REVIEW

RJME Romanian Journal of Morphology & Embryology http://www.rjme.ro/

Giant left atrial myxoma – literature review and case presentation

VICTOR CORNEL RAICEA[1)], HORAŢIU SUCIU[2,3)], ANDREI DAN RAICEA[2)], GHEORGHE COSMIN MACARIE[4,5)], TIBOR MEZEI[6,7)], MARIA SMARANDA MAIER[8,9)]

[1)]*Clinic of Cardiovascular Surgery, Emergency County Hospital, Craiova, Romania*

[2)]*Clinic of Cardiovascular Surgery, Emergency Institute for Cardiovascular Diseases and Transplant, Târgu Mureş, Romania*

[3)]*Department of Surgery, George Emil Palade University of Medicine, Pharmacy, Science, and Technology of Târgu Mureş, Romania*

[4)]*Clinic of Cardiology, Emergency Institute for Cardiovascular Diseases and Transplant, Târgu Mureş, Romania*

[5)]*Department of Internal Medicine, George Emil Palade University of Medicine, Pharmacy, Science, and Technology of Târgu Mureş, Romania*

[6)]*Department of Pathology, George Emil Palade University of Medicine, Pharmacy, Science, and Technology of Târgu Mureş, Romania*

[7)]*Department of Pathology, Mureş County Emergency Clinical Hospital, Târgu Mureş, Romania*

[8)]*Department of Neurology, George Emil Palade University of Medicine, Pharmacy, Science, and Technology of Târgu Mureş, Romania*

[9)]*Neurology Clinic I, Mureş County Emergency Clinical Hospital, Târgu Mureş, Romania*

Abstract

Primary cardiac tumors are an extremely rare pathology, representing only 5–10% of cardiac neoplasms, but among them, the most common are cardiac myxomas, that appear to originate from multipotent mesenchymal cells of the subendocardial and endocardial stroma. The incidence of cardiac myxomas is higher in females and they are usually diagnosed between the fourth and sixth decade of life. Most often, they are located in the left atrium, having the site of attachment at the level of the interatrial septum, especially at the level of the *fossa ovalis* and the adjacent limbus. Due to the increased risk of systemic embolization and intracardiac obstruction, cardiac myxomas have a definite indication for emergency surgical treatment. Cardiac myxomas are a very rare cause of transient ischemic attacks and stroke. We present the case of a 38-year-old patient who experienced four recurrent transient ischemic attacks and strokes. At the fourth cerebrovascular event, echocardiography was performed and it revealed a giant tumor located in the left atrium that was surgically removed. Pathological examination confirmed the diagnosis of cardiac myxoma. The postoperative evolution was favorable, both from a neurological and cardiac point of view. Although cardiac myxomas represent a rare cause of transient ischemic attacks and stroke, they must be considered as part of the assessment protocol for cerebrovascular events.

Keywords: cardiac myxoma, benign cardiac tumor, heart diseases, recurrent ischemic strokes.

Introduction

Cardiac tumors represent a rare pathology, and primary tumors are estimated to have an incidence 100 times lower than secondary tumors, with a prevalence of 0.001–0.03% in autopsy studies [1, 2]. The most frequent benign heart tumors are cardiac myxomas, which originate from multipotent mesenchymal cells (MCs) in the endocardium and account for up to 80% of all primary heart tumors. Myxomas are most prevalent in female patients aged 30 to 60 years and are located in the left atrium in 75% of cases. Due to its various clinical manifestations, which can mimic a multitude of systemic diseases or heart conditions, cardiac myxoma is a diagnostic challenge. Even if it is a benign tumor in most cases, delaying the correct diagnosis of this condition can have very serious consequences, especially due to the increased risk of systemic embolization of tumor fragments that can cause severe ischemic strokes, but also due to the risk of developing heart failure secondary to atrioventricular valve obstruction. Most patients also experience a wide range of constitutional symptoms, but the underlying mechanism is not completely understood. Early diagnosis of cardiac myxomas by echocardiography or cardiac magnetic resonance imaging (MRI), followed by prompt surgical treatment is associated with an excellent long-term evolution and a low risk of recurrence [1, 3–8].

Aim

The aim of this paper was to present the data from the literature on a rare disease with nonspecific symptoms and severe complications, and also to report a case of a giant left atrial myxoma presenting with recurrent ischemic strokes, in a young female patient.

Epidemiology

The estimated incidence of cardiac myxomas is about 0.5 per million people per year. Cardiac myxomas are more

common in women compared to men, with some studies reporting a 3:1 ratio between women and men [9, 10].

In terms of localization, the incidence of cardiac myxomas with localization at the level of the right atrium (10–20%) is smaller compared to those located at the level of the left atrium (about 75–80%). In a relatively small percentage of cases (5–10%), cardiac myxomas can be located in both atria or in the ventricles. The most common site for tumor attachment is the interatrial septum. Tumors are usually mobile and frequently prolapse in the ventricle [9–13].

Cardiac myxomas are most commonly diagnosed between the fourth and sixth decade of life, with an average patient age of 51 years at the time of surgery in some studies [9].

In approximately 90% of cases, cardiac myxomas occur sporadically, and less than 10% of cases occur in the family context, particularly in the context of Carney syndrome, an autosomal dominant X-linked disease characterized by the presence of multiple neoplasms represented by cardiac and extracardiac myxomas, endocrine tumors, schwannomas, and pigmented skin tumors [4, 14, 15].

Pathophysiology

Although there is much debate about the origin of cardiac myxomas, they appear to originate from multipotent MCs of the subendocardial and endocardial stroma that are capable of both neural and endothelial differentiation. The hypothesis of origin from endocardial neural tissue has not been proven and is unlikely [4, 16].

According to data from the literature, cardiac myxomas most commonly have dimensions between 1.5 cm and 15 cm. From a morphological standpoint, cardiac myxomas can be solid tumors, with a smooth, regular surface and a globular or multilobular appearance, or they can present as papillary tumors, which are friable and have a gelatinous appearance with a morphology often similar to cauliflower. Rare cases have also been described in which the myxoma was surrounded by a capsule. Within the cardiac myxoma there are described, *via* echocardiogram, areas of calcification, areas of hemorrhage or necrosis, and most frequently, echolucent areas [13, 17].

Pathologically, cardiac myxomas are composed of bland, stellate, ovoid, or plump spindle myxoma cells that are usually mononuclear, with a round, oval, or elongated nucleus and eosinophilic cytoplasm. They are rarely solitary, usually arranged in clusters and cords around small blood vessels, showing rare mitotic figures and no cytological atypia. The myxoid stroma is composed of mucopolysaccharides, type IV collagen, and elastin. Inflammatory cells are frequently present, especially at the site of attachment to the atrial wall; occasional blood vessels with focal hemorrhage, thrombi, and calcifications may also be seen [4, 16, 17].

Clinical features

The clinical manifestations encompass a myriad of symptoms, which can be best described by the triad of constitutional, obstructive (mitral valve obstruction), and embolic (central and peripheral) symptoms [1, 3, 4].

The most common symptoms reported in patients with left atrial myxoma are those caused by mitral valve obstruction and left-sided heart failure, resulting in secondary pulmonary hypertension, with about half of the patients presenting with dyspnea, followed by orthopnea and pulmonary edema. In the case of cardiac myxoma located in the right atrium, the symptoms are due to tricuspid valve stenosis and right heart failure and are represented by dyspnea, hepatomegaly, or ascites. Both locations of the cardiac myxoma may be associated with heart rhythm disorders due to myocardial penetration. In some clinical trials, embolic events were reported in one-third of patients with cardiac myxomas. The most frequent manifestations of left-sided atrial myxoma are transient neurological symptoms such as strokes, while the most frequent manifestation of right-sided atrial myxoma is pulmonary embolism. Other locations of systemic embolization of atrial myxomas reported in the literature are the kidneys, spleen, iliac or femoral arteries, and the abdominal aorta. Constitutional symptoms are found in about 40% of patients and are usually represented by anorexia, weight loss, fatigue, arthralgia, and fever. In rare cases, atrial myxoma may occur as part of the Carney's complex [9, 13, 18–22].

Diagnosis

In approximately 50% of cases, the diagnosis of cardiac myxoma is established late, when symptoms appear due to mitral valve obstruction or when the tumor causes thromboembolic events in the brain, lung, or periphery [9].

Two-dimensional (2D) echocardiography is currently considered the method of choice for the screening and diagnosis of cardiac myxoma, due to the temporal and spatial resolution that allows for the differentiation of cardiac tumors from valvular vegetations or intracardiac thrombi. Transthoracic echocardiography, which has a sensitivity of 95%, can be complemented by transesophageal echocardiography, which facilitates a sensitivity of 100% in the diagnosis of cardiac myxoma. Typically, cardiac computed tomography (CT) and MRI examinations do not bring additional benefits to justify the significantly increased costs, but their advantage is that they allow a more accurate assessment of the presence and size of the implantation peduncle and its implantation site, as well as a better view of the thoracic structures. These imaging techniques are also superior in excluding tumor infiltration of the adjacent myocardium [10, 23, 24].

Coronary angiography is not routinely indicated in patients with suspected cardiac tumors, except to rule out the presence of atherosclerotic coronary lesions in elderly patients [25].

2D echocardiography should be performed in all patients with signs of valvular obstruction or embolic events, or in patients with the above-mentioned constitutional signs for which no other cause is identified. The first diagnosis of cardiac myxoma by 2D echocardiography was reported in 1968 [10, 26].

Differential diagnosis

The differential diagnosis of cardiac myxomas is made primarily with other primary cardiac tumors, both benign (*e.g.*, lipoma, papillary fibroelastoma, rhabdomyoma, leiomyoma, lymphangioma) [27, 28] and malignant (*e.g.*, angiosarcoma, mesenchymoma, leiomyosarcoma, fibromyxosarcoma); with metastatic tumors that invade the

heart, which are up to four times more common than the primary tumors; and with an organized thrombus [2, 4], or with other congenital or ischemic heart disease [29].

Complications

Even though cardiac myxomas are in most cases benign tumors, without early recognition, the effects can be catastrophic. Among the most common complications of cardiac myxomas are systemic embolizations, reported in most clinical trials in about 50% of patients. Embolic events are caused either by the development of thrombi on the tumor surface and their subsequent dissemination, or by tumor fragmentation and detachment. Embolic manifestations are most common in the cerebral circulation and at the level of the retinal artery, followed by the arteries of the lower limbs, the visceral arteries and abdominal aorta. Rare cases of embolism in the coronary arteries have also been described, which together with the complete obstruction of the mitral valve, represent the causes of sudden death in patients with cardiac myxoma. The most important risk factors for embolic events in patients with cardiac myxomas appear to be the macroscopic appearance of the tumor, its location, an increased platelet count and the mobility of the tumor [21, 7, 30–33]. In almost a third of cases, the main complication of heart myxomas is chronic heart failure, especially in solid, large tumors that obstruct the atrioventricular valves. Complete acute obstruction of atrioventricular communication is a potentially fatal complication and requires emergency surgery [5, 34].

Treatment

After establishing the diagnosis of cardiac myxoma, the patient should be referred to a cardiac surgery service as soon as possible, due to the increased risk of systemic embolization or mitral valve obstruction, in the case of left-sided atrial myxomas, especially considering the completely curable potential of this condition [5]. The first successful removal of a cardiac myxoma was performed in 1954 by Clarence Crafoord, in Stockholm, in a 40-year-old female patient who showed signs of mitral valve stenosis as symptomatology [35].

The treatment of cardiac myxomas is eminently surgical; medical treatment is currently non-existent [36]. The objective is the removal of the tumoral formation and the adjacent healthy tissue as soon as the diagnosis has been established, to avoid adjacent complications (obstructive and emboligenic) [37]. For patients over 50 years of age, who do not have a family history of the disease, the elective treatment is simple surgical excision; however, for young patients with significant family history, the treatment is complex and aggressive [38, 39].

The common surgical approach is through a median longitudinal sternotomy. Because of the intracavitary localization of the myxoma, the use of total cardio-pulmonary bypass with bicaval cannulation is mandatory. The base of the implantation pedicle is excised, together with the healthy surrounding tissue in a circumference of at least 5 mm. It is recommended that the excised tissue should incorporate the superior half of the *fossa ovalis*, as this tissue is abundant in precursor cells of the myxoma [40]. In either cases, the surgeon should extract the formation as a whole, to avoid subsequent embolization of tumoral fragments [41]. After the excision of the tumor is completed, cardiac cavities are rinsed abundantly with saline, while aggressively aspirating its contents to extract the remaining fragments. If the base of insertion of the tumor is situated in the atrial wall, it is ideal to excise the entire thickness of the atrial wall. If the localization of the base of implantation makes it impossible to excise the entire thickness of the wall, then it is mandatory to excise the adjacent atrial endocardium, ideally also incorporating a part of the muscular wall. The defect created through this excision will be closed through a simple suture or using a patch of autologous or heterologous pericardium [40].

Ventricular myxomas, whether they are located in the left or right ventricle, do not require complete resection of the ventricular wall, which is a dangerous procedure. Using this less aggressive form of resection, no relapse of the tumoral formation has been recorded [42, 43]. In the case of right ventricular myxomas, it is mandatory that the left and right atria are inspected, as 15% of cases present an associated left or right atrial tumor [42]. In rare cases, associated with the extraction of the myxomatous tumoral formation, surgical intervention of the adjacent atrioventricular valves is necessary, consisting of annuloplasty procedures, or in the rare case in which the insertion of the pedicle is adjacent to or at the level of the valve, valvular replacement becomes necessary [40].

Prognosis

The prognosis after surgery is usually very good. The recurrence rate is very low, in approximately 7% of cases, and recurrence most frequently occurs within five years of the operation. In a retrospective study by Bjessmo & Ivert (1997) [9], the 20-year survival rate after surgery was 85%. Most patients who were diagnosed with recurrence of cardiac myxoma had risk factors for recurrence, such as a family history of the tumor, multifocal myxoma, or a location other than the atrial septum. The most important causes of cardiac myxoma recurrence, in patients without a family history, appear to be tumoral re-implantation during resection and incomplete resection. For the identification of a recurrence, it is recommended to perform transthoracic echocardiography one year after the surgery, and subsequently at an interval of five years for patients with risk factors for recurrence. According to recent studies, cardiac CT or MRI has greater accuracy for early diagnosis of a recurrence after surgery. The recognition of a familial implication and Carney syndrome is important in guiding the surgical treatment, planning patient follow-up, and predicting recurrence [9, 10, 12, 42, 44–46].

Case presentation

We describe the case of a 38-year-old female patient with no significant medical history; in March and May of 2020, she presented with two consecutive episodes of right limb motor deficit lasting approximately five minutes each. In June, the patient visited the Emergency

Department, complaining of a right limb motor deficit, partially regressive but persistent. CT scan of the brain revealed no pathological changes, and the diagnosis of an ischemic stroke was established. The patient was admitted to the Neurology Department. Throughout the first hospitalization, the following laboratory tests were performed and were in normal range: complete blood count, biochemistry, coagulation, erythrocyte sedimentation rate, protein C, protein S, antithrombin III, Leyden factor V mutation, factor II mutation G20210A, antiphospholipid antibodies, anticardiolipin antibodies, lupus anticoagulant, anti-double stranded deoxyribonucleic acid (dsDNA) antibodies, antinuclear antibodies (ANA) profile test, serum protein electrophoresis and immunofixation electrophoresis, anti-proteinase 3 antibodies [classical anti-neutrophil cytoplasmic antibodies (cANCA)], and anti-myeloperoxidase antibodies [perinuclear ANCA (pANCA)].

Ultrasound imaging of the carotid and vertebral arteries was normal, with no atherosclerotic plaques or differences in velocities observed. Due to the reorganization of internal Hospital Departments caused by the coronavirus disease 2019 (COVID-19) pandemic (our hospital being an emergency hospital with COVID-19 support), the limitation of inter-clinical consultations and the reduction of the hospitalization period made it impossible to perform the echocardiographic examination, a routine examination in the protocol of stroke diagnosis. The patient was started on antiplatelet therapy and transferred to a Neuromotor Recovery Service. In September 2020, the patient presented in the Emergency Department with vertigo, nausea, repetitive vomiting, and balance impairment, and was therefore admitted to our Neurology Clinic. The general clinical examination was within normal limits.

The neurological examination revealed right central facial palsy, bilateral horizontal nystagmus, right limb hemiparesis grade 4 Medical Research Council (MRC) Scale, right limb superficial hemi-hypoesthesia, global brisk deep tendon reflexes, right Babinski sign, and right limb dysmetria at both index–nose and heel–knee–shin maneuver, with a National Institutes of Health (NIH) Stroke Scale (NIHSS) of six points. The cerebral MRI revealed right cerebellar ischemic stroke. In the T2 sequence, numerous hypersignal lesions were distributed in both cerebral hemispheres and the vermis; the three-dimensional time of flight (3D TOF) sequences revealed no signal or morphological differences in the cerebral arteries (Figure 1, a and b). We established the diagnosis of vertebrobasilar stroke. The patient was not a candidate for intravenous thrombolysis; she presented to the Emergency Department nine hours after the onset of symptoms.

2D transthoracic echocardiography, which was ordered to determine the cause of the recurrent ischemic strokes, revealed a 6×5 cm cardiac mass, with imprecise margins, located in the left atrium and attached to the interatrial septum. The anterior mitral valve was spared of tumoral invasion. Due to the considerable dimensions, the mitral valve orifice was obstructed during the systolic phase, which led to a large-to-medium functional stenosis and mitral ring dilation (33 mm); in the diastolic phase, it prolapsed into the left ventricle, free pericardial space, 6 mm, with no compression on the right cavities (Figure 2, a and b).

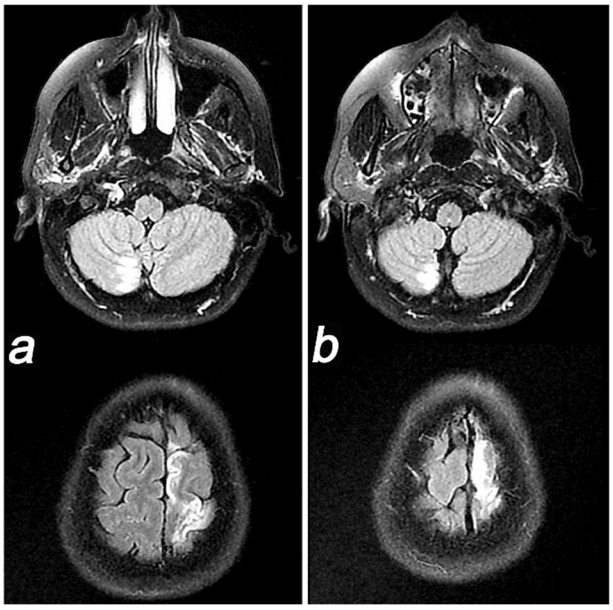

Figure 1 – ***(a and b) Cerebral MRI, axial T2 FLAIR sequences revealed right ischemic cerebellar stroke and left hemispheric stroke. FLAIR: Fluid-attenuated inversion recovery; MRI: Magnetic resonance imaging.***

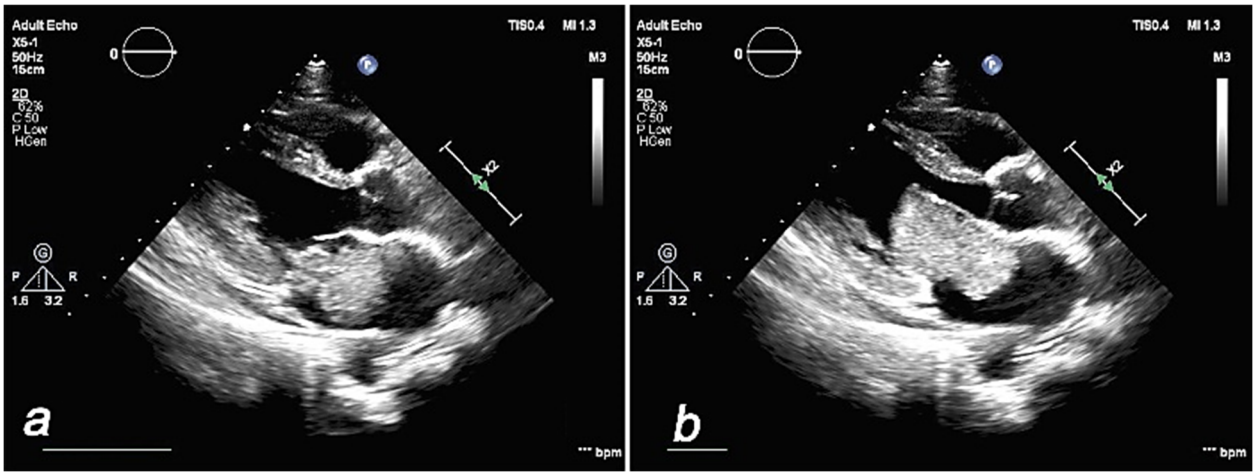

Figure 2 – ***(a and b) Presurgical 2D transthoracic echocardiography showed a cardiac mass located in the left atrium, with imprecise margins, attached to the interatrial septum. 2D: Two-dimensional.***

The thoracoabdominal–pelvic CT scan revealed a tumoral mass situated in the left atrium, inhomogeneous, with imprecise margins and minimal enhancement after the contrast administration, measuring 67×46×45 mm. Additionally, a native and post-contrast administration hypodense lesion was located in the spleen, measuring 53×32 mm – splenic infarction (Figure 3, a and b). Thus, the patient was diagnosed with recurrent transitory ischemic attacks and ischemic strokes secondary to cerebral emboli arising from the left atrial myxoma (either tumoral fragments, blood clots, or both). The treatment was adapted towards low-molecular-weight Heparin and the patient was transferred to the Cardiothoracic Surgery Clinic two weeks after the ischemic stroke. Intraoperatively, the mass appeared polypoid and multilobulated, originating from the secondary atrial septum. The myxoma was excised under total cardiopulmonary bypass, approached by right and left atriotomy. The procedure involved excising the secondary interatrial septum with 5 mm margins from the tumoral border and reconstructing the interatrial septum with a heterologous pericardial patch. Concomitantly, mitral annuloplasty was performed with a full ring (Medtronic No. 28) to correct the mitral insufficiency secondary to the myxoma protruding in the left ventricle during the diastolic phase (Figure 4, a and b).

Tissue samples were sent to the Morphopathology Laboratory. Macroscopically, the samples appeared nodular, with shiny surfaces and a myxoid, semi-transparent aspect, and a total diameter of 50×40×30 mm. Two of these samples had attached endocardial fragments. The tissue samples were interpreted by microscopy and immunohistochemical staining, as follows: moderate cellular tumoral proliferation, composed of fusiform, monomorphous cells, distributed in a mild basophilic stroma with a myoxid aspect; extensive hemorrhagic areas with siderophage inclusions; at the site of the tumoral origin, multiple tumoral emboli were observed in the blood vessels from the subendocardial muscular tissue and the blood vessel walls appeared thickened; the tumoral cells were intensely positive for calretinin; the proliferation index as assessed by Ki67 immunomarker was reduced (Figure 5, a–c). The post-surgical evolution of the patient was entirely favorable; no complications were noted either from a cardiological or a neurological standpoint. The postsurgical echocardiography noted the absence of the tumoral mass, no shunt at the site of the interatrial septum, and a competent mitral valve (Figure 6, a and b). One month after the surgical intervention, the patient presented with a mild right limb motor deficit, full regression of the cerebellar signs, and an NIHSS of two points.

Discussions

We described the case of a young female patient with cardiac myxoma who initially presented with recurrent ischemic strokes. This complication was the consequence of the late diagnosis and delayed adequate treatment for the primary cardiac tumor.

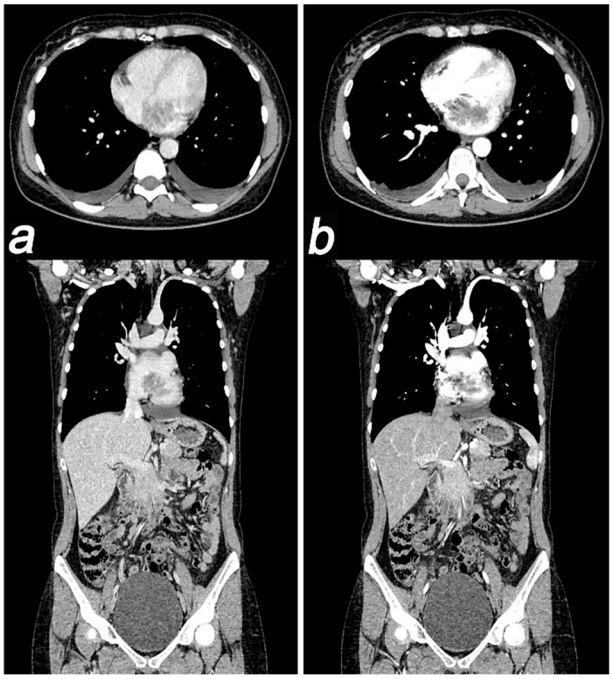

Figure 3 – *(a and b) Thoracoabdominal–pelvic CT scan showed a tumoral mass in the left atrium with minimal enhancement after contrast administration, splenic lesion suggestive of splenic infarction. CT: Computed tomography.*

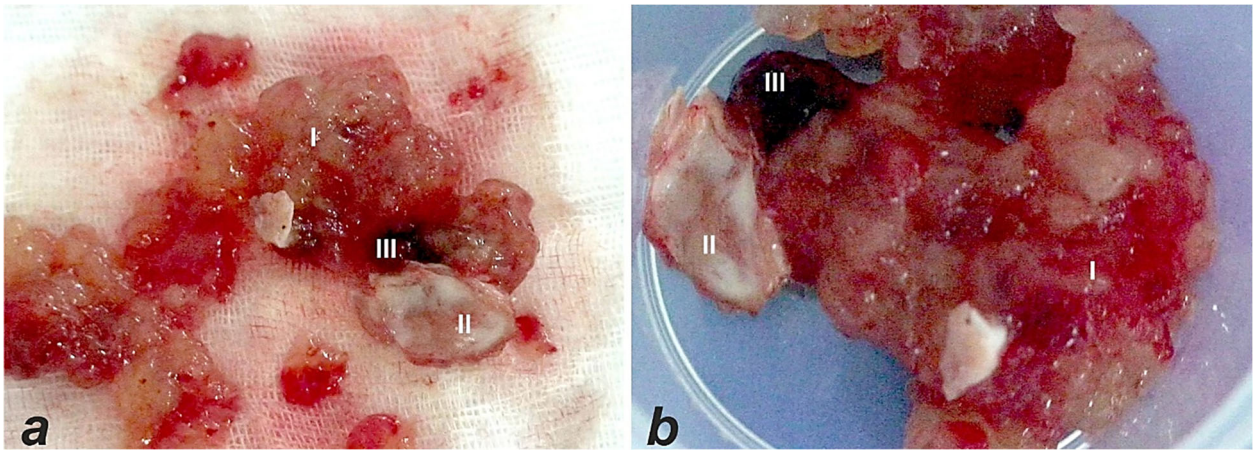

Figure 4 – *(a and b) Macroscopic aspect of the tumoral mass: gelatinous and polylobulated aspect of the myxoma (I); the tumoral mass is pediculated, with origin at the level of the interatrial septum – fragment resected from the interatrial septum (II); the presence of isolated secondary thrombi (III) on the tumor surface.*

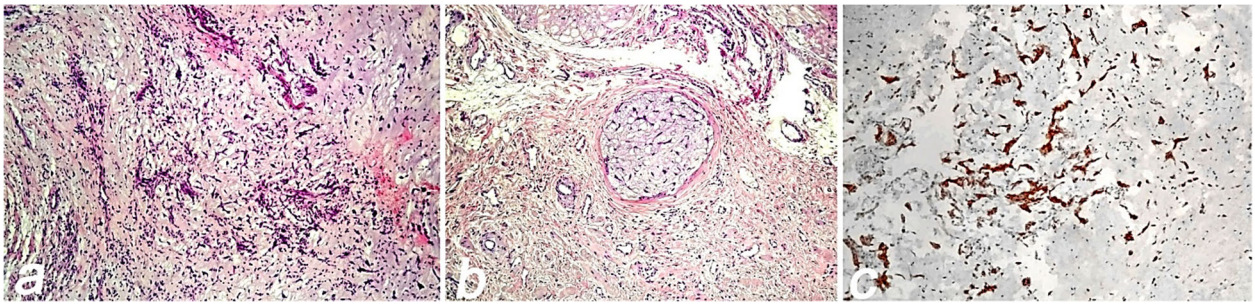

Figure 5 – ***(a) Defining cellular characteristics are observed. Predominantly hypocellular areas with rare hypercellular foci composed of bland, stellate, ovoid or plump spindle myxoma cells, showing no mitotic activity with variable numbers of inflammatory cells in the background. Cells are embedded in a slightly basophilic matrix; occasional blood vessels with focal hemorrhage are also seen. (b) Larger, thick-walled vessels are regularly seen at the implantation site (or base) of the lesion, occasionally with tumor emboli such as the one depicted in the microphotograph. (c) Myxoma cells (also called lepidic cells) are marked with anti-calretinin antibodies; somewhat more cellular areas are observed here. HE staining: (a and b) ×100. DAB chromogen, immunohistochemical staining: (c) ×200. DAB: 3,3'-Diaminobenzidine; HE: Hematoxylin–Eosin.***

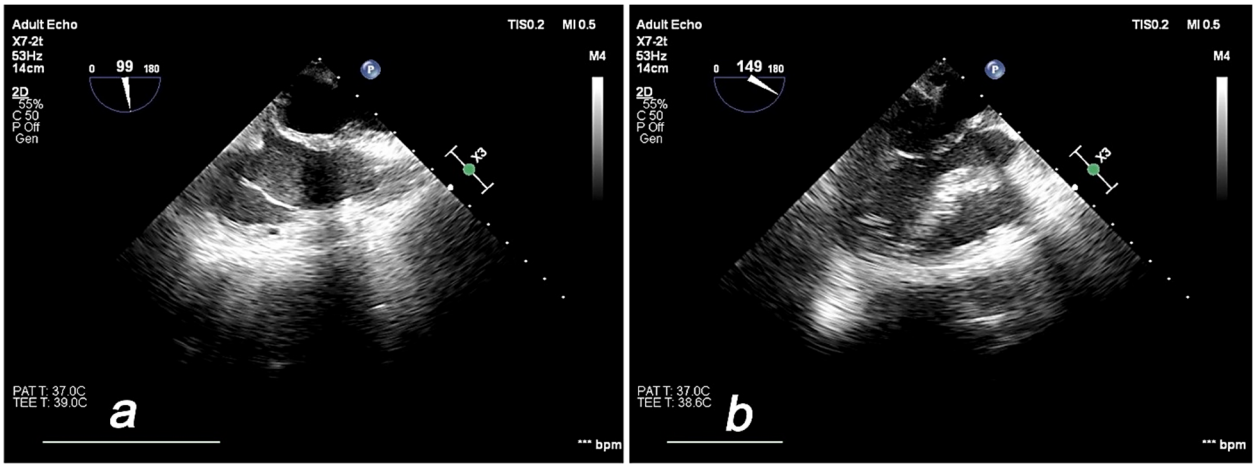

Figure 6 – ***(a and b) Postsurgical 2D transthoracic echocardiography showed the absence of the tumoral mass, no shunt at the site of the interatrial septum and a competent mitral valve. 2D: Two-dimensional.***

Neurological manifestations appear in up to 45% of patients with cardiac myxomas, and in most cases they are represented by cardioembolic ischemic strokes. In rare cases, the presence of intracranial hemorrhage has been associated with atrial myxomas, secondary to the migration of tumoral fragments which, after embolization, nest at the site of the small cerebral vessels and lead to endothelial destruction or, by infiltrating the blood vessel wall, are involved in the genesis of aneurysms or pseudo-aneurysms [47, 48]. The embolic events are the consequence of tumoral tissue detachments from the cardiac myxoma or formation of thrombi at the surface of the tissue mass [49, 50]. Apart from the peripheral and central embolic complications that appear in 50–70% of patients, cardiac myxomas may manifest through constitutional symptoms, such as weight loss, fever, asthenia, or arthralgia, and these symptoms have been described in more than half of the cases. Most frequently, the symptoms that suggest the possibility of a myxoma diagnosis are secondary to those of intracardiac obstruction (vertigo, palpitations, dyspnea, and cardiac insufficiency), which appear in up to 70% of patients. In less than 10% of cases, atrial myxomas are diagnosed incidentally and are asymptomatic [1, 4, 50–52]. In our case, the constitutional and intracardiac obstruction symptoms were absent, with our patient having only central and peripheral embolic manifestations (cerebral ischemic stroke and splenic infarction).

The COVID-19 pandemic caused immense dysfunction in the medico-sanitary system. A significant delay between the first symptom and the diagnosis was unfortunately noted: seven months from the first transient ischemic attack to the diagnosis of atrial myxoma, a timeline in which, regrettably, our patient experienced three more cerebrovascular events with significant secondary motor deficits. Although the incidence of cardiac myxomas is low, this case highlights the importance of a full workup protocol for ischemic stroke, including routine transthoracic echocardiography in ischemic stroke patients, especially in those with no traditional cardiovascular risk factors. Early diagnosis is facilitated by non-invasive, easily accessible transthoracic echocardiography with high sensitivity (95%) for the detection of cardiac myxomas. Rapid, adequate surgical treatment prevents further complications from an embolic or a cardiac origin, such as sudden death secondary to a valvular obstruction [44, 52–54].

In the literature, data are scarce and contradictory regarding the ideal timing for surgical excision of an atrial myxoma diagnosed after an ischemic stroke. In the absence of clear guidelines, some authors opted for early, emergency surgical intervention, which is the only therapeutic option that can prevent recurrence of cerebrovascular events. However, surgical intervention to remove an atrial myxoma requires open-heart surgery, cardiopulmonary bypass, and

systemic anticoagulation, which significantly increase the risk of a brain hemorrhagic transformation in the case of acute stroke patients [51, 55–59]. Considering that our patient was hemodynamically stable and had no cardiac symptoms, and the risk of hemorrhagic transformation was considerable, we opted to delay the surgical intervention two weeks after the event, time in which the patient underwent low-molecular-weight Heparin treatment and was restricted to bed. The anticoagulant treatment, which is the medical option endorsed by some authors to delay the tumoral excision, prevents the migration of the thrombo-embolic fragments but has no therapeutic effects upon the tumoral emboli [46, 56, 60].

Conclusions

Although cardiac myxomas represent a rare cause of transient ischemic attacks and stroke, they must be considered as part of the assessment protocol for cerebrovascular events. A transthoracic 2D echocardiogram is a mandatory investigation for this category of patients, especially when traditional risk factors such as hypertension and atrial fibrillation are absent. In our case, a young and apparently healthy woman presented with four consequent cerebrovascular events due to a delay in diagnostic protocol caused by the COVID-19 pandemic. Considering the size of the intracardiac tissue mass, prolonging the delay in diagnosis could have been fatal, as in cases of sudden death secondary to valvular obstruction.

Conflict of interests

The authors declare that they have no conflict of interests.

References

[1] Pérez Andreu J, Parrilla G, Arribas JM, García-Villalba B, Lucas JJ, Garcia Navarro M, Marín F, Gutierrez F, Moreno A. Neurological manifestations of cardiac myxoma: experience in a referral hospital. Neurologia, 2013, 28(9):529–534. https://doi.org/10.1016/j.nrl.2013.03.006 PMID: 23751554

[2] Yu K, Liu Y, Wang H, Hu S, Long C. Epidemiological and pathological characteristics of cardiac tumors: a clinical study of 242 cases. Interact Cardiovasc Thorac Surg, 2007, 6(5): 636–639. https://doi.org/10.1510/icvts.2007.156554 PMID: 17670730

[3] Thompson J, Kapoor W, Wechsler LR. Multiple strokes due to atrial myxoma with a negative echocardiogram. Stroke, 1988, 19(12):1570–1571. https://doi.org/10.1161/01.str.19.12.1570 PMID: 3201518

[4] Velez Torres JM, Martinez Duarte E, Diaz-Perez JA, Rosenberg AE. Cardiac myxoma: review and update of contemporary immunohistochemical markers and molecular pathology. Adv Anat Pathol, 2020, 27(6):380–384. https://doi.org/10.1097/PAP.0000000000000275 PMID: 32732585

[5] Garatti A, Nano G, Canziani A, Gagliardotto P, Mossuto E, Frigiola A, Menicanti L. Surgical excision of cardiac myxomas: twenty years experience at a single institution. Ann Thorac Surg, 2012, 93(3):825–831. https://doi.org/10.1016/j.athoracsur.2011.11.009 PMID: 22296980

[6] Roschkov S, Rebeyka D, Mah J, Urquhart G. The dangers of cardiac myxomas. Prog Cardiovasc Nurs, 2007, 22(1): 27–30. https://doi.org/10.1111/j.0889-7204.2007.05884.x PMID: 17342003

[7] Uner A, Dogan M, Sal E, Peker E. Stroke and recurrent peripheral embolism in left atrial myxoma. Acta Cardiol, 2010, 65(1):101–103. https://doi.org/10.2143/AC.65.1.2045899 PMID: 20306900

[8] Vahedi K, Amarenco P. Cardiac causes of stroke. Curr Treat Options Neurol, 2000, 2(4):305–318. https://doi.org/10.1007/s11940-000-0048-4 PMID: 11096756

[9] Bjessmo S, Ivert T. Cardiac myxoma: 40 years' experience in 63 patients. Ann Thorac Surg, 1997, 63(3):697–700. https://doi.org/10.1016/s0003-4975(96)01368-9 PMID: 9066386

[10] MacGowan SW, Sidhu P, Aherne T, Luke D, Wood AE, Neligan MC, McGovern E. Atrial myxoma: national incidence, diagnosis and surgical management. Ir J Med Sci, 1993, 162(6):223–226. https://doi.org/10.1007/BF02945200 PMID: 8407260

[11] Li H, Guo H, Xiong H, Xu J, Wang W, Hu S. Clinical features and surgical results of right atrial myxoma. J Card Surg, 2016, 31(1):15–17. https://doi.org/10.1111/jocs.12663 PMID: 26585438

[12] Castells E, Ferran V, Octavio de Toledo MC, Calbet JM, Benito M, Fontanillas C, Granados J, Obi CL, Saura E. Cardiac myxomas: surgical treatment, long-term results and recurrence. J Cardiovasc Surg (Torino), 1993, 34(1):49–53. PMID: 8482704

[13] Goswami KC, Shrivastava S, Bahl VK, Saxena A, Manchanda SC, Wasir HS. Cardiac myxomas: clinical and echocardiographic profile. Int J Cardiol, 1998, 63(3):251–259. https://doi.org/10.1016/s0167-5273(97)00316-1 PMID: 9578352

[14] Carney JA, Gordon H, Carpenter PC, Shenoy BV, Go VL. The complex of myxomas, spotty pigmentation, and endocrine overactivity. Medicine (Baltimore), 1985, 64(4):270–283. https://doi.org/10.1097/00005792-198507000-00007 PMID: 4010501

[15] Deshpande A, Kumar S, Chopra P. Recurrent, biatrial, familial cardiac myxomas. Int J Cardiol, 1994, 47(1):71–73. https://doi.org/10.1016/0167-5273(94)90136-8 PMID: 7868289

[16] Pucci A, Gagliardotto P, Zanini C, Pansini S, di Summa M, Mollo F. Histopathologic and clinical characterization of cardiac myxoma: review of 53 cases from a single institution. Am Heart J, 2000, 140(1):134–138. https://doi.org/10.1067/mhj.2000.107176 PMID: 10874274

[17] Swartz MF, Lutz CJ, Chandan VS, Landas S, Fink GW. Atrial myxomas: pathologic types, tumor location, and presenting symptoms. J Card Surg, 2006, 21(4):435–440. https://doi.org/10.1111/j.1540-8191.2006.00265.x PMID: 16846432

[18] Kolluru A, Desai D, Cohen GI. The etiology of atrial myxoma tumor plop. J Am Coll Cardiol, 2011, 57(21):e371. https://doi.org/10.1016/j.jacc.2010.09.085 PMID: 21596227

[19] Seol SH, Kim DI, Jang JS, Yang TH, Kim DK, Kim DS. Left atrial myxoma presenting as paroxysmal supraventricular tachycardia. Heart Lung Circ, 2014, 23(2):e65–e66. https://doi.org/10.1016/j.hlc.2013.05.641 PMID: 23891308

[20] Ma G, Wang D, He Y, Zhang R, Zhou Y, Ying K. Pulmonary embolism as the initial manifestation of right atrial myxoma: a case report and review of the literature. Medicine (Baltimore), 2019, 98(51):e18386. https://doi.org/10.1097/MD.0000000000018386 PMID: 31861001 PMCID: PMC6940114

[21] Wang Z, Chen S, Zhu M, Zhang W, Zhang H, Li H, Yuan G, Zou C. Risk prediction for emboli and recurrence of primary cardiac myxomas after resection. J Cardiothorac Surg, 2016, 11:22. https://doi.org/10.1186/s13019-016-0420-4 PMID: 26832806 PMCID: PMC4736655

[22] Shetty Roy AN, Radin M, Sarabi D, Shaoulian E. Familial recurrent atrial myxoma: Carney's complex. Clin Cardiol, 2011, 34(2):83–86. https://doi.org/10.1002/clc.20845 PMID: 21298650 PMCID: PMC6652706

[23] Engberding R, Daniel WG, Erbel R, Kasper W, Lestuzzi C, Curtius JM, Sutherland GR, Lambertz H, von Hehn A, Lesbre JP, Bogunovic N, Biasi S, Caruso A, Lengyel M, Iliceto S; The European Cooperative Study Group. Diagnosis of heart tumours by transoesophageal echocardiography: a multicentre study in 154 patients. Eur Heart J, 1993, 14(9):1223–1228. https://doi.org/10.1093/eurheartj/14.9.1223 PMID: 8223737

[24] Reddy DB, Jena A, Venugopal P. Magnetic resonance imaging (MRI) in evaluation of left atrial masses: an *in vitro* and *in vivo* study. J Cardiovasc Surg (Torino), 1994, 35(4):289–294. PMID: 7929538

[25] Reynen K, Köckeritz U. Right atrial myxoma. Clin Res Cardiol, 2006, 95(1):3. https://doi.org/10.1007/s00392-006-0318-6 PMID: 16598439

[26] Schattenberg TT. Echocardiographic diagnosis of left atrial myxoma. Mayo Clin Proc, 1968, 43(9):620–627. PMID: 5710588

[27] Teodoru CA, Preda MA, Borugă VM, Şuţă MC, Dărăbuş DM, Toth AE, Al Barri L, Cornea RF, Grigorescu AE, Bonţe DC, Stanca S, Feier HB. Giant and multiple cardiac papillary fibroelastomas masquerading as acute cerebrovascular events. Rom J Morphol Embryol, 2020, 61(3):947–951. https://doi.org/10.47162/RJME.61.3.36 PMID: 33817739 PMCID: PMC8112784

[28] Mahmoud H, Nicolescu AM, Filip C, Nicolae G, Duică G, Bălgrădean M, Cinteză EE. Complex atrial septal defect closure in children. Rom J Morphol Embryol, 2019, 60(1):49–57. PMID: 31263827

[29] Ţieranu EN, Donoiu I, Istrătoaie O, Găman AE, Ţieranu ML, Ţieranu CG, Gheonea DI, Ciurea T. Rare case of single coronary artery in a patient with liver cirrhosis. Rom J Morphol Embryol, 2017, 58(4):1505–1508. PMID: 29556648
[30] Lee VH, Connolly HM, Brown RD Jr. Central nervous system manifestations of cardiac myxoma. Arch Neurol, 2007, 64(8): 1115–1120. https://doi.org/10.1001/archneur.64.8.1115 PMID: 17698701
[31] Kawabata T, Kasahara S, Ohtsuki S, Kuroko Y, Kotani Y, Fujii Y, Yoshizumi K, Arai S, Sano S. Left ventricular myxoma occluding the suprarenal abdominal aorta in an infant. Ann Thorac Surg, 2015, 100(1):309–311. https://doi.org/10.1016/j.athoracsur.2014.08.066 PMID: 26140776
[32] He DK, Zhang YF, Liang Y, Ye SX, Wang C, Kang B, Wang ZN. Risk factors for embolism in cardiac myxoma: a retrospective analysis. Med Sci Monit, 2015, 21:1146–1154. https://doi.org/10.12659/MSM.893855 PMID: 25900256 PMCID: PMC4418206
[33] Bulkley BH, Hutchins GM. Atrial myxomas: a fifty year review. Am Heart J, 1979, 97(5):639–643. https://doi.org/10.1016/0002-8703(79)90193-5 PMID: 433739
[34] Tsang FHF, Cheng LC. Giant myxoma causing right ventricular outflow tract obstruction. Hong Kong Med J, 2011, 17(3):242–244. PMID: 21636873
[35] Chitwood WR Jr. Clarence Crafoord and the first successful resection of a cardiac myxoma. Ann Thorac Surg, 1992, 54(5): 997–998. https://doi.org/10.1016/0003-4975(92)90676-u PMID: 1417305
[36] Hill M, Cherry C, Maloney M, Midyette P. Surgical resection of atrial myxomas. AORN J, 2010, 92(4):393–406, quiz 407–409. https://doi.org/10.1016/j.aorn.2010.06.012 PMID: 20888942
[37] Gür AK, Aykaç MC. Surgical treatment of cardiac myxomas: a 23-case experience. Heart Surg Forum, 2018, 21(5):E370–E374. https://doi.org/10.1532/hsf.1987 PMID: 30311887
[38] McCarthy PM, Piehler JM, Schaff HV, Pluth JR, Orszulak TA, Vidaillet HJ Jr, Carney JA. The significance of multiple, recurrent, and "complex" cardiac myxomas. J Thorac Cardiovasc Surg, 1986, 91(3):389–396. PMID: 3951243
[39] Waller DA, Ettles DF, Saunders NR, Williams G. Recurrent cardiac myxoma: the surgical implications of two distinct groups of patients. Thorac Cardiovasc Surg, 1989, 37(4):226–230. https://doi.org/10.1055/s-2007-1020322 PMID: 2799794
[40] Kouchoukos NT, Kirklin JW. Kirklin/Barratt-Boyes cardiac surgery: morphology, diagnostic criteria, natural history, techniques, results, and indications. 4th edition, Elsevier/Saunders, Philadelphia, USA, 2013. https://www.worldcat.org/title/kirklinbarratt-boyes-cardiac-surgery-morphology-diagnostic-criteria-natural-history-techniques-results-and-indications/oclc/778040134
[41] Chamberlin SW, Carter JR, Richardson RL. Intraoperative coronary-artery embolization from left atrial myxoma. Anesthesiology, 1977, 47(3):301–302. https://doi.org/10.1097/00000542-197709000-00014 PMID: 889119
[42] Bortolotti U, Mazzucco A, Valfré C, Valente M, Pennelli N, Gallucci V. Right ventricular myxoma: review of the literature and report of two patients. Ann Thorac Surg, 1982, 33(3): 277–284. https://doi.org/10.1016/s0003-4975(10)61926-1 PMID: 7073369
[43] Boulafendis D, Heine J, Samaan HA. Right ventricular myxoma. Int J Cardiol, 1984, 5(2):216–219. https://doi.org/10.1016/0167-5273(84)90150-5 PMID: 6698647
[44] Gray IR, Williams WG. Recurring cardiac myxoma. Br Heart J, 1985, 53(6):645–649. https://doi.org/10.1136/hrt.53.6.645 PMID: 4005088 PMCID: PMC481829
[45] Lin Y, Xiao J, Chen J, Hong J, Peng H, Kang B, Wu L, Wang Z. Treating cardiac myxomas: a 16-year Chinese single-center study. J Cardiovasc Med (Hagerstown), 2016, 17(1):44–53. https://doi.org/10.2459/JCM.0000000000000114 PMID: 24933197
[46] Schaff HV, Mullany CJ. Surgery for cardiac myxomas. Semin Thorac Cardiovasc Surg, 2000, 12(2):77–88. https://doi.org/10.1053/ct.2000.5079 PMID: 10807430
[47] Ekinci EI, Donnan GA. Neurological manifestations of cardiac myxoma: a review of the literature and report of cases. Intern Med J, 2004, 34(5):243–249. https://doi.org/10.1111/j.1444-0903.2004.00563.x PMID: 15151670
[48] Burton C, Johnston J. Multiple cerebral aneurysms and cardiac myxoma. N Engl J Med, 1970, 282(1):35–36. https://doi.org/10.1056/NEJM197001012820109 PMID: 5409468
[49] Damásio H, Seabra-Gomes R, da Silva JP, Damásio AR, Antunes JL. Multiple cerebral aneurysms and cardiac myxoma. Arch Neurol, 1975, 32(4):269–270. https://doi.org/10.1001/archneur.1975.00490460085013 PMID: 1124989
[50] Knepper LE, Biller J, Adams HP Jr, Bruno A. Neurologic manifestations of atrial myxoma. A 12-year experience and review. Stroke, 1988, 19(11):1435–1440. https://doi.org/10.1161/01.str.19.11.1435 PMID: 3188128
[51] Pinede L, Duhaut P, Loire R. Clinical presentation of left atrial cardiac myxoma. A series of 112 consecutive cases. Medicine (Baltimore), 2001, 80(3):159–172. https://doi.org/10.1097/00005792-200105000-00002 PMID: 11388092
[52] Tetsuka S, Ikeguchi K. Prevention of cerebral embolism progression by emergency surgery of the left atrial myxoma. Case Rep Med, 2015, 2015:151802. https://doi.org/10.1155/2015/151802 PMID: 25954312 PMCID: PMC4411460
[53] Obrenović-Kirćanski B, Mikić A, Parapid B, Djukić P, Kanjuh V, Milić N, Kovačević-Kostić N, Velinović M, Seferović P, Vraneš M. A 30-year-single-center experience in atrial myxomas: from presentation to treatment and prognosis. Thorac Cardiovasc Surg, 2013, 61(6):530–536. https://doi.org/10.1055/s-0032-1322545 PMID: 22865091
[54] Stefanou MI, Rath D, Stadler V, Richter H, Hennersdorf F, Lausberg HF, Lescan M, Greulich S, Poli S, Gawaz MP, Ziemann U, Mengel AM. Cardiac myxoma and cerebrovascular events: a retrospective cohort study. Front Neurol, 2018, 9:823. https://doi.org/10.3389/fneur.2018.00823 PMID: 30337904 PMCID: PMC6178925
[55] Zisbrod Z, Rose DM, Jacobowitz IJ, Kramer M, Acinapura AJ, Cunningham JN Jr. Results of open heart surgery in patients with recent cardiogenic embolic stroke and central nervous system dysfunction. Circulation, 1987, 76(5 Pt 2):V109–V112. PMID: 3665007
[56] Vogel B, Thomas D, Mereles D, Rottbauer W, Katus HA. Systemic embolization and myocardial infarction due to clinically unrecognized left atrial myxoma. Case Rep Med, 2011, 2011: 159024. https://doi.org/10.1155/2011/159024 PMID: 22203848 PMCID: PMC3235785
[57] da Silva IRF, de Freitas GR. Is it safe to proceed with thrombolytic therapy for acute ischemic stroke in a patient with cardiac myxoma? Case report and review of the literature. Eur Neurol, 2012, 68(3):185–186. https://doi.org/10.1159/000340019 PMID: 22922212
[58] Sethi NK. Is it safe to proceed with thrombolytic therapy for acute ischemic stroke in a patient with cardiac myxoma? Eur Neurol, 2013, 69(2):67. https://doi.org/10.1159/000345117 PMID: 23154305
[59] Al-Said Y, Al-Rached H, Baeesa S, Kurdi K, Zabani I, Hassan A. Emergency excision of cardiac myxoma and endovascular coiling of intracranial aneurysm after cerebral infarction. Case Rep Neurol Med, 2013, 2013:839270. https://doi.org/10.1155/2013/839270 PMID: 24109531 PMCID: PMC3787621
[60] Florescu C, Mustafa ER, Târtea EA, Florescu DR, Albu VC. Antiplatelet therapy in secondary ischemic stroke prevention – a short review. Rom J Morphol Embryol, 2019, 60(2):383–387. PMID: 31658310

Corresponding author
Andrei Dan Raicea, MD, Resident Physician for Cardiovascular Surgery, Clinic of Cardiovascular Surgery, Emergency Institute for Cardiovascular Diseases and Transplant, 50 Gheorghe Marinescu Street, 540136 Târgu Mureş, Mureş County, Romania; Phone +40758–552418, e-mail: raicea_andrei@yahoo.com

Received: May 25, 2021 *Accepted: December 20, 2021*