Caspian Journal of Internal Medicine 2025 (Winter); 16(1): 178-184
DOI: 10.22088/cjim.16.1.178

Case Report

Recurrent prosthetic mitral valve thrombosis: First report of an unusual feature of systemic mastocytosis, a case report and review of the literature

Amirhossein Akbarzadehpasha (MD) [1¥]
Zahra Lotfi (MD) [2¥]
Razieh Omidvar (MD) [1*]
Azadeh Goodarzi (MD) [2]
Saeid Hosseini (MD) [1]
Afsaneh Sadeghzadeh Bazargan (MD) [2]
Kambiz Kamyab Hesari (MD) [3]

1. Rajaie Cardiovascular Medical and Research Center, School of Medicine, Iran University of Medical Sciences, Tehran, Iran
2. Department of Dermatology, Rasool Akram Medical Complex Clinical Research Development Center (RCRDC), School of Medicine, Iran University of Medical Sciences, Tehran, Iran
3. Department of Dermatopathology, Raazi Hospital, Tehran University of Medical Sciences, Tehran, Iran

*** Correspondence:**
Razieh Omidvar,
Department of Dermatology, Rasool Akram Medical Complex Clinical Research Development Center (RCRDC), School of Medicine, Iran University of Medical Sciences, Tehran, Iran

E-mail: amirhosseinap73@gmail.com
Tel: +98 2123921

¥These authors contributed equally in writing this article.

Received: 3 Sep 2023
Revised: 15 Oct 2023
Accepted: 24 Dec 2024
Published: 27 Oct 2024

Abstract

Background: Mastocytosis is a systemic disease involving the clonal expansion of mast cells in multiple organs. Given that immune system overreaction and excessive histamine release are among the most prominent events in mastocytosis, the incidence of complications caused by immune reactions is expected to increase across various organs. While systemic manifestations of mastocytosis have been reported frequently, cardiac complications are less often discussed. These Cardiac complications can be early indicators of the disease but such uncommon features may lead to delays in diagnosis. The significance of mast cells and histamine release in the cardiovascular system is acknowledged in prior studies.

Case Presentation: This study presents a case of recurrent prosthetic mitral valve malfunction in a 52-year-old patient with a history of cutaneous mastocytosis, who underwent mitral valve replacement three times over ten years. Despite being on appropriate anticoagulation therapy (INR: 2.5-3.5), the patient experienced recurrent prosthetic valve thrombosis. This is, to our knowledge, the first report of prosthetic mitral valve thrombosis in a patient with mastocytosis.

Conclusion: Interestingly, cardiac complications may be the first presentation of systemic mastocytosis, diagnosed long after the initial symptoms. The majority of such cases had no visible cutaneous manifestations (table 1). Regarding our case report, we recommend our colleagues to closely monitor and remain vigilant for possible cardiac symptoms of mastocytosis patients with prosthetic cardiac valves.

Keywords: Mastocytosis, cutaneous mastocytosis, prosthetic mitral valve, mitral valve thrombosis, Mastocytosis cardiac complications, thrombosis related to mastocytosis.

Citation:
Akbarzadehpasha A, Lotfi Z, Omidvar R, et al. Recurrent prosthetic mitral valve thrombosis: First report of an unusual feature of systemic mastocytosis, a case report and review of the literature. Caspian J Intern Med 2025; 16(1): 178-184.

Systemic mastocytosis (SM) is characterized by clonal expansion of mast cells (MCs) in various organs (1). The prevalence of SM has been reported to be 1 per 10,000 in the adult population (2). SM is classified among the myeloproliferative neoplasms (MPNs), which have been found to cause an increased risk of thromboembolic morbidity (3). The mechanism by which this disease could affect the heart and cause heart failure remains unclear. Kim et al. posited that abnormally high histamine levels are associated with the development of heart failure (4). Kolck et al. reported that neither mast-cell infiltration nor continuously elevated histamine secretion caused changes in heart chamber sizes or ejection fraction in their patients (5). The importance of mast cells and histamine in the cardiovascular system is accepted. In a controlled study, blockage of histamine 2 receptors favored the improvement of the pathophysiology of CHF (4), but the exact mechanism of mastocytosis effects on the cardiovascular system was not completely understood.

As is known, eosinophils activate mast cells to release histamine. Excessive histamine release has adverse effects on the cardiovascular system like cardiac arrhythmia (especially tachyarrhythmia (6, 7)), coronary artery spasm (8), deep vein thrombosis, and pulmonary embolism (9). There have been several studies about cardiovascular symptoms in hypereosinophilic syndrome including dyspnea, heart failure, mitral regurgitation, arrhythmia, myocardial inflammation, and mural thrombosis. Due to the correlation between eosinophils and histamine release of mastocytosis, it is predictable that similar symptoms might be observed in mastocytosis, but there are not enough studies taken place yet. In this article, we report a case of recurrent prosthetic mitral valve thrombosis in a patient with mastocytosis. Also, we conducted a brief review of the previous studies of cardiovascular manifestations in mastocytosis.

Case Presentation

A 52 y/o gentleman with a 40-year history of generalized pigmented skin lesions and mechanical mitral valve replacement surgery presented to our cardiology department with exertional dyspnea. The absence of a good metallic sound in auscultation guided us towards considering prosthetic valve thrombosis. Echocardiography revealed fixation of the medial leaflet of the prosthetic MV (figure 1, 2 A, B), with increased transvalvular gradients (MG: 13mmHg, EV: 2.5m/s, PHT: 135ms, and DVI: 3.4). More importantly, a relatively large (1.1*0.5cm) and partially organized immobile clot was reported, entrapped in the medial hinge point of the medial leaflet of prosthetic MV, in both atrial and ventricular sides.

Also, another smaller semi-mobile clot (0.3*0.35cm) was seen on the atrial side of the same hinge point (figure 2 C, D). Coronary CT angiography revealed normal coronary arteries. So, the patient underwent a fourth time redo mitral valve replacement (MVR), with a good postoperative course and was discharged on the 12th postop day. Unfortunately, they were re-admitted due to sternal dehiscence and mediastinitis (figure 3), which could also be related to their underlying skin condition. The aforementioned complication was treated by antibiotic therapy, wound care, and pectoral flap. The patient was discharged again in good condition.

This could have been a common case of prosthetic valve malfunction surgery (performed several times each year at our center); however, the key point here is that this was the fourth time the patient had undergone mitral valve surgery in the last decade (see figure 4): About 11 years ago, months before the first surgery, the patient presented with dyspnea and generalized weakness to another medical center. As the patient recalls, a series of cardiac workups were performed, but sadly, we do not have access to the documents currently. Subsequently, the patient was operated on for mechanical MVR. Considering inaccessibility to said medical files, the reason for the first MVR surgery remains unknown to us.

13 months after the first surgery, mechanical prosthetic mitral valve malfunction due to thrombosis resulted in the second open heart surgery (a prosthetic valve cleaning surgery). Almost 3 years after the second surgery, the patient went through another MVR surgery, due to prosthetic valve malfunction. This was their first time undergoing surgery in our center. The fourth major surgery they went through was the one that we wrote about in detail just above and it was performed about 6 years after the third surgery. As confirmed with the patient and their physician, during all these years, INR levels were kept in the therapeutic range for mechanical MV prosthesis thrombosis prophylaxis. The recurrence of prosthetic valve malfunction and thrombosis, in spite of proper anticoagulation, triggered a comprehensive investigation of the patient's skin condition and its possible contribution to the situation at hand, as suggested by our cardiac surgeon.

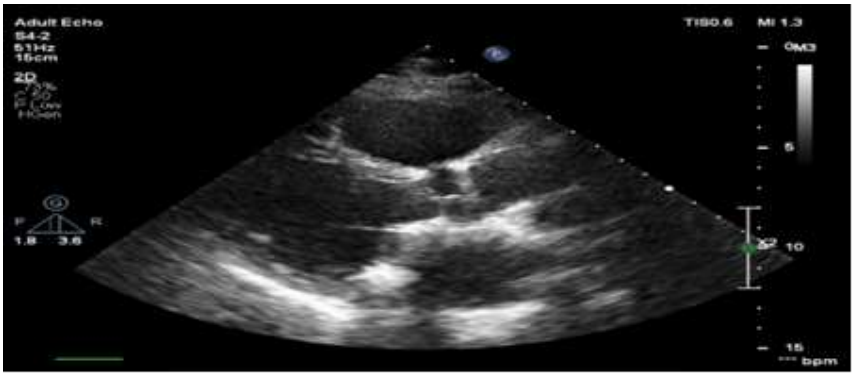

Figure 1. Preoperative transthoracic echocardiography. Fixed medial leaflet of prosthetic mitral valve (white arrow), in comparison to the other leaflet (black arrow).

Caspian Journal of Internal Medicine 2025 (Winter); 16(1): 178-184
Akbarzadehpasha A, et al.

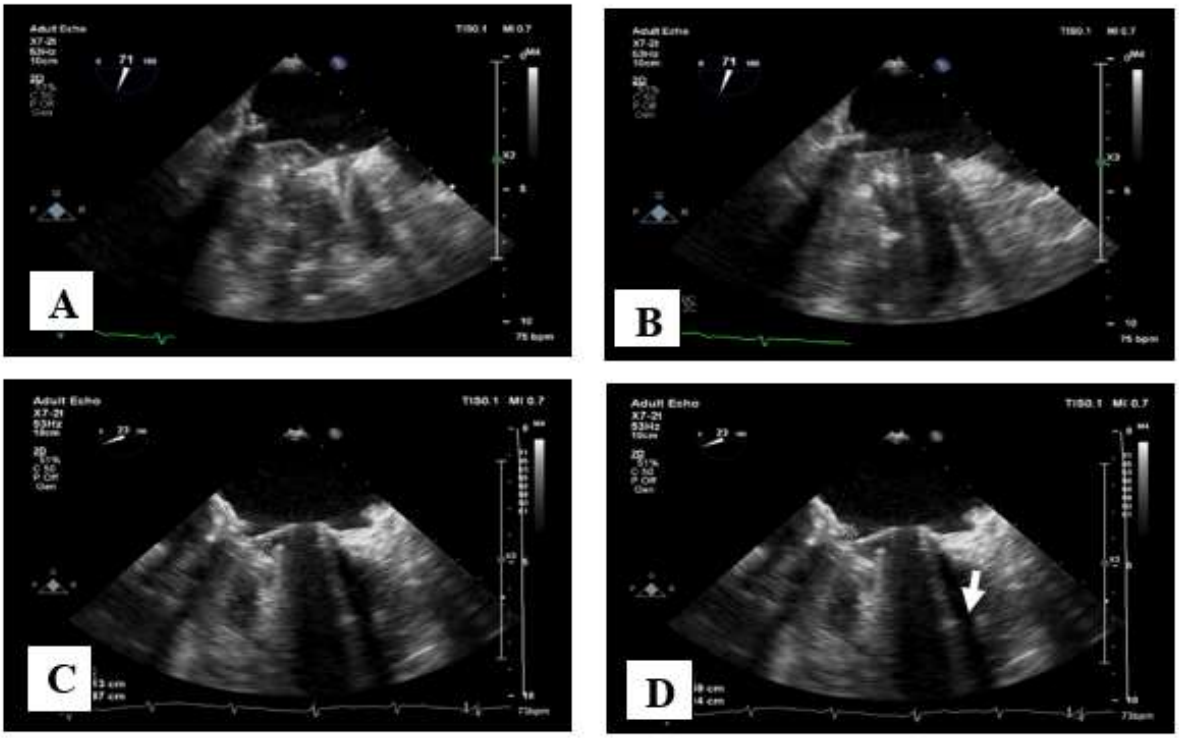

Figure 2. Pre-pump (cardiopulmonary bypass) intraoperative transesophageal echocardiography. A) Prosthetic MV in systole (both leaflets closed) B) Prosthetic MV in diastole - fixed medial leaflet (white arrow). C) Large immobile clot (1.1*0.5cm) entrapped in the medial hinge point of the medial leaflet. D) Smaller semi-mobile clot (0.3*0.35cm) on the atrial side of the mentioned hinge point.

The blood tests revealed anemia (Hb: 10.6g/dL, RBC: $4.05*10^6$ cells/mm^3, MCV: 81.7FL), Eosinophilia (WBC: 9000 cells/mm^3, Neutrophils: 53%, Lymphocytes: 18%, Monocytes: 12%, Eosinophils: 15%, and Band cells: 2%), and normal platelet count ($267*10^3$/mm^3). Also SGOT, SGPT, Alkaline Phosphatase, and Bilirubin levels were within normal limits. There were no symptoms of bone pain and lymphadenopathy. Also, physical examination and imaging studies did not show any significant lymphadenopathy or hepatosplenomegaly.

The patient's physical examination revealed generalized tan red-brown macules since childhood, which were diagnosed (by skin biopsy) about a year after the first surgery, as a case of urticaria pigmentosa (UP) (figure 3). They were not taking any specific medications at the time (except antihistamines). They were also treated with limited sessions of phototherapy, which did not lead to any improvement in their underlying skin condition. We consulted our dermatology department for evaluation and treatment of the skin condition, to prevent further systemic complications. The dermatologist we consulted with, performed another biopsy to reconfirm the diagnosis. The biopsy was taken by regional blocking of the skin around the lesion, to avoid excessive mast cell accumulation. The pathology results confirmed mastocytosis - urticaria pigmentosa (figure 5).

After consulting with different specialties, it was deduced that the recurrent prosthetic MV thrombosis must have happened under the effect of excessive histamine release, caused by mastocytosis; therefore, systemic corticosteroids were prescribed for the patient. Since serum tryptase and urinary methyl histamine testing is not available in our country, we ordered the other available workup: bone marrow biopsy. Due to the patients' lack of cooperation and unwillingness to undergo such testing during inpatient admission, we scheduled outpatient hematology visits for further evaluation of systemic and hematologic manifestations. Unfortunately, the patient has not attended these appointments, yet. Considering the interesting cardiac manifestation in this patient, we decided to publish the data as soon as possible, so that it would be available as an alerting beacon on such an uncommon cardiac feature of mastocytosis; Hence, long-term follow-up of the treatment results in the case is not yet available.

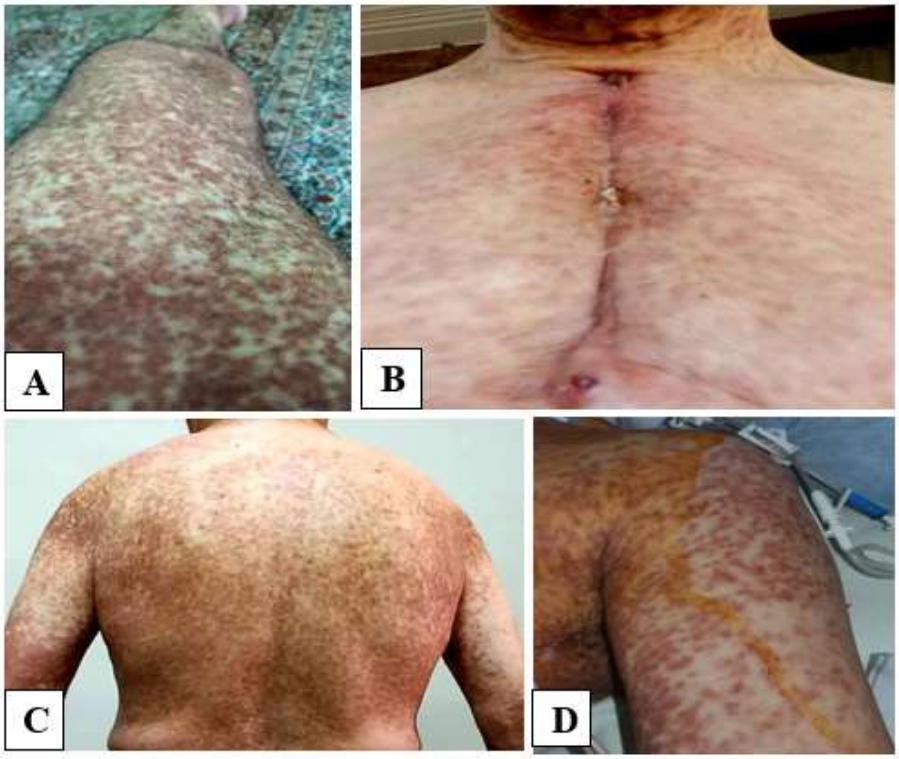

Figure 3. Cutaneous manifestations. A, B, C, and D) Generalized tan red-brown macules and patches spread all over the trunk and extremities. B) Non-healing sternotomy wound after the fourth MVR surgery.

Figure 4. Timeline of the major surgeries.

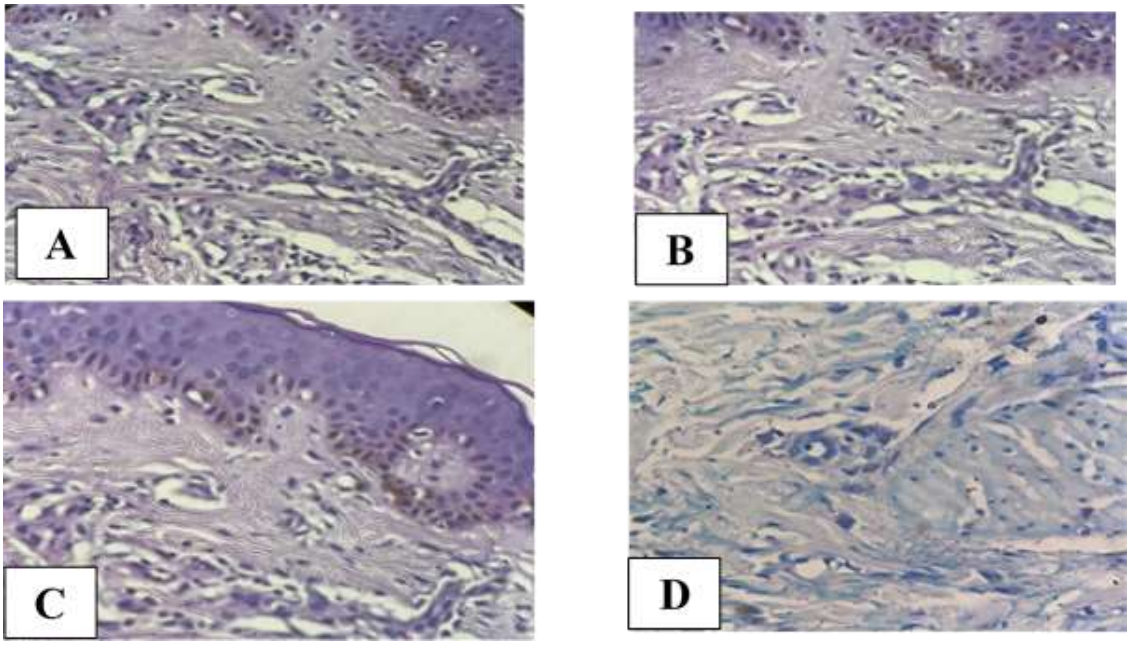

Figure 5. A, B, and C) Partially filled papillary dermis by mononuclear cell, with small round nuclei and granular cytoplasm. D) Toluidine blue stain shows metachromatic granules.

Discussion

Mastocytosis is a rare and complex disease that can invade several organs. Clinical presentations may vary from pruritic rashes to unexplained syncope and sudden death. Patients with mastocytosis often have a long history of chronic and acute symptoms that have remained unrecognized for a long time (10). Several cardiac complications associated with mastocytosis are reported in previous studies. Recurrent syncope and pulseless cardiac arrest have been reported frequently. While arrhythmias such as VF, AF, and atrioventricular block are presented in 3 case reports, dilated cardiomyopathy and diastolic dysfunction were only reported once. On the other hand, pleural effusion and pericardial effusion resulting in cardiac tamponade have been discussed in 4 case reports. One case report presents a patient with a history of hypotension and flushing with diffuse ST depression in ECG. Another points out myocardial injury and Ventricular fibrillation in a patient with urticaria pigmentosa. As mentioned before, there are no reports of prosthetic valve malfunction in mastocytosis available so far. The results of the studies mentioned in this paragraph are discussed briefly in table 1.

Although several studies have been conducted to evaluate the specific cardiovascular conditions of mastocytosis patients in receiving anesthetic medications (11, 12), there are not enough studies emphasizing cardiac complications of mastocytosis in general. Kounis syndrome is defined as concurrent episodes of acute coronary syndrome, associated with mast cell activation due to allergy, hypersensitivity, or anaphylactic reactions. Several papers have been published regarding the Kounis syndrome in mastocytosis (13-15), but other cardiovascular symptoms triggered by excessive mast cell activity have not been thoroughly investigated yet. Given the high burden of chronic cardiovascular diseases and the lesser-known cardiac manifestations of mastocytosis, we decided to gather and review articles reporting its cardiac complications to draw the attention of specialists to this important issue. It is interesting that in some cases, cardiac complications were the first presentation of systemic mastocytosis, which was diagnosed long after the initial symptoms. More interestingly, the majority of the patients had no visible cutaneous manifestations (table 1). Regarding our case report, we recommend our colleagues to closely follow and be extra-sensitive towards possible cardiac symptoms of mastocytosis patients with prosthetic cardiac valves. It is also recommended that reports of new cases of cardiac complications in mastocytosis be gathered in review articles to help specialists in this field properly diagnose, treat, and manage such complications.

Our study had one limitation. We have not yet followed up with the patient in long term, after initiating the treatment. The reasoning behind this is the fact that after a decade of the underlying cause of prosthetic mitral valve malfunction going unnoticed, the patient's condition has just been diagnosed and the treatment started. Considering how fatal such a cardiac complication could be, the authors decided to release the information as soon as possible, so that it would be available to other researchers and colleagues for further investigation. We will actively keep in touch with the patient and consider reporting long-term follow-up in upcoming years. However, we believe the importance of our study lies within reporting a unique and new manifestation, as it is the first reported case of recurrent prosthetic mitral valve thrombosis and malfunction due to mastocytosis.

Table 2. Uncommon cardiac manifestations of mastocytosis in previous studies

Study	Findings	Cutaneous manifestations	Cardiac symptoms as presenting sign of mastocytosis
Marianna Suppa, et al. (16)	Pleural effusion Acute coronary syndrome		No
Jose Amoro, et al. (11)	Dilated cardiomyopathy Diastolic dysfunction	Generalized erythematous macules and patches on posteior and anterior trunk	No
Elizabeth D Paratz, et al. (15)	Recurrent syncope Cardiac arrest		Yes
Vineeth K Sukritan, et al. (17)	Recurrent syncope Cardiac tamponade	Maculopapular rash and urticaria	No
A Wong, et al. (18)	Cardiac tamponade	Telangiectasia macularis and Eruptive perstans	Yes

Study	Findings	Cutaneous manifestations	Cardiac symptoms as presenting sign of mastocytosis
Butterfield J.H. et al. (19)	Pulseless electrical activity Cardiac arrest resistant to cardiac pacemaker		Yes
Erminia Ridolo et al. (20)	Pulseless cardiac arrest		Yes
Erminia Ridolo et al. (20)	Hypotension Flushing Diffuse ST depression		Yes
Susan M et al. (21)	Dyspnea Palpitation VF Myocardial injury	Urticaria pigmentosa	Yes
L Ricciardi et al. (22)	Recurrent paroxysmal atrial fibrillation		No
Dasanu C A et al. (23)	Recalcitrant coronary syndrome		No
Thomas D et al. (24)	Atrioventricular block Pericardial effusion		No

Acknowledgments

The authors would like to thank Rajaei Heart Center and Rasool Akram Medical Complex Clinical Research Development Center for their technical and editorial assistance.

Funding: We received no funding for this project.

Ethics approval: This study was reviewed and approved by the Research Ethics Committee of Rajaie Cardiovascular Medical and Research Center, under the approval code IR.RHC.REC.1401.056.

Conflicting interests: All the authors declare that there is no conflict of interest

Author's contribution: All authors contributed to the preparation of data and finalization of this article.

Data availability: The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Informed consent: Written informed consent was obtained from the patient for participation in the study and the rights of the subject were protected. To observe ethical principles, the name of the patient was not mentioned in the paper.

References

1. Metcalfe DD. Mast cells and mastocytosis. Blood 2008; 112: 946-56.
2. Cohen SS, Skovbo S, Vestergaard H, et al. Epidemiology of systemic mastocytosis in Denmark. Br J Haematol 2014; 166: 521-8.
3. Barbui T, Carobbio A, Cervantes F, et al. Thrombosis in primary myelofibrosis: incidence and risk factors. Blood 2010; 115: 778-82.
4. Kim J, Ogai A, Nakatani S, et al. Impact of blockade of histamine H2receptors on chronic heart failure revealed by retrospective and prospective randomized studies. J Am Coll Cardiol 2006; 48: 1378-84.
5. Kolck UW, Alfter K, Homann J, von Kügelgen I, Molderings GJ. Cardiac mast cells: implications for heart failure. J Am Coll Cardiol 2007; 49: 1107-8.
6. Wolff AA, Levi R. Histamine and cardiac arrhythmias. Circ Res 1986; 58: 1-6.
7. Genovese A, Spadaro G. Highlights in cardiovascular effects of histamine and HI-receptor ansgonists. Allergy 1997; 52: 67-78.
8. Ginsburg R, Bristow MR, Kantrowitz N, Baim DS, Harrison DC. Histamine provocation of clinical coronary artery spasm: implications concerning pathogenesis of variant angina pectoris. Am Heart J 1981; 102: 819-22.
9. Budnik I, Brill A. Immune factors in deep vein thrombosis initiation. Trends Immunol 2018; 39: 610-23.

10. Alto WA, Clarcq L. Cutaneous and systemic manifestations of mastocytosis. Am Fam Physician 1999; 59: 3047-54.
11. Moro JA, Almenar L, Jarque I, et al. Heart transplantation in a patient with systemic mastocytosis. J Heart Lung Transplant 2008; 27: 689-91.
12. Różewicz-Juraszek M, Hryniewiecki T, Faber K, et al. Case report on aortic valve replacement in adult woman with systemic mastocytosis (RCD code: VIII). J Rare Cardiovasc Dis 2017; 3: 54-5.
13. de la Fuente Tornero E, Castro AV, de Sierra Hernández PÁ, et al. Kounis syndrome during anesthesia: presentation of indolent systemic mastocytosis: a case report. A A Case Rep 2017; 8: 226-8.
14. Kounis NG, Mazarakis A, Tsigkas G, Giannopoulos S, Goudevenos J. Kounis syndrome: a new twist on an old disease. Future Cardiol 2011; 7: 805-24.
15. Paratz ED, Khav N, Burns AT. Systemic mastocytosis, kounis syndrome and coronary intervention: case report and systematic review. Heart Lung Circ 2017; 26: 772-8.
16. Suppa M, Marino L, Piccari P, Masselli G, Gradini R. Cardiac complications in a patient affected by systemic mastocytosis and primitive myelofibrosis: A case report. Clin Case Rep 2021; 9: e04972.
17. Sukrithan VK, Salamon JN, Berulava G, Sibinga NE, Verma A. Systemic mastocytosis presenting as cardiac tamponade with CD25+ pericardial mast cells. Clin Case Rep 2016; 4: 279-81.
18. Wong A, Toh J, Jerschow E. O009 Systemic mastocytosis presenting as cardiac tamponade. Ann Allergy Asthma Immunol 2016; 117: S4.
19. Butterfield JH, Weiler CR. Presentation of untreated systemic mastocytosis as recurrent, pulseless-electrical-activity cardiac arrests resistant to cardiac pacemaker. Int Arch Allergy Immunol 2014; 163: 130-4.
20. Ridolo E, Triggiani M, Montagni M, et al. Mastocytosis presenting as cardiac emergency. Intern Emerg Med 2013; 8: 749-52.
21. Rohr SM, Rich MW, Silver KH. Shortness of breath, syncope, and cardiac arrest caused by systemic mastocytosis. Ann Emerg Med 2005; 45: 592-4.
22. Ricciardi L, Saitta S, Isola S, et al. Systemic mastocytosis associated with recurrent paroxysmal atrial fibrillation. Allergy 2005; 60: 542-3.
23. Dasanu CA, Keating MJ, Tsai H. Systemic Mastocytosis Presenting with a Recalcitrant Coronary Syndrome. Conn Med 2018; 82: 23.
24. Thomas D, Dragodanne C, Frank R, et al. Systemic mastocytosis with myo-pericardial localization and atrioventricular block. Arch Mal Coeur Vaiss 1981; 74: 215-21. [in French]