CASE REPORT

Embryonal rhabdomyosarcoma of cardiac origin: case report

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Rhabdomyosarcoma is considered a mesenchymal neoplasm. Due to its infrequency, there is no precise and protocolized treatment standard at national and worldwide level. We present the case of a young patient with symptoms of progressive deterioration of functional class, dyspnea associated with physical activity, orthopnea and paroxysmal nocturnal dyspnea, is protocolized by suspicion of myxoma versus intracardiac thrombus by echocardiography. Subsequently, it was diagnosed as embryonal rhabdomyosarcoma with histological studies obtained after tumor excision.

Key words: Cardiac malignancy; Embryonal rhabdomyosarcoma; Left atrial tumor; Myxoma.

El rabdomiosarcoma se considera una neoplasia mesenquimal. Por su poca frecuencia, no existe un estándar de tratamiento preciso y protocolizado a nivel nacional y mundial. Presentamos el caso de un paciente joven, con síntomas de deterioro progresivo de la clase funcional, disnea asociada a actividad física, ortopnea y disnea paroxística nocturna, se protocolizó por sospecha de mixoma versus trombo intracardiaco por ecocardiografía. Posteriormente, se diagnosticó como rabdomiosarcoma embrionario con la histología obtenida tras la exéresis tumoral.

Palabras clave: Neoplasia maligna cardiaca; Rabdomiosarcoma embrionario; Tumor de aurícula izquierda; Mixoma.

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Primary cardiac tumors have a reported incidence of 0.0017% to 0.019%. Benign tumors at the cardiac level are common, in order of frequency are rhabdomyoma, fibroma, myxoma, teratoma, hemangioma and others [1]. Malignant primary cardiac tumors are infrequent. Among the sarcomas previously published are angiosarcoma, undifferentiated pleomorphic sarcomas and rhabdomyosarcoma. Usually with asymptomatic course, until they are advanced and produce non-specific symptoms [2].

The description of cases in the literature of primary cardiac neoplasms is not recent. In 1559 and 1835, Colomnus and Alberts, respectively, made descriptions of this type of post-mortem neoplasms. In 1902, Von Recklinhausen described a rhabdomyoma (being the first report of a primary cardiac neoplasm with muscular differentiation). In 1931, Yates reported for the first time some cases of cardiac myxomas [3]. Barnes reported the first primary sarcoma of the heart in 1934. In 1951, Prichard postulated the impossibility of its surgical treatment and claimed that its pre-mortem diagnosis was coincidental [4]. The first in vivo diagnosis was made using angiography in 1952 by Goldberg, with Crawford being the first to perform a successful resection of an atrial myxoma in 1955 [5].

Subsequently, occasional cases of primary cardiac neoplasms have been reported, with series reporting benign tumors (72%) led by myxoma, followed by rhabdomyoma, fibroma, papillary fibroelastoma, solitary fibrous tumor, and lipoma [6]. Malignancies constitute 28%, and are headed by angiosarcoma, followed by rhabdomyosarcoma, malignant mesothelioma, fibrosarcoma, lymphoma, leiomyosarcoma, liposarcoma, and osteosarcoma [7].

Malignant primitive cardiac tumors have some general characteristics that distinguish them from benign ones [8]. Namely, a) they usually settle in the right cardiac chambers, mostly in the right atrium, and from here invade other cardiac structures; b) they have a variable configuration and shape, but mostly polypoid, infiltrative or intracavitary; c) most common presentation in the third, fourth or fifth decades of life; d) Male gender is the most affected; e) rapid, infiltrative or invasive growth in mediastinal and thoracic structures; f) they have a great tendency to produce distant metastases, especially in the lung, kidney, liver, adrenal glands and bone; g) clinically, they cause varied symptomatology, from

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the presence of chest pain, dyspnea, palpitations, syncope, atrial or ventricular arrhythmias and atrioventricular block, to causing constrictive pericarditis due to tumor infiltration and very characteristically, hematic pericardial effusion or cardiac tamponade, and also can manifest with heart failure, peripheral or pulmonary tumor embolization and nonspecific constitutional syndrome; h) Diagnosis and typing of the type of tumor can only be confirmed by extensive biopsy of the tumor mass, electrocardiogram may show ST-segment elevation in neoplasms with myocardial infiltration or atrioventricular block if there is invasion of the conduction tissue, cardiomegaly, changes in the cardiac silhouette, widened mediastinum or signs of pericardial effusion can be observed in the simple chest X-ray; i) echocardiography, especially 2D echocardiography and transesophageal echocardiography adequately detect intramural and intracavitary tumors, and thoracic CT scan and MRI provide information on the degree of extension or invasion into the mediastinum.

Speaking of the clinical case herein, rhabdomyosarcoma is a malignant neoplasm composed of striated muscle cells [9], previously referred to as rhabdomyoblastoma, myosarcoma and malignant rhabdomyoma, which derives from the mesenchyme of the mesodermal splanchnic sheets that originate the angiogenic cumulus [10]. It has a low incidence ranging between 0.002% to 0.3%. It is the most common primary cardiac neoplasm in children and adolescents (75% of cardiac sarcomas in children under one year of age); its presentation in adulthood is very rare. It is more common in males [11]; therefore, the present case in an adult female with pre-mortem diagnosis, is extremely unusual.

Unlike other primary cardiac neoplasms, rhabdomyosarcomas do not have a predilection for one location and involve multiple locations in the heart (60%) [12]. This causes half of the patients to present obstruction of at least one valve, although pericardial involvement is also frequent (50%) [13]. Most of the tumor is intraparietal, but it can protrude outwards or intracavitary invading the cardiac valves, atrial and ventricular cavities. It is characterized by rapid growth and involves both cardiac sides and adjacent structures, producing multiple tumors with hematogenous or continuity spread [14].

Rhabdomyosarcoma generally produces nonspecific clinical symptoms (fever, anorexia, weight loss and dyspnea), or it may also offer no symptoms until metastases are present; or until its rapid growth compromises pericardial structures causing effusion and consequently cardiac tamponade [15]. The most specific symptoms are repeated syncope, secondary to valvular compromise and the sensation of palpitations due to compromise of cardiac conduction, although cases of sudden death have also been reported [16].

In general, clinical manifestations can vary in 4 mechanisms: obstruction of flow by interference in the functioning of a valve, local invasion causing arrhythmias or pericardial effusion with tamponade (presenting in up to 29%), thromboembolic phenomena and the spectrum of dyspnea, syncope, chest pain, fever and malaise [17].

In the diagnostic approach, the electrocardiogram is usually normal except for possible arrhythmias. Chest radiography does not show important data unless pulmonary metastases develop. Echocardiography is the method of choice for the initial diagnosis of intracardiac tumors because it provides relevant data on their location, extent and density [18]. Initiating the approach with transthoracic cardiac ultrasound is of great utility when related to general symptoms such as dyspnea, syncope and arrhythmias or when performed during a routine study. When an intracardiac tumor is found, the differential diagnosis should be made with thrombi, vegetation, benign and malignant tumors. Generally, the most mistaken diagnosis is the differentiation between sarcoma and myxoma, the latter generally located in the interatrial septum, pedunculated and projecting towards the left atrium, as in the case of our patient, while rhabdomyosarcoma is more commonly found in the ventricles [19].

As for diagnostic tools, transesophageal echo is very useful in the examination of atrial tumors, and gives more detailed information about the size, mobility and presence of satellite lesions within the heart. 3D ultrasound provides more precise information on the site and dimensions of the tumor, as well as its relationship with neighboring structures. CT allows the evaluation of small tumors and other intrathoracic tumors. Magnetic resonance imaging is very useful for differentiating between thrombi and tumors and can be helpful in discriminating between malignant and benign tumors. PET scanning provides additional information on the metabolic activity of the tumor [20].

Rhabdomyosarcomas are usually extensive neoplasms involving a large part of the heart, nodular in shape, soft, with central necrosis. In histopathology, two forms of presentation are differentiated, a juvenile (embryonal or alveolar) and an adult. The finding of rhabdomyoblasts is fundamental for the diagnosis [21].

Rhabdomyosarcoma presents great histologic variability, with pleomorphism and anaplasia. Within the same tumor there may be myxoid, spindle cell and solid areas; areas of necrosis and hemorrhage may also be observed. The nuclei are frequently large and vesicular in shape. Giant cells may be observed, with presence of abnormal mitoses. Rhabdomyoblasts can adopt different morphologies: tadpole shape, racquet shape with eccentric nucleus, rounded shape with one nucleus and abundant cytoplasm, giant cell shape with multiple nuclei and abundant cytoplasm, and spider web shape with peripheral vacuoles [9].

The cytoplasm of rhabdomyoblasts is eosinophilic and granular, with transverse striations detected at high magnification (indicating striated muscle differentiation). These striations are identified by light microscopy in only 20% to 30%, but under electron microscopy they can be seen in up to 90% of cases [22].

Immunohistochemistry with positivity for specific muscle actin, desmin, and myoglobin should be used for certainty diagnosis. Poorly differentiated rhabdomyoblasts can be detected with HHF35 or myogenin, also these lesions show histochemical reactivity for PAS with diastase [23].

The prognosis of cardiac sarcomas is dismal due to the advanced stage of the tumor at diagnosis, nonspecific symptomatology and low suspicion, all of which results in delayed diagnosis. The organs most frequently involved by metastases are the lungs, kidneys, liver, supra-adrenal glands and bones [10].

Regarding the treatment of sarcomas, the established standard, when there is no metastatic disease is wide resection with margins of at least 1 cm, classifying it as R0 if there are tumor-free margins, R1 if there is microscopic invasion of the margins, and R2 if there is residual tumor at the margins. Improved survival has not been proven with adjuvant chemotherapy, but it may improve the disease-free period and its use should be considered especially in incomplete resections. When dealing with metastatic disease, neoadjuvant chemotherapy is mandatory, as well as in large or unresectable tumors. The most commonly used scheme is IFO (Ifosfamide) and ANTHRA (Doxorubicin and Epidoxorubicin). The prognosis of sarcomas is poor in the long term, with very low survival at 5 years. The most important prognostic factor is to achieve R0 surgery [20].

Regarding the surgical technique for tumor exeresis, simple tumor resection can be performed in the case of benign tumors such as myxomas, resecting from the root of the septum; however, in complex tumors of the right heart, the right half of the organ can be resected, ensuring pulmonary blood flow through the Fontan circulation. In the event that the tumor involves the posterior wall of the left atrium or the dorsal great vessels, ex situ resection can be performed, removing the heart for a more complete resection and reimplanting it at the end of the resection. Finally, cardiac transplantation can be considered as a treatment option in individualized cases in which metastatic disease has been excluded [24].

Surgical resection of tumors when they are small is possible; however, this tumor presents great aggressiveness, with a high frequency of local and distant metastases at the time of diagnosis, which makes this therapeutic strategy little used and, in many cases, palliative strategies are chosen for the treatment of these tumors [25]. Furthermore, these patients have poor response to treatment with chemotherapy and radiotherapy thus limiting their survival, in many cases, to less than 12 months, with no reported case of survival greater than five years. Recently some reports have proposed cardiac transplantation as an alternative for the treatment of these neoplasms [26].

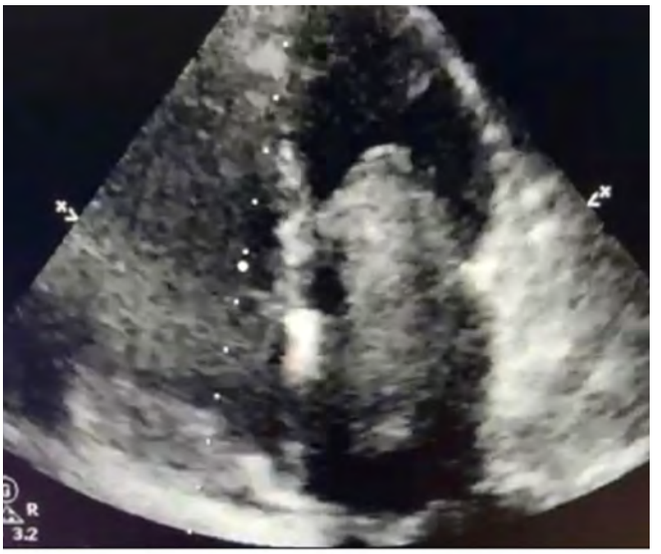

Figure 1. Echocardiogram four chamber projection of rhabdomyosarcoma. A tumor is observed in the left atrium, with a wide implantation base, prolapsing to the left ventricle and causing severe mitral stenosis.

CLINICAL CASE

A 30-year-old female patient, who one month prior to admission presented progressive deterioration of functional class, adding dyspnea associated with physical activity up to NYHA II, orthopnea and paroxysmal nocturnal dyspnea, with treatment in a private home for lower respiratory tract infection with partial improvement, but persistence of symptoms and progression to dyspnea at rest. She was admitted at emergency room in our institution with hemodynamic instability, respiratory failure and acute pulmonary edema requiring advanced airway management and vasopressor support. With high suspicion of pulmonary embolism, angiotomography was performed without identifying apparent alterations, calling attention to incidental finding of a tumor in the left atrium. Subsequently, clinical deterioration progressed to asystole on the monitor, requiring cardiopulmonary resuscitation maneuvers, with successful recovery.

Transthoracic echocardiogram showed a non-dilated left ventricle, with a left ventricular ejection fraction of 60%, with dilated left atrium and image suggestive of thrombus adhered to interatrial septum, mobile characteristics, non-vascularized, homogeneous content, with defined borders of 67x36 mm, prolapsing to the left ventricle, conditioning transmitral acceleration gradient G maximum 30 mmHg, mean G 19 mmHg by lateral wall and mild-moderate mitral regurgitation eccentric jet. Right cavities were not dilated, TAPSE 19, S wave 10, moderate tricuspid regurgitation, PSAP 72 mmHg, with high probability of pulmonary hypertension and moderate tricuspid regurgitation (**Fig.1**).

Low output data and shock state persisted, requiring admission to coronary intensive care unit for cardiogenic shock, requiring double vasopressor and inotropic, with persistent

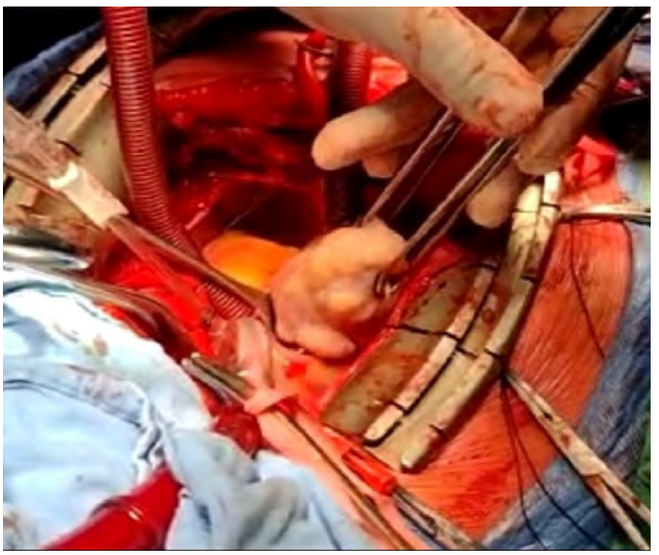

Figure 2. Surgical excision of the tumor and edges of the interatrial septum, showung a pedunculated base of approximately 1 cm, adherent to interatrial septum.

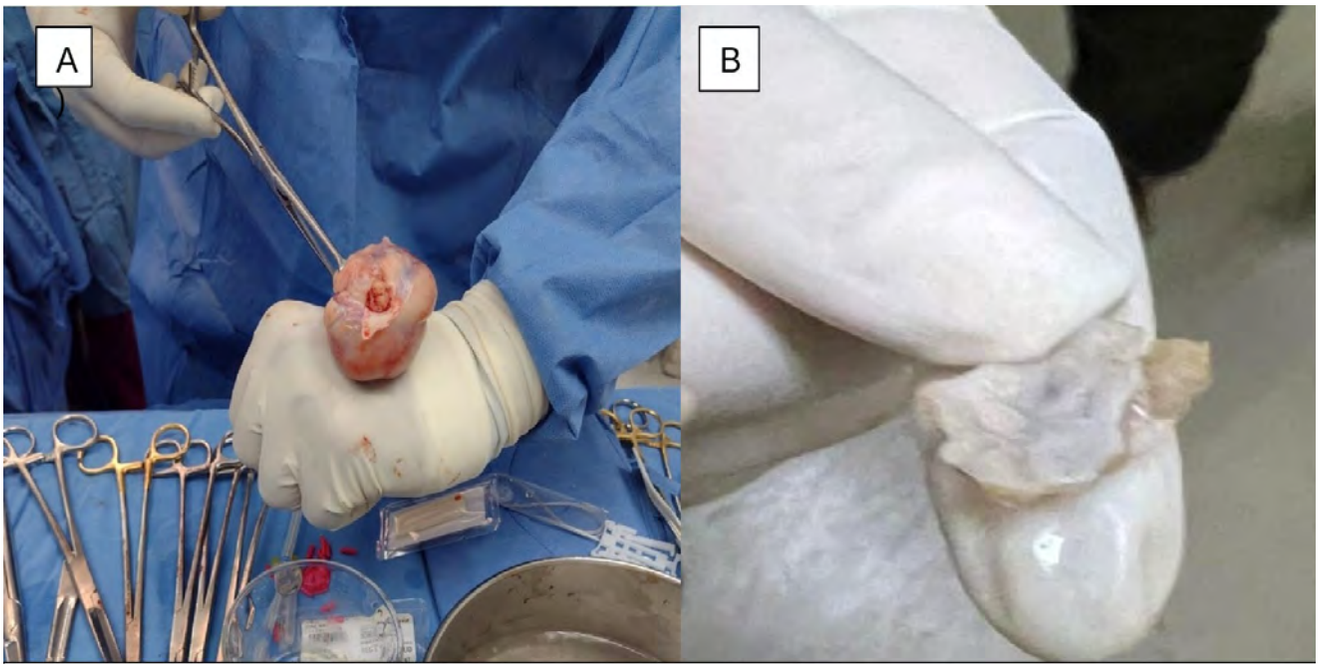

Figure 3. A. Surgical excision specimen of cardiac embryonal rhabdomyosarcoma of the left atrium measuring 7 cm by 5 cm; B. Interatrial septum,with necrotic spot which was adherent to the resected tumor, with borders free of tumor.

respiratory impairment, requiring urgent surgical management. Surgical findings were a tumor in left atrium of approximately 7 cm x 5 cm, which prolapsed through the mitral valve with minimal regurgitation by intraoperative echocardiogram; aortic valve without insufficiency, without presence or residue of tumor (**Fig. 2**). A serohematic left pleural effusion of 150 ml was drained. Cardiopulmonary bypass time and aortic cross-clamping time were 66 minutes and 43 minutes, respectively.

The postoperative course was uneventful, free of complications. The patient was discharged from ICU, the approach was complemented with simple and contrasted thoracoabdominal-pelvic tomography with no evidence of tumor activity. Histopathology study reported embryonal rhabdomyosarcoma histological grade 5, FNCLCC Grade 2. Mitotic count 8 in 2 mm2, focal necrosis, unidentified lymphovascular invasion (**Fig. 3**). Surgical margins were negative for malignancy. The case was discussed with the oncology department who indicated outpatient follow-up. Before in-hospital discharge, transthoracic echocardiogram showed no primary valvular damage, normal biventricular systolic function, normal left ventricular diastolic function, low probability of pulmonary hypertension, non-dilated or hypertrophic left ventricle, with normal global and segmental mobility, LVEF 64%; left atrium was not dilated, without thrombus inside. Mitral valve of normal thickness and mobility, without insufficiency; mild tricuspid insufficiency, PSAP 22 mm Hg.

Histopathological study microscopic description was as follows: immunohistochemistry MY0D1 +, Desmin +, TLE 1 + FL 1 +, Ki67 +, HHH3 +, CD34 -, CD31 -, ERG -. (**Fig. 4**).

Twelve days after operation, simple and contrasted thoracoabdominal pelvic tomography was performed with no evidence of tumor activity at the time of examination.

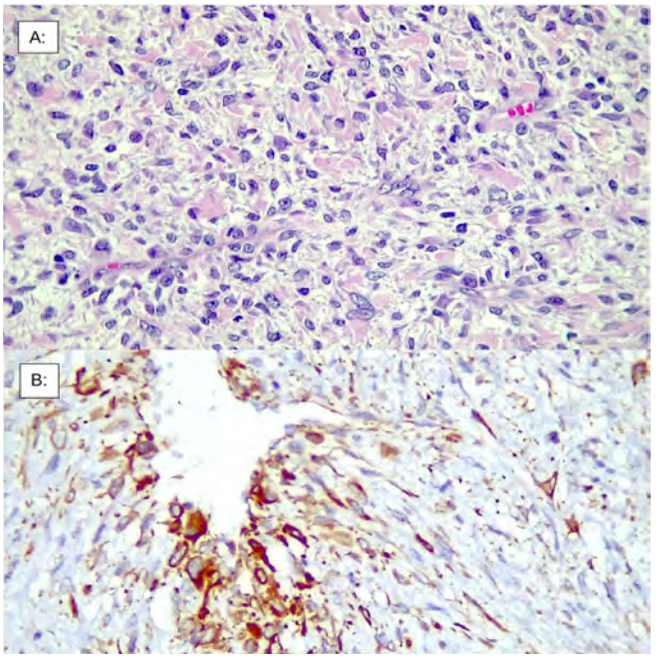

Figure 4. A. The most characteristic feature of this tumor is observed, cells with irregular, eosinophilic, dense, fibrillary cytoplasm with morphologically eccentic nuclei, compatible with rhabdomyoblasts. B. Inmonuhistological reaction with desmin, with intense and focal positivity in cytoplasm, with cells with characteristic morphology of rhabdomyoblasts.

COMMENT

This was a young patient, meeting the age range of presentation, according to previous published literature, arriving at the emergency department in poor general condition, due to the occupational process in the mitral valve, requiring emergency surgery, with a presumptive diagnosis of intracardiac thrombus with suspicion that it was secondary to recent COVID-19 disease, given the fact that there has been seen an increase in the incidence of cases in our hospital [27]. With a surprising result at the time of surgery to find a tumor in left atrium prolapsing into the left ventricle whose morphological characteristics were not compatible with myxoma or thrombus. which was an unexpected finding supported by the histopathological result as cardiac embryonal rhabdomyosarcoma.

In closing, the histological variety defines the type of therapy recommended in the postoperative period for adequate control. In addition, the importance of achieving a resection with negative borders is of paramount importance. Subsequent multidisciplinary management to improve the patient's survival and quality of life is absolutely recommended.

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REFERENCES

1. González LR, Toloza AC, Reyes MR, et al. Primary cardiac tumors. Experience in 72 cases. Rev méd Chile. 2020. 148(3). doi: 10.4067/S0034-98872020000300327.
2. Gamboa AY, Arguedas GJ, González M. Rabdomiosarcoma cardíaco. Acta pediátr costarric. 2008; 20(1): 44-47.
3. Castorino F, Masiello P, Quattrocchi E, Di Benedetto G. Primary cardiac rhabdomyosarcoma of the left atrium: an unusual presentation. Tex Heart Inst J. 2000;27(2):206-8.
4. Induni E, Pucc J, Soto L. Tumores Intracardíacos. Revista costarric cardiol 2002; 4(1):7-11.
5. Skopin II, Serov RA, Makushin AA, Sazonenkov MA. Primary rhabdomyosarcoma of the right atrium. Interact Cardiovasc Thorac Surg. 2003;2(3):316-8. doi: 10.1016/S1569-9293(03)00059-8.
6. McAllister HA Jr, Hall RJ, Cooley DA. Tumors of the heart and pericardium. Curr Probl Cardiol. 1999;24(2):57-116.
7. Prichard rW. Tumors of the heart. review of the subject and report of one hundred and fifty cases. Arch Pathol 1951; 51:98-128.
8. Thomas CR, Johnson GW, Stoddard MF, et al. Primary malignant cardiac tumors: update 1982. Med Pediatr Oncol 1992; 20: 519-531.
9. McAllister HA, Fenoglio JJ. Tumors of the cardiovascular system. Atlas of Tumor Pathology. Washington: Armes Forces Institute of Pathology, 1978; 73-119.
10. Köbbert C, Möllmann C, Schäfers M, et al. Transgenic model of cardiac rhabdomyosarcoma formation. J Thorac Cardiovasc Surg. 2008;136(5):1178-86. doi: 10.1016/j.jtcvs.2008.04.022.
11. Cubides CAS, Salazar G, Muñoz A, et al. Tumores cardíacos primarios. rev Col Cardiol 2003; 10:472-485.
12. McAllister HA. Tumors of the heart and pericardium. En: Silver MD, editor. Cardiovascular patology. Nueva York, Churchill Livingstone, 1983;2:936-937.
13. Tavil Y, Turkoglu S, Tacoy G, Cemri M. Huge biatrial cardiac rhabdomyosarcoma resulting in bilateral atrioventricular valve obstruction. Cardiovasc Pathol. 2006;15(6):354-5. doi: 10.1016/j.carpath.2006.07.008.
14. Zacaria VE, Pereira R. Arévalos F. et al. Rabdomiosarcoma cardíaco: reporte de un caso en el Servicio de Oncología Clínica del Instituto de Previsión Social (IPS). Rev. salud pública Parag. 2022; 12(1): 48-51. doi: 10.18004/rspp.2022.junio.48.
15. Poterucha TJ, Kochav J, O'Connor DS, Rosner GF. Cardiac Tumors: Clinical Presentation, Diagnosis, and Management. Curr Treat Options Oncol. 2019;20(8):66. doi: 10.1007/s11864-019-0662-1.
16. Bombi JA, Fitó R. Varón de 24 años con hemopericardio. Med Clin 1989; 92:29-35.
17. Shanmugam G. Primary cardiac sarcoma. Eur J Cardiothorac Surg. 2006;29(6):925-32. doi: 10.1016/j.ejcts.2006.03.034.
18. Villacampa VM, Villarreal M, Ros LH, Alvarez R, Cózar M, Fuertes MI. Cardiac rhabdomyosarcoma: diagnosis by MR imaging. Eur Radiol. 1999;9(4):634-7. doi: 10.1007/s003300050723.
19. Díaz-Pérez JA, Gómez-Arbeláez D, Hurtado-Gómez GA. Rabdomiosarcoma primario de corazón como causa de síncope recurrente en el adulto. Arch Mex Cardiol 2011;81(4):313-316.
20. Lestuzzi C, De Paoli A, Baresic T, Miolo G, Buonadonna A. Malignant cardiac tumors: diagnosis and treatment. Future cardiology 2015; 11(4), 485–500. doi: 10.2217/fca.15.10.
21. Abad C. Tumores cardíacos (II). Tumores primitivos malignos. Tumores metastásicos. Tumor carcinoide. Rev Esp Cardiol 1998; 51:103-114.
22. Enzinger FM, Weiss SW. Soft tissue tumors. St. Louis: Mosby; 1995. 539-568.
23. Attanasio A, Romitelli S, Mauriello A, Palmieri G, Stefani A, Pierangeli L. Cardiac rhabdomyosarcoma: a clinicopathologic and electron microscopy study. G Ital Cardiol. 1998;28(4):383-6.
24. Hoffmeier A, Sindermann JR, Scheld HH, Martens S. Cardiac tumors--diagnosis and surgical treatment. Dtsch Arztebl Int. 2014;111(12):205-11. doi: 10.3238/arztebl.2014.0205.
25. Shapiro LM. Cardiac tumours: diagnosis and management. Heart. 2001;85(2):218-22. doi: 10.1136/heart.85.2.218.
26. Satoh M, Horimoto M, Sakurai K, Funayama M, Igarashi K, Yamashiro K et al. Primary cardiac rhabdomyosarcoma exhibiting transient and pronounced regression with chemotherapy. Am Heart J 1990; 120(1): 458-460. doi: 10.1016/0002-8703(90)90267-2.
27. Martínez A, Echeverry M, Estrada H. et al. Incidence of intracardiac thrombi in times of Covid 19, Cir Card Mex 2022; 7(4): 65-69.