction

Due to the unique structure and function of the heart, cardiac tumors are the rarest cardiovascular conditions. Cardiac tumors have an estimated prevalence of 0.002–0.33% of all the autopsy cases [1, 2]. They may be benign or malignant, primary or secondary. Benign tumors represent about 75% and include: myxoma, fibroma, rhabdomyoma, lipoma, fibroelastomas, hemangioma and paraganglioma, and the malignant represent 25%, such as: sarcomas, mesotheliomas or lymphomas [3].

Metastatic cardiac tumors are 20–40 times more frequent than primary malignant tumors [4, 5]. Similarly to other organs, primitive cardiac malignant tumors may give metastases. According to some studies, approximately 20% of primary cardiac tumors give metastases in the lungs, liver, bones, mediastinal lymph nodes and brain [6].

In 2015, *World Health Organization* (WHO) proposed a new classification of heart tumors as being benign, malignant, intermediate with an unpredictable subsequent evolution, while including a special section for germinal tumors and pericardial tumors [7].

Primary cardiac tumors were identified in 0.17% to 0.19% of the cases during the necropsy performed on individuals deceased because of cardiovascular diseases. More recent analyses have shown an increasing rate of cases of cardiac tumors over the last years, due to the improvements brought to the imagistic techniques.

Primitive cardiac tumors affect both men and women

at same rate, most often being diagnosed around the age of 50 years old. Regarding frequency, most tumors were diagnosed in the right atrium, followed by the left atrium, and the least in the ventricles [2].

In adults, 50% of the primary benign tumors are represented by myxoma, followed, by decreasing order of occurrence, by the cardiac fibroma, lymphoma, angioma and fibroelastoma. Cardiac myxoma is rarer in children, the most frequent benign cardiac tumor being the rhabdomyoma (32%).

The patients with primary cardiac tumors may present a series of symptoms that simulate a cardiac disease. The clinical signs are mostly determined by the localization, size, structure, growth rate and invasiveness of the tumor [3].

We present two cases of myxomas, with a different localization, which showed varied clinical signs and raised problems of positive and differential diagnosis.

### ✉ Case presentations

#### Case No. 1

Fifty-six-year-old female patient, with no previous known heart problems, claims to have had, for around three months, physical asthenia, dyspnea when performing medium physical effort, and episodes of atypical pain in her chest, which lasted for a short period and ended suddenly. Her symptoms became heavier during the physical effort times and when she changed the position

of her body. Over the last two weeks prior to the admission to the hospital, the patient had arthralgia, underfebrility (body temperature  $37.5^{\circ}\text{C}$ ), and two episodes of syncope.

The clinical examination showed there is a diastolic blow of varying intensity, which is influenced by the position of the body and it is suggestive for the “poplar tree tumor”.

The electrocardiogram (EKG) routes repeated revealed: sinus rhythm, with 70–85 beats per minute, without changes of the repolarizing phase.

The echocardiography helped identify a normal-sized left ventricle with normal segment-level and overall kinetics (the left ventricular ejection fraction 60%). The left atrium was oversized (72/59 mm) and, inside its cavity, there was some tumor with average erogeneity, quite homogeneous and properly delimited (63/50 mm), inserted into a pedicle with a large attachment basis at the level 1/3 mediums of the interatrial septum. The mitral valve was not modified, nor did it have a cooptation deficit (Figure 1).

The right-sided cardiac cavities were not modified in terms of their sizes, but some elements were found: tricuspid regurgitation of the I<sup>st</sup>–II<sup>nd</sup> degree, with a maximal systole gradient right ventricle (RV)–right atrium (RA) 32 mmHg.

Considering the aforementioned clinical elements and since the echocardiogram confirmed there is a massive tumor in the left-side atrium, which has got direct effects into altering the mechanic function of the mitral valve and into determining a major embolism-causing risk, the doctors decided to immediately perform a surgical intervention on the patient’s temporarily stopped heart, to remove the tumor.

The surgery was performed through a classical approach: an incision at the middle of the sternum, under circumstances of extracorporeal blood circulation, normal body temperature, and after having stopped the heart’s functioning. The tumor was removed, by eliminating the entire attachment basis at the level of the interatrial sternum and recovering the tissue using a patch of autologous pericardium (Figure 2).

The macroscopic image of the removed tumor, during the surgery, was characteristic for myxoma (Figure 3).

Still, for confirming the positive and especially for an accurate differential diagnosis, the fragment of surgical exeresis was sent to the Laboratory of Pathological Anatomy, where it was fixed in 10% formaldehyde and included in paraffin, according to the usual histopatho-

logical protocol. There were performed 4- $\mu\text{m}$  sections in the microtone that were subsequently stained with Hematoxylin–Eosin (HE) and with the green light trichrome, the Goldner–Szekely (GS) technique. For the immunohistochemical (IHC) study, there were used the following antibodies: anti-CD20 (monoclonal mouse anti-human CD20cy, clone L26, 1:50 dilution, Dako) for highlighting B-lymphocytes; anti-CD3 (monoclonal mouse anti-human CD3, clone F7.2.38, 1:25 dilution, Dako) for highlighting T-lymphocytes; anti-CD34 (monoclonal mouse anti-human CD34 class II, clone C8/144B, 1:100 dilution, Dako) for highlighting vascular endothelia; anti-Ki67 (monoclonal mouse anti-human Ki67, clone MIB-1, 1:50 dilution, Dako) for highlighting the proliferative ability of the cells in the tumoral stroma; anti-Bcl-2 (monoclonal mouse anti-human Bcl-2, clone 100, 1:50 dilution, Dako) for highlighting the lymphomatous transformation of B-lymphocytes.

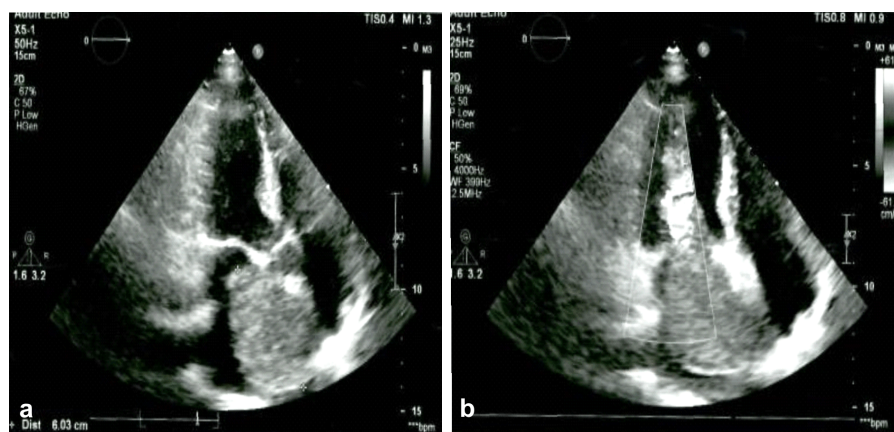
The microscopic examination highlighted the presence of some cells with a varied morphology (fusiform, stellate, polyhedral), with abundant, eosinophil cytoplasm, with large and normochromic nuclei, arranged isolated or as cordons or islands, with varied shapes and sizes, most often included in a myxoid stroma, rich in fundamental, amorphous, slightly eosinophilic substance (Figures 4 and 5). The cells identified by us presented the aspect of mesenchymal or fibroblast cells.

Overall, the tumoral stroma presented a myxoid aspect, but we also identified areas with a densely fibrillary stroma (Figure 6), rich in collagen fibers with a heterogeneous arrangement. Also, in the myxoma structure, there were identified some areas with a strong inflammatory infiltrate, especially lymphocytes (Figure 7), together with hemorrhagic areas (Figure 8).

The IHC study highlighted the presence of a small quantity of B-lymphocytes, most often diffusely and heterogeneously disseminated (Figure 9) and only rarely agglutinated in the form of lymph nodes (Figure 10). In the myxoid stroma, there were also identified T-lymphocytes that, most often, were diffusely spread and only sometimes-formed dense cellular infiltrates (Figures 11 and 12).

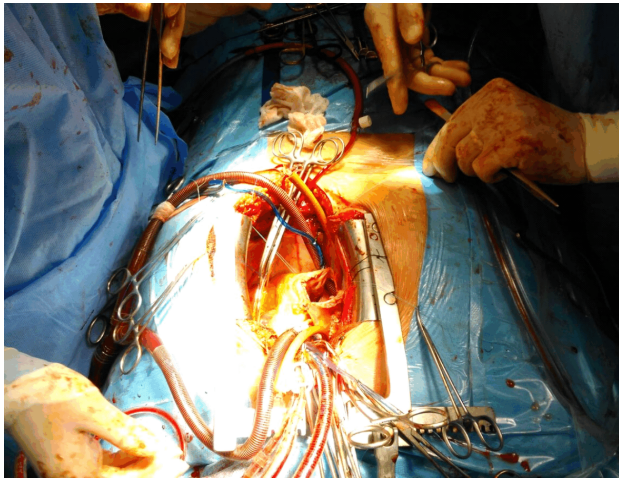
The use of anti-CD34 allowed us to remark that most of the stromal cells were CD34 positive (Figure 13). Some of these cells formed new vessels (Figure 14).

The immunomarkings with Ki67 and Bcl-2 were negative, a proof that the tumor had benign characteristics.

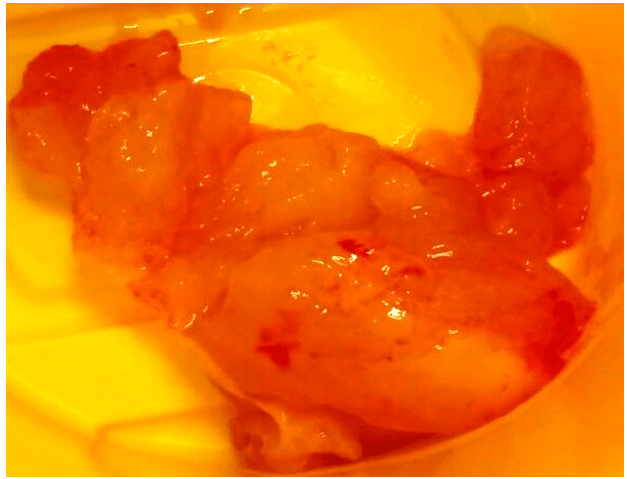


**Figure 1 – Transthoracic echocardiography in apical incidence four chambers, revealing an atrium-level tumor with a 6.3/5 cm diameter, of homogeneous structure and smooth edges, a large attachment basis at the level of the interatrial septum, which does not fully penetrates the diastole through a mitral valve hole and which thus causes a medium dynamic mitral stenosis effect.**

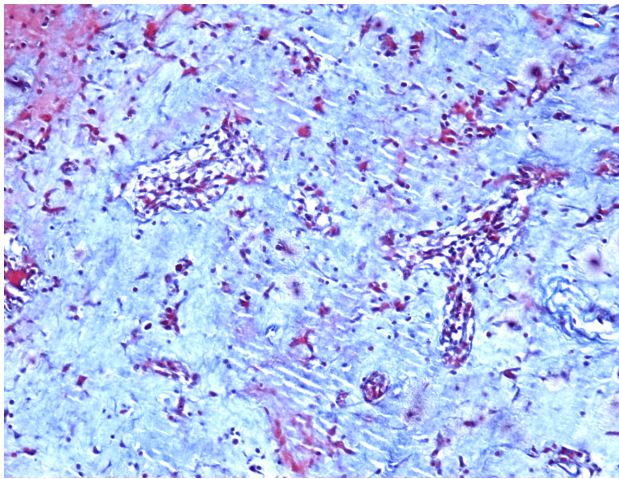




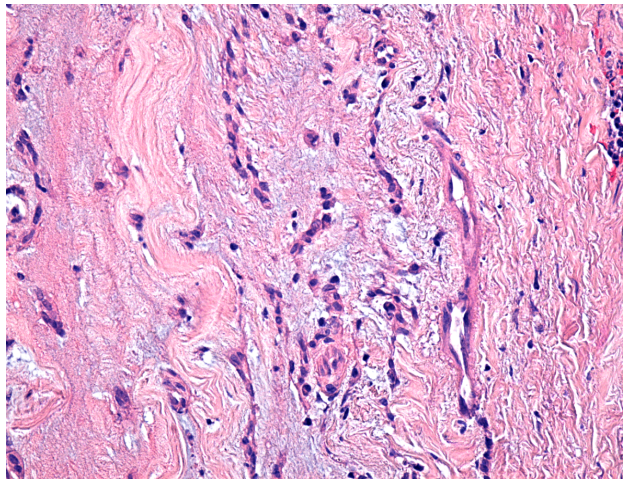
**Figure 2** – Photo taken during the surgery: classical thoracotomy, fluted heart, operating in an extracorporeal circulation.



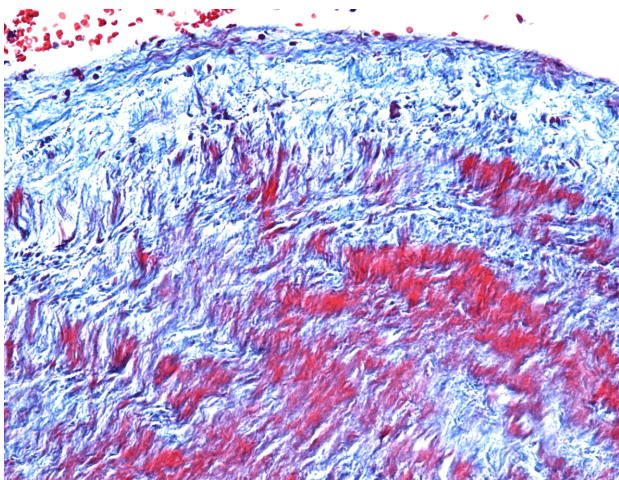
**Figure 3** – A macroscopic anatomic part: polyp-like yellow tumor with a smooth surface, a jelly-like consistency, with hemorrhagic areas.



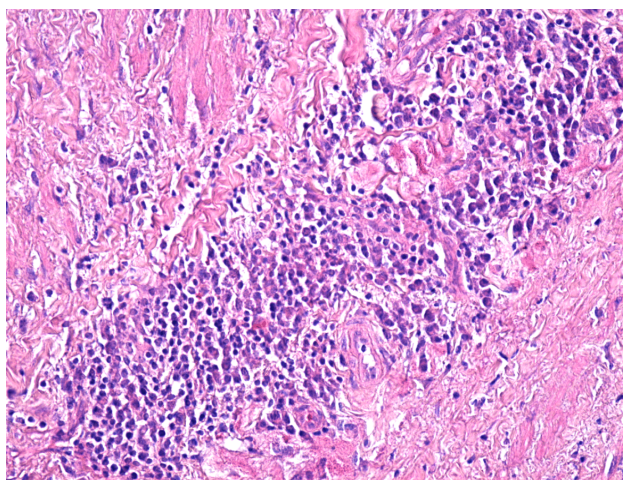
**Figure 4** – Isolated cells grouped in cords or islands arranged in a myxoid stroma rich in amorphous fundamental substance (GS trichrome staining,  $\times 100$ ).



**Figure 5** – Fusiform, polyhedral, stellate, fibroblast cells with an acidophilic cytoplasm, arranged isolated or as cords (HE staining,  $\times 200$ ).

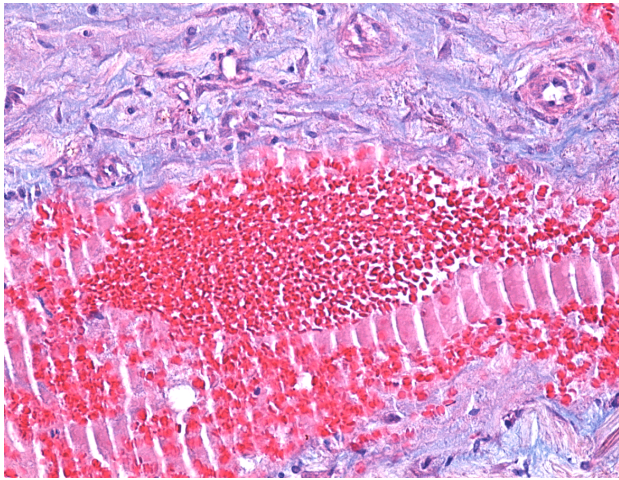


**Figure 6** – Tumoral stroma rich in collagen fibers (GS trichrome staining,  $\times 200$ ).

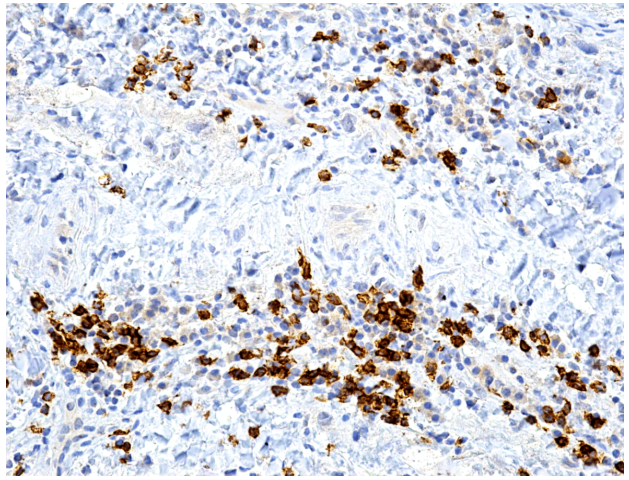


**Figure 7** – Tumoral stroma infiltrated with lymphocyte cells (HE staining,  $\times 200$ ).

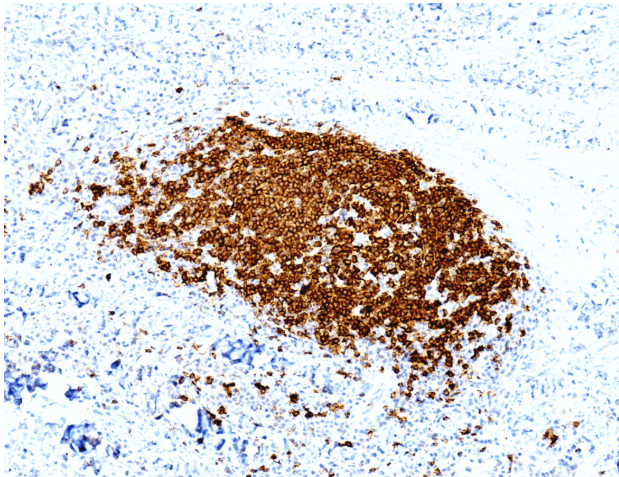




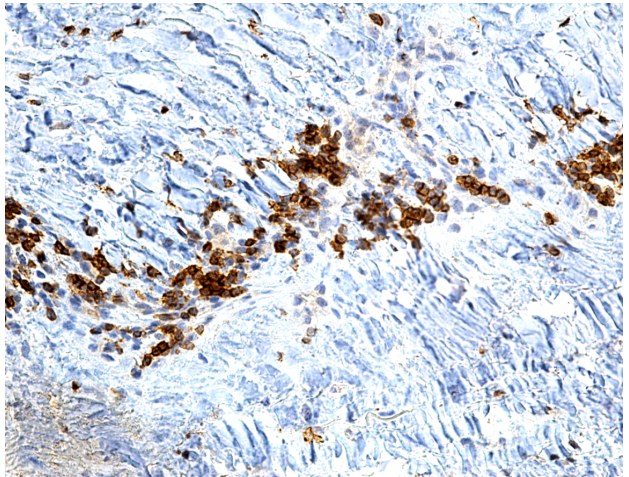
**Figure 8** – Tumoral stroma with an old hemorrhagic focus, with partially lysed red blood cells (HE staining, ×200).



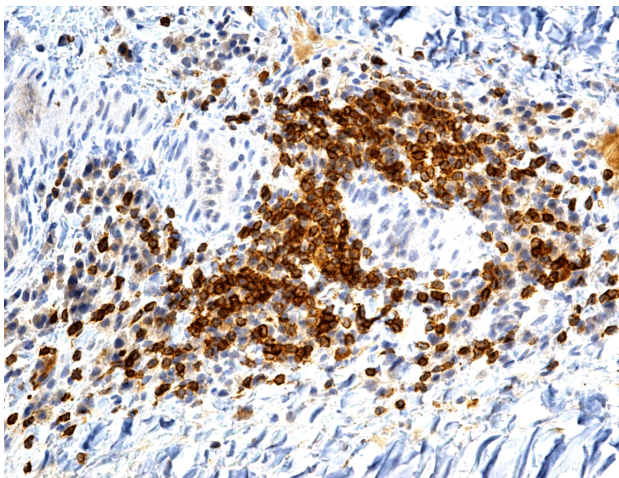
**Figure 9** – B-lymphocytes diffusely and heterogeneously disseminated in the tumoral stroma (Anti-CD20 antibody immunomarking, ×200).



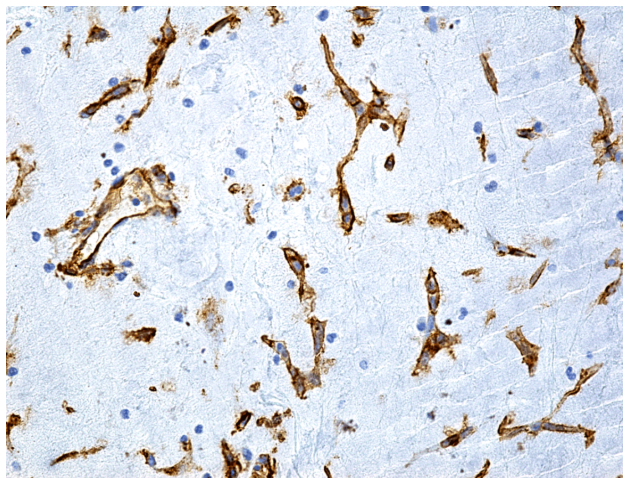
**Figure 10** – B-lymphocytes arranged as a lymph node (Anti-CD20 antibody immunomarking, ×100).



**Figure 11** – T-lymphocytes arranged heterogeneously in the myxoid stroma (Anti-CD3 antibody immunomarking, ×200).

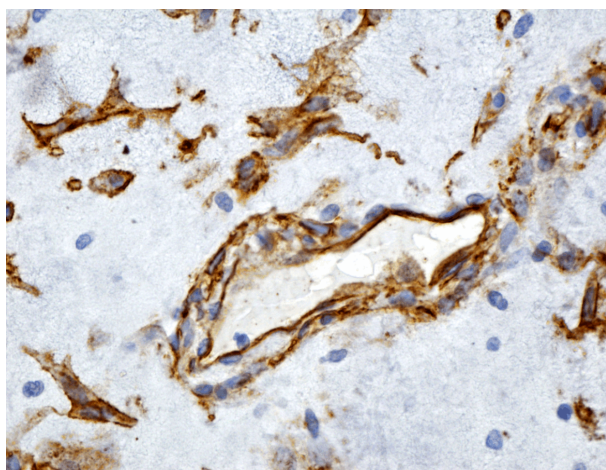


**Figure 12** – Tumoral stroma strongly infiltrated with T-lymphocytes (Anti-CD3 antibody immunomarking, ×200).



**Figure 13** – Stromal cells, isolated and arranged in cords, CD34 positive (Anti-CD34 antibody immunomarking, ×100).





**Figure 14 – Angiogenesis blood vessels with the wall formed of numerous CD34-positive endothelial cells (Anti-CD34 antibody immunomarking,  $\times 200$ ).**

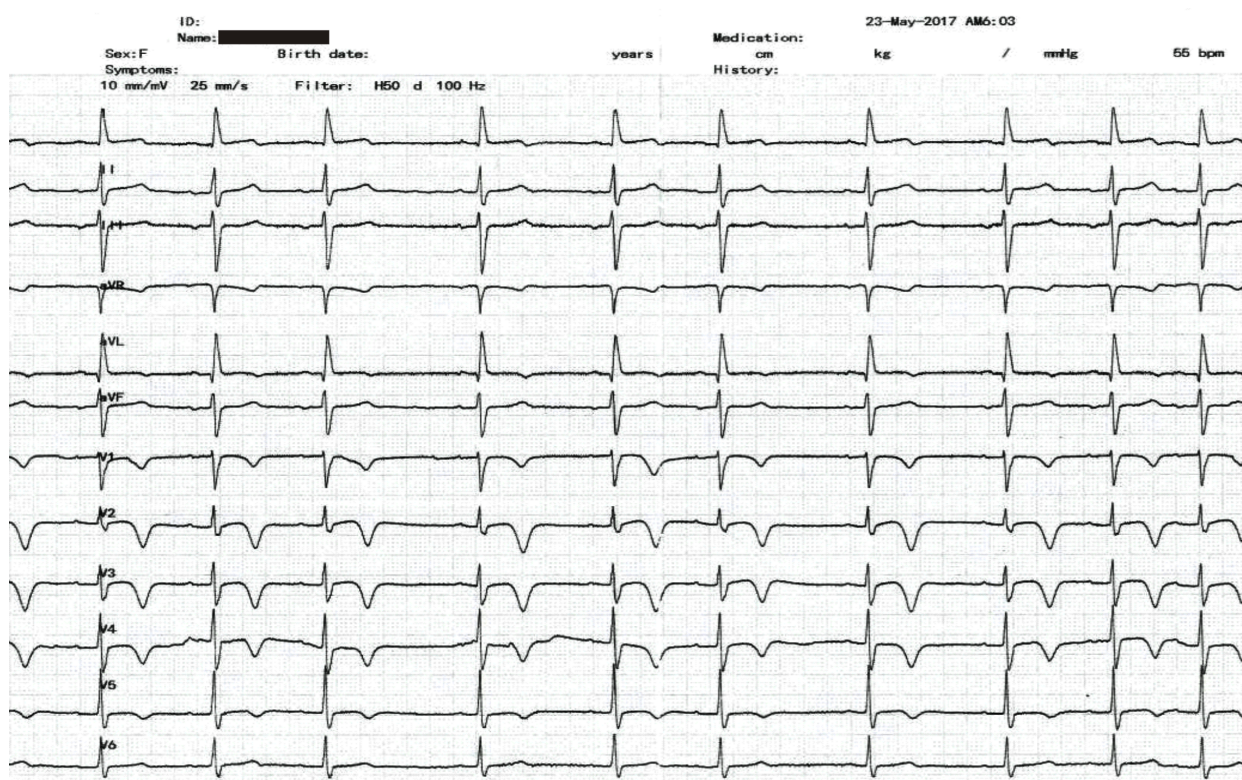
## Case No. 2

F.I., 48-year-old female patient, a smoker suffering from dyslipidemia, claims to have had precordial pains (lasting less than 5 minutes, and influenced by physical effort and the position of the body) for around one month.

The clinical examination does not reveal any pathological heart blow. From a paraclinical perspective, the patient does not have either an inflammatory syndrome, or myocardial necrosis enzymes.

The still electrocardiogram, done several times, reveals suggestive changes of the repolarizing phase, *i.e.*, some ischemic elements in the precordial derivations during the angina crises (Figure 15).

The transthoracic echocardiographic examination revealed normal-sized a cardiac cavities with normal segment-level and overall kinetics at both ventricles, without valve regurgitations.



**Figure 15 – Electrocardiogram: sinus rhythm, atrioventricular 55 beats/min, T-wave negative in V1-V5, a suggestive aspect of myocardial ischemia in the anterior territory.**

A tumor was identified at the aortic valve level, attached to the vascular side of the left coronary cusp. Since the transthoracic echocardiographic window did not allow for undoubtful assessments of the complex anatomy at this level, the doctors decided to perform a transpharyngeal echography (Figure 16).

The electrocardiographic investigation made it mandatory to also perform the angiographic examination, which revealed permeable coronary arteries.

Based on the clinical, EKG-generated and echographic data, a differential diagnosis was established which took into account three clinical entities: aortic valve vegetation, valve thrombosis, and primary aortic valve tumor.

The doctors rejected the probability of cardiac thrombosis because of the rare occurrence of this condition at the aortic valve level, especially without some clinical predisposition (such as the atrial fibrillation) or without echographic criteria indicating an abnormally structured heart (such a predisposition).

The aortic valve thrombosis on the normal heart valve is practically excluded.

The valve septic graft (the vegetation) is a quite frequent clinical condition at the valve level. In the case of our patient, the tumor location on the vascular side of the valve, without valve destruction or aortic regurgitation, were not clear arguments for establishing the diagnosis for septic etiology.



Under these circumstances, the most probable diagnosis was that of a valve tumor, the papillary fibro-elastoma being the tumor the most frequently located at this level.

Taking into account the clinical angina symptoms and the high risk of heart embolism, the doctors decided to remove the tumor. For this purpose, the classical incision was performed – open-heart surgery with normal body temperature –, by removing the tumor and replacing the aortic valve with a double-disk mechanical prosthesis.

The macroscopic examination suspected the tumor as a myxoma, although this localization is extremely rare.

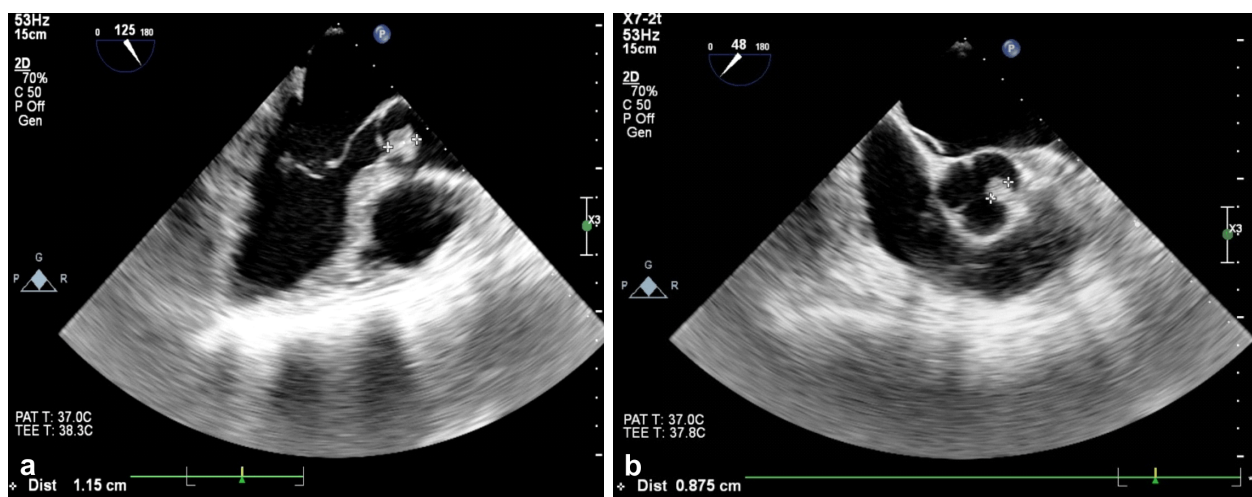
The pathological examination of the pieces included in paraffin highlighted the presence of some stellate, fusiform, polyhedral or elongated cells, arranged in a loose myxoid stroma (Figure 17) or in a dense stroma, rich in collagen (Figure 18). In this case, we observed the

presence of a higher quantity of dense, fibrillary stroma, in comparison to the atrial myxoma, probably caused by the presence of arterial pressure. In the tumoral stroma, there were identified siderophages (proof of local micro-hemorrhages), disseminated inflammatory cells, mostly diffuse, and some small calcium deposits.

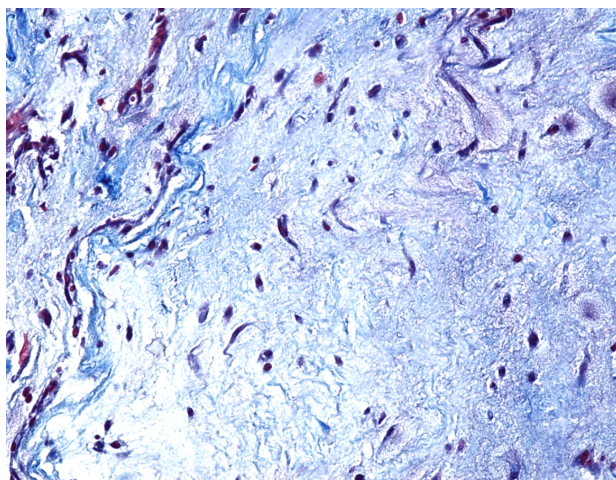
The IHC examinations confirmed the presence of B- and T-lymphocytes, diffusely disseminated (Figures 19 and 20).

Regarding the CD34-positive cells, there were also identified numerous intensely positive stromal cells, arranged isolated, as cordons or islands (Figures 21 and 22). Some of these formed capillary structures. The extremely varied aspects of CD34-positive cells suggest that these may have various functions not only that of forming new blood vessels.

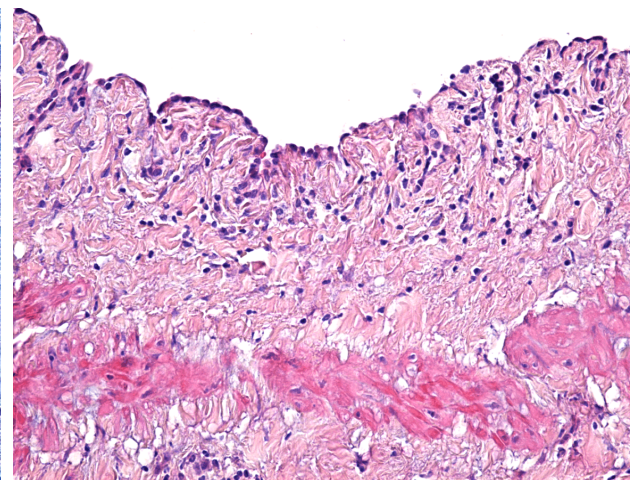
The IHC reactions to anti-Ki67 and anti-Bcl-2 antibodies were negative in this case, as well.



**Figure 16** – The transesophageal echocardiography revealed the existence of a 1.15/0.875 mm diameter tumor at the level of the left-side coronary cusp, which was mobile and attached through a small pedicle to the valve tissue, on the vascular side of the left coronary cusp.

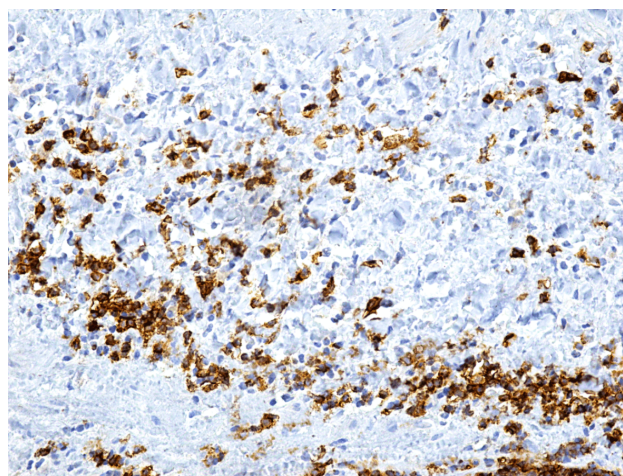


**Figure 17** – Elongated, fusiform cells, arranged isolated in the myxoid stroma (GS staining,  $\times 200$ ).

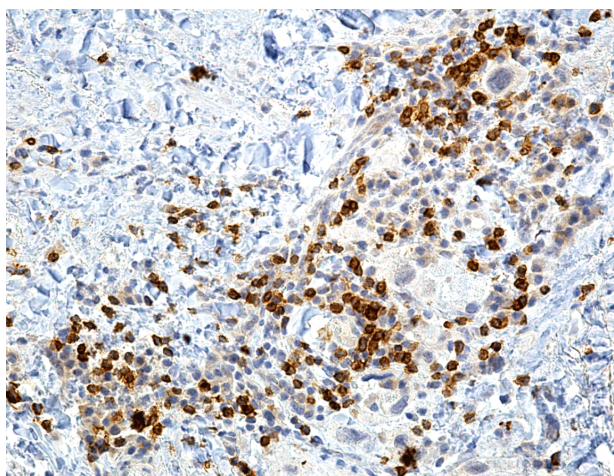


**Figure 18** – Dense tumoral stroma rich in collagen (HE staining,  $\times 200$ ).

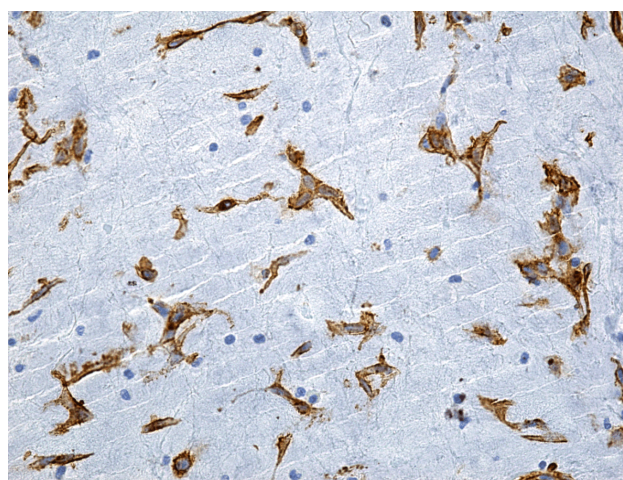




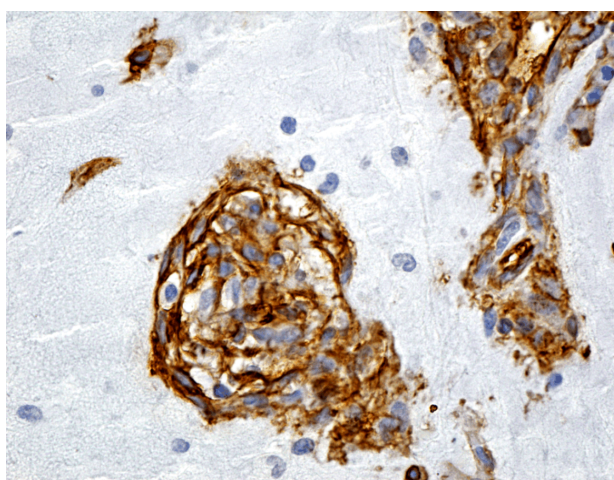
**Figure 19** – *B-lymphocytes disseminated diffusely and heterogeneously in the tumoral stroma (Anti-CD20 antibody immunomarking, ×200).*



**Figure 20** – *Area of tumoral stroma infiltrated with numerous T-lymphocytes (Anti-CD3 antibody immunomarking, ×200).*



**Figure 21** – *CD34-positive stromal isolated cells or arranged in cords, stellate or elongated, with numerous elongations (Anti-CD34 antibody immunomarking, ×100).*



**Figure 22** – *Intensely CD34-positive stromal cells arranged as islands (Anti-CD34 antibody immunomarking, ×200).*

## Discussions

The cardiac myxoma is the most frequent primary benign cardiac tumor – representing 40–50% of the primitive cardiac tumors and 80% of the benign tumors in adults. It is difficult to establish the diagnosis for cardiac tumors because of the non-specific clinical signs of this condition. The cardiac signs are mainly determined by the anatomic location of the tumor. The symptoms mimic other heart conditions, and can also have extra-cardiac aspects (embolic ones) in a large range, from a total absence of symptoms to the most serious sign, sudden cardiac death.

Most cases of cardiac myxomas are isolated, still 10% are familial ones, autosomal dominant genetically transmitted, by genetic mutations in chromosome pair 12, within the Carney syndrome, characterized by the occurrence of cardiac myxomas, endocrine anomalies, skin pigmentation and neurological diseases [8–11].

Most cases of cardiac myxoma are diagnosed between 40 and 60 years old, but they may appear at any age.

Myxoma is a benign tumor of the endocardium, which develops inside cavities, with a risk of causing

nuisance to all the heart cavities. This condition is especially located in the atrium. Around 75% of cases are located in the left atrium, at the level of the *fossa ovalis*, 25% can be found in the right atrium, and there are also rare cases in which myxoma is formed in the ventricle. The rarest cases are located in the valve (less than 1.5% of the occurrences). The cardiac myxoma is often a single intra-cavity tumor. In the forms occurring in families, there might be multiple tumors with an atypical location, with a beginning earlier than 30 years old, with an increased trend of recovering subsequently to surgical removal, and they frequently also occur in other areas outside the heart (at the breasts or the skin level), joined by pigment spots and endocrine hyperactivity [12, 13].

One of our cases presented a myxoma with a rare localization (in the aortic valve), which caused ischemic changes on the electrocardiogram. Javed *et al.* (2014) stated that there were reported only nine cases of myxomas localized on the aortic valves [14].

The pathological aspect, both macroscopically, but mostly the microscopically one, establishes the diagnosis



and provides important pieces of information regarding the prognostic and evolution.

The most frequently encountered are indefinite forms, villous, with variable colors (gray, yellow), with bleeding spots, viscous, gelatinous consistency, increased mobility, pedunculated, with wide implantation base, variable seat (most common exist at the interatrial septum, at the *fossa ovalis*) [15], of variable dimensions, which can reach in the severe cases 15 cm [16, 17], with high embolic risk [18, 19]. In the other cases, it was described well-defined tumor formations with smooth surface, embedded, firm consistency, sessile with a narrow base of implantation and low embolic risk.

Macroscopically, our cases presented a smooth surface, yellowish color with hemorrhagic spots and soft consistency, almost gelatinous. The myxoma localized on the aortic valve presented a harder consistency, comparative to the one with atrial localization.

The microscopic examination we performed showed in the myxoma structures the presence of conjunctive cells, with stellate, polygonal, round form, with or without elongations, present in an abundant stroma of myxoid aspect. By using anti-CD34 antibody, we observed that many of the stromal cells were CD34-positive that could have been stem mesenchymal cells, endothelial progenitor cells, endothelial cells of blood vessels. Some authors consider that the presence of CD34 antigen on non-hematopoietic cells in various adult tissues show the phenotype of progenitor cells even on adult stem cells [20]. Other studies showed that myxomas contain mesenchymal multipotent cells, capable of differentiating into endothelial cells, fibroblasts, angioblasts, smooth muscular cells and even cartilaginous cells [21, 22].

In our cases, we observed the fact that the stroma aspect was uneven, in some areas being infiltrated with red blood cells, because of local microhemorrhages. In other areas, the stroma was densely fibrillary. Also, in the stroma, there were identified T- and B-lymphocytes, most often arranged diffusely, but in some areas, the inflammatory infiltrate was quite intense. For the differential diagnosis between malignant lymphoma or sarcoma, we used two IHC markers: anti-Ki67 and anti-Bcl-2 antibodies. The negative reaction to these antibodies, associated with a diffuse reaction to CD20 excluded a lymphoma, and also another primary or secondary malignant tumor [23–28].

The diagnosis of atrial myxoma is suggested by the clinical examinations and medical imaging (cardiac echography, computed tomography, nuclear magnetic resonance), but the certainty diagnosis is established by the histopathological and IHC examination.

Cardiac myxoma is a serious condition that may give multiple complications: rhythm disorders, valvular failure, heart failure, ischemic phenomena, embolic phenomena and even sudden death. Therefore, its treatment is a relative emergency. The surgical resection of the myxoma is the treatment at choice, the surgical intervention being considered safe, with a low morbidity and mortality [29, 30].

Monitoring the evolution of patients with atrial myxoma after surgery is essential for the prevention of local and general complications (emboli) and for the detection of relapses.

## Conclusions

Atrial myxomas represent a tumoral pathology with an extremely varied clinical symptomatology, which may raise problems of positive and differential diagnosis. The investigations of medical imaging allow the identification and localization of the cardiac tumor, but only the histopathological examination may confirm the positive and differential diagnosis. The surgical treatment remains the most used nowadays and the postoperative prognosis remains a good one.

## Conflict of interests

The authors declare that they have no conflict of interests.

## References

- [1] Corradi D, Contini GA, Gherli T, Nicolini F. A left atrial myxomalike rhabdomyosarcoma. *J Thorac Cardiovasc Surg*, 2012, 144(1):e7–e10.
- [2] Zapata Laguado MI, Palacios Rojas JO, Gómez Lopez EA, Velasco Morales ML, Orozco de la Hoz CE. High-grade left atrial pleomorphic sarcoma: case report and review. *Case Rep Oncol*, 2017, 10(3):1138–1143.
- [3] Fathala A, Abouzied M, AlSugair AA. Cardiac and pericardial tumors: a potential application of positron emission tomography–magnetic resonance imaging. *World J Cardiol*, 2017, 9(7):600–608.
- [4] Fernandes F, Soufen HN, Ianni BM, Arteaga E, Ramires FJ, Mady C. Primary neoplasms of the heart. Clinical and histological presentation of 50 cases. *Arq Bras Cardiol*, 2001, 76(3):231–237.
- [5] Butany J, Leong SW, Carmichael K, Komeda M. A 30-year analysis of cardiac neoplasms at autopsy. *Can J Cardiol*, 2005, 21(8):675–680.
- [6] McManus B, Lee CH. Chapter 69: Primary tumors of the heart. In: Libby PP, Bonow RO, Mann DL, Zipes DP (eds). *Braunwald's heart disease: a textbook of cardiovascular medicine*. 8<sup>th</sup> edition, Elsevier Science, Philadelphia, 2008, 1815–1828.
- [7] Burke A, Tavora F. The 2015 WHO classification of tumors of the heart and pericardium. *J Thorac Oncol*, 2016, 11(4):441–452.
- [8] Aroca A, Mesa JM, Dominguez F, Oliver JM, Ramirez U, Centeno JE. Multiple recurrence of a “sporadic” (non-familial) cardiac myxoma. *Eur J Cardiothorac Surg*, 1996, 10(10):919–921.
- [9] Imai Y, Taketani T, Maemura K, Takeda N, Harada T, Nojiri T, Kawanami D, Monzen K, Hayashi D, Murakawa Y, Ohno M, Hirata Y, Yamazaki T, Takamoto S, Nagai R. Genetic analysis in a patient with recurrent cardiac myxoma and endocrinopathy. *Circ J*, 2005, 69(8):994–995.
- [10] Lone RA, Ahanger AG, Singh S, Mehmood W, Shah S, Lone G, Dar A, Bhat M, Sharma M, Lateef W. Atrial myxoma: trends in management. *Int J Health Sci (Qassim)*, 2008, 2(2):141–151.
- [11] Jia X, Kohli A, Jarjour J, Chen CJ, Gilmore B, Tabbaa R, Poythress EL. Recurrent biatrial myxoma in a 41-year-old woman after left atrial myxoma resection. *Tex Heart Inst J*, 2017, 44(6):402–404.
- [12] Martin-Suárez S, Botta L, Dell'Amore A, Camurri N, Mikus E, Leone O, Marinelli G, Di Bartolomeo R. Mitral valve myxoma involving both leaflets. *Cardiovasc Pathol*, 2007, 16(3):189–190.
- [13] Cetin G, Gursoy M, Ugurlucan M, Uzunhasan I, Hatemi AC, Tireli E, Kucukoglu S, Kansiz E. Single-institutional 22 years experience on cardiac myxomas. *Angiology*, 2010, 61(5):504–509.
- [14] Javed A, Zalawadiya S, Kovach J, Afonso L. Aortic valve myxoma at the extreme age: a review of literature. *BMJ Case Rep*, 2014, 2014:bcr2013202689.
- [15] Burke AP, Virmani R. Cardiac myxoma. A clinicopathologic study. *Am J Clin Pathol*, 1993, 100(6):671–680.



- [16] Dong A, Lu J, Zuo C. Multiple peripheral pulmonary artery aneurysms in association with a right atrial myxoma. *Circulation*, 2016, 133(4):444–446.
- [17] Roberts WC. Primary and secondary neoplasms of the heart. *Am J Cardiol*, 1997, 80(5):671–682.
- [18] Altundag MB, Ertas G, Ucer AR, Durmus S, Abanuz H, Calikoğlu T, Ozbagi K, Demirkasimoglu A, Kaya B, Bakkal BH, Altundag K. Brain metastasis of cardiac myxoma: case report and review of the literature. *J Neurooncol*, 2005, 75(2):181–184.
- [19] Raut MS, Maheshwari A, Swain B. Unsolved enigma of atrial myxoma with biventricular dysfunction. *Ann Card Anaesth*, 2018, 21(1):105–106.
- [20] Sidney LE, Branch MJ, Dunphy SE, Dua HS, Hopkinson A. Concise review: evidence for CD34 as a common marker for diverse progenitors. *Stem Cells*, 2014, 32(6):1380–1389.
- [21] Reynen K. Cardiac myxomas. *N Engl J Med*, 1995, 333(24):1610–1617.
- [22] Grant M, Douglass S, Roberge E, Shry E. Cardiac magnetic resonance imaging and a rare case of an atrial myxoma causing an atrial septal defect. *Radiol Case Rep*, 2017, 12(4):658–663.
- [23] Mankad R, Herrmann J. Cardiac tumors: echo assessment. *Echo Res Pract*, 2016, 3(4):R65–R77.
- [24] Jonavicius K, Salcius K, Meskauskas R, Valeviciene N, Tarutis V, Sirvydis V. Primary cardiac lymphoma: two cases and a review of literature. *J Cardiothorac Surg*, 2015, 10:138.
- [25] Pătraşcu AM, Rotaru I, Olar L, Pătraşcu Ş, Ghiluş MC, Neamţu SD, Nacea JG, Gluhovschi A. The prognostic role of Bcl-2, Ki67, c-MYC and p53 in diffuse large B-cell lymphoma. *Rom J Morphol Embryol*, 2017, 58(3):837–843.
- [26] Ayedi I, Chaabouni H, Akrouit M, Boudawara T, Toumi N, Khanfir A, Frikha M. Cardiac metastases: 4 cases report. *Tunis Med*, 2017, 95(6):429–433.
- [27] Sun D, Wu Y, Liu Y, Yang J. Primary cardiac myxofibrosarcoma: case report, literature review and pooled analysis. *BMC Cancer*, 2018, 18(1):512.
- [28] Xiao J, Song J, Liu H, Sun Y, Wang C. Rare cardiac metastasis of soft tissue sarcoma: a case report and literature review. *Medicine (Baltimore)*, 2018, 97(13):e9814.
- [29] Keeling IM, Oberwalder P, Anelli-Monti M, Schuchlenz H, Demel U, Tilz GP, Rehak P, Rigler B. Cardiac myxomas: 24 years of experience in 49 patients. *Eur J Cardiothorac Surg*, 2002, 22(6):971–977.
- [30] Shah IK, Dearani JA, Daly RC, Suri RM, Park SJ, Joyce LD, Li Z, Schaff HV. Cardiac myxomas: a 50-year experience with resection and analysis of risk factors for recurrence. *Ann Thorac Surg*, 2015, 100(2):495–500.

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