

CASE REPORT

Diagnosis of the right atrial myxoma after treatment of COVID-19: A case report

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Key Clinical Message: Atrial myxoma is a rare disease but has a broad clinical presentation and complication that involves several systems- heart, lungs, brain, and systemic. An interdisciplinary approach is very important to optimize the outcome in patients with atrial myxomas. A thorough examination by primary care providers is crucial. Then radiologists or cardiologists can help with imaging modalities that can help diagnose and characterize the tumor. Prior to surgical resection by cardiothoracic surgeons, patients need to be evaluated by pulmonologists, cardiologists, and anesthesiologists for preoperative risk stratifications. In patients with neurological complications, pulmonary complications, or infectious endocarditis, input from neurologists, hematologists, infectious disease specialists is essential for patient care. In case antiplatelet/anticoagulation therapy or antibiotic treatment is warranted, pharmacists can provide valuable recommendations.

Abstract: Myxoma is the most common benign cardiac primary tumor, occurring in the right atrium in only 15%–20% of cases. This disease is asymptomatic initially depending upon size of the tumor, and symptoms develop as the tumor spreads. Atrial myxomas are associated with a triad of complications, including obstruction, emboli, and constitutional symptoms (such as fever and weight loss). This regard, embolization of the pulmonary circulation system is a complication of right myxoma. The patient was a 40-year-old male who presented to the emergency department complaining of fever and confusion. He had been previously hospitalized due to COVID-19 and treated with Remdesivir and plasmapheresis. He had tachycardia, tachypnea, thrombocytopenia, and increased liver enzymes. Chest imaging showed nodular lesions with necrotic areas and cavitory lesions in both lungs and the right atrium infected clot was seen in echocardiography. He was treated with intravenous antibiotics and finally underwent heart surgery due to the diagnosis of pulmonary septic embolism. The patient was finally diagnosed with right atrial myxoma according to heart mass histopathology. It is worth noting that the patient's thrombosis had already developed on the right atrial myxoma, which delayed the diagnosis in this patient. This thrombus formation

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was due to the hypercoagulability state of COVID-19 and following the insertion of a central venous catheter to perform plasmapheresis as a complication of treatment. Special attention should be paid to thromboprophylaxis and the early diagnosis of intravascular and intracardiac thrombosis in COVID-19 patients. Furthermore, the use of imaging modalities is recommended to differentiate thrombus from myxoma.

KEYWORDS

COVID-19, myxoma, plasmapheresis, thrombosis

1 | BACKGROUND

COVID-19 can range in severity from asymptomatic cases to multi-organ involvement, Acute respiratory distress syndrome (ARDS), and shock that led to death in severe cases.^{1,2} Higher activity of the inflammatory cascade and cytokine storm could be seen in severe cases.^{3,4} In this disease, the hyper inflammatory condition was associated with the formation of intravascular clots or thromboembolism both in the acute phase and after several weeks of the disease.⁵⁻⁷

Plasmapheresis is a therapeutic method to reduce the hyperinflammatory condition in COVID-19 patients.^{4,8,9} Although it is known as a safe treatment,⁹ infection and thrombosis caused by central venous catheter insertion (CVC) have also been reported as side effects.^{10,11} Furthermore, there have been cases of right atrial thrombus after CVC, especially in deeper insertion. Deeper insertion of CVC within the right atrial may increase the risk of thrombus versus those placed at the superior vena cava,¹² possibly making it difficult to distinguish these thrombi from myxomas inside the heart cavities.¹³

Primary cardiac tumors are rare, and three-quarters of them are benign. Myxomas account for almost 50% of benign cardiac tumors.¹⁴ Approximately 75% of myxomas are in the left atrium, and only 15%–20% are in the right atrium.^{14,15}

The main factors involved in the development and type of clinical manifestations of myxomas include their locations, sizes, and mobility. However, small tumors may have no clinical symptoms^{14,16,17} and are often diagnosed after imaging tests for other reasons.¹⁸ Some patients may experience symptoms such as shortness of breath, angina pectoris, syncope, dizziness, fatigue, cough, and fever.^{19,20} Furthermore, several cases of emboli have been reported in patients with myxoma, and more systemic emboli have been reported due to the increased prevalence of these left-sided primary cardiac tumors.^{21,22} Moreover, an embolism caused by right atrial myxoma involves the pulmonary blood flow system.²³ Infectious cardiac myxoma is a

rare condition that manifests with high fever and emboli in other organs.²⁴ Myxoma indicates an emergency, and surgery should be performed as soon as possible after diagnosis to avoid embolization and valve obstruction as acute complications of postponing surgery.^{19,20}

2 | CASE PRESENTATION

The patient was a 40-year-old man who visited the emergency department with complaints of fever, chills, sweating, and confusion. According to his medical history, 8 days ago, he was hospitalized for COVID-19 in the same center's intensive care unit and underwent Remdesivir, anti-inflammatory, and anticoagulants treatment with a prophylactic dose. Due to the relative level of pulmonary involvement and hypoxemia, plasmapheresis was performed three times at an interval of 48 h, and finally, he was discharged in good general condition and with stable vital signs. The patient had no history of an underlying disease and did not consume alcohol, cigarettes, or opium. On admission to the emergency department, he was found to have tachycardia, tachypnea (RR:22 bpm), and a fever of 38.3 C. SPO2 without supplemental oxygen was 89%, and the patient's blood pressure was 115/78 mm Hg. On examination of body systems, the patient was slightly drowsy, but other neurological examinations were normal, the cardiac examination was normal, and a small crackle was heard on lung auscultation at the left lung base. No skin lesions were seen, but a herpes simplex lesion was seen on the right lower lip. In laboratory examinations, the CBC test showed thrombocytopenia, leukocytosis, and a normal hemoglobin level. Other tests also showed hyponatremia, increased liver enzymes, and higher levels of serum inflammatory factors. [Table 1](#) presents laboratory tests at the time of patient admission.

Then, the patient was admitted to the ICU due to confusion and worse clinical conditions. Four hours after being admitted to the ICU, he showed symptoms of high fever and delirium.

According to clinical symptoms and a possible diagnosis of herpetic encephalitis, a brain CT scan without contrast was requested for the patient. The result was

TABLE 1 Laboratory tests at the beginning of admission to the emergency room and 1 month after discharge.

Blood test	Value	
	Emergency room	One month after discharge
WBC ($\times 10^3/\mu\text{L}$)	18,100	8500
Hemoglobin (mg/L)	14.7	14.5
PLT ($\times 1000\mu\text{L}$)	46,000	249,000
PT (s)	14	NA
PTT (s)	26	NA
INR	1.1	NA
Na (mmol/L)	121	NA
K (mmol/L)	4.1	NA
Ca (mg/dL)	8.3	NA
phosphorous (mg/dL)	3.9	NA
Magnesium (mg/dL)	2.2	NA
Albumin (g/L)	3.8	NA
BUN (mg/dL)	29	NA
Creatinine (mg/dL)	1.1	NA
AST (U/L)	94	17
ALT (U/L)	131	15
Alp (U/L)	289	321
Blood sugar (mg/dL)	116	NA
CRP	2+	Negative
ESR (mm/h)	58	22

normal, then the lumbar puncture was performed and the cerebrospinal fluid sample was sent for biochemical purposes. A bacterial smear and culture, a PCR for HSV, and Wright's test were performed on this sample. However, because the clinical condition was worsening, it was treated empirically with intravenous antibiotics and Acyclovir. Following up on the cerebrospinal fluid results revealed no abnormalities.

During the patient's hospitalization, high-resolution computed tomography (HRCT) of the lungs was performed based on tachypnea and hypoxemia using pulse oximetry. Bilateral nodular lesions with necrotic areas were seen in the fields of both lungs (Figure 1). Transthoracic echocardiography (TTE) was performed for the patient suspected of endocarditis according to the patient's clinical conditions, including fever and lung imaging, and the history of central venous catheter insertion for plasmapheresis during a previous hospitalization. There was no evidence of skin infection at the previous location of the central venous catheter (right subclavian). In TTE, there were a hypermobile mass and an infected clot in the right atrium moving into the right ventricle. Left ventricular ejection fraction was reported as 60% and no abnormality was seen in heart valves. There was no increased pulmonary artery pressure, heart cavity wall thickness, movements, or pericardial effusion (Figure 2). According to the TTE result, a blood culture was performed using the BACTEC method, and the procalcitonin serum level was checked. After 18 h, *Staphylococcus aureus* grew in the patient's blood culture, and 13.4 ng/mL procalcitonin was reported.

Regarding the patient's blood culture results, antibiotic treatment with Vancomycin and Gentamicin was started and Acyclovir was stopped for him. After 3 days, the patient's fever stopped and his procalcitonin level reached 0.93 ng/mL after 12 days. The general condition of the

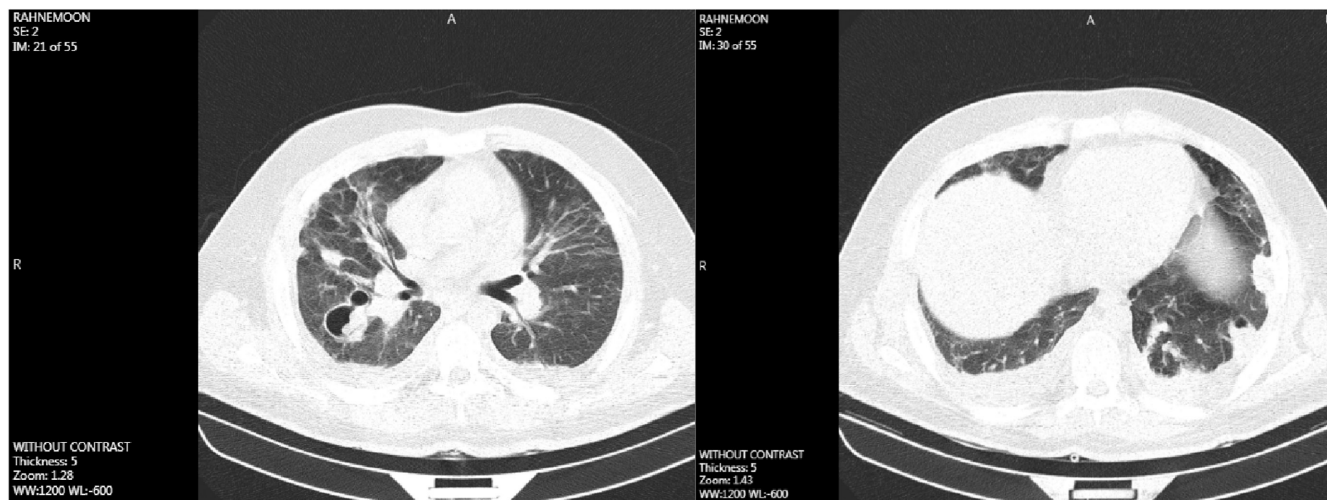


FIGURE 1 Changes in peripherals of both lungs due to Bilateral nodular lesions with necrotic areas in a cut of HRCT on the first day of hospitalization.



FIGURE 2 Hypermobile mass and infected clot in the right atrium moving into the right ventricle in TEE.

patient was also improved. After 2 weeks of treatment, echocardiography was performed on the patient again. No specific change in the size, form, or movement of the heart mass was seen compared to the previous echocardiography; hence, transesophageal echocardiography (TEE) was recommended for a more detailed examination. According to the TEE report, the systolic function of the right ventricle was normal, and there were no changes in the thickness and movements of the heart chambers. The right atrium was observed to have a very large size (7×44 mm) hypermobile mass with a moving particle at its tip. This mass has a broad attachment to the RV wall at the Eustachian valve site, and is observed to protrude into the tricuspid valve during diastole. Based on clinical data, it is thought to be an infected clot.

According to the echocardiography results and consultation with the cardiac surgeon, the patient was a candidate for surgery to remove the mass (Figure 3). After surgery, the sample was sent to the pathologist for examination, and the patient was discharged after completing the post-operative period with the prescription of oral antibiotics. Finally, the pathology report revealed that the patient had a right atrial myxoma 1 month later at the next visit. The patient's general condition significantly improved and he did not report any surgical complications. Additionally, the new HRCT scan also showed a completely improved lung involvement (Figure 4). Table 1 presents the tests related to 1 month after discharge.

3 | DISCUSSION

In this case, an infectious thrombus in the right heart caused a septic embolism in the lungs and clinical signs

of infection in the patient. Septic pulmonary emboli is usually seen in IV drug users, but its occurrence has been reported in patients with artificial heart valves, central venous catheters, and intra-cardiac devices.²⁵ Myxoma infection is rare^{25–28} and their infection increases the risk of embolism in these patients.^{29–31}

Considering the lack of evidence of intravenous drug abuse in the patient's history, it seems that the central venous catheter insertion in the previous hospitalization for plasmapheresis and the diagnosis of COVID-19 led to infection and intracardiac thrombus in the right atrial myxoma. Therefore, central venous catheter insertion in patients is associated with the creation of thrombosis, and intravascular thrombosis increases the patients' mortality rate.^{32,33} Various mechanisms have been proposed for the creation of thrombus due to central venous catheter insertion. These mechanisms include damage and mechanical stimulation of the right atrium wall, decreased vascular blood flow rate caused by the catheter, and emboli caused by peripheral vein thrombosis.^{33–37} Coagulopathy and intravascular thrombosis are known as the most common severe complications of COVID-19.^{38–40} In these patients, higher complement activity and cytokine storm are the causes of this hypercoagulability state.^{38,41,42} The risk of thrombosis is significantly higher in patients with COVID-19 even in the cases of using anticoagulant drugs as prophylaxis.³⁸ In addition to the above mentioned factors, some local factors may also cause a thrombus on the atrial myxoma, including the irregular surface of the myxoma, bleeding, or stasis caused by the tumor size and obstruction of blood flow.^{43,44} In this case, the reason for thrombus formation was the CVP line catheter, abutting against the right atrial mass leading to thrombus formation. Left atrial thrombus are probably well protected

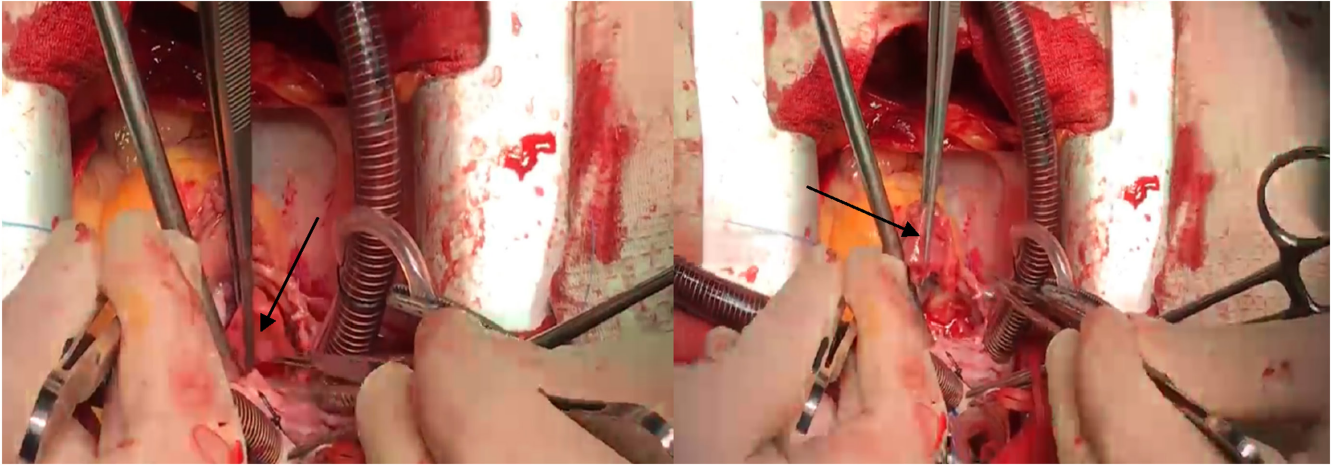


FIGURE 3 Resecting myxoma at a size of 2×0.52 cm during surgery.

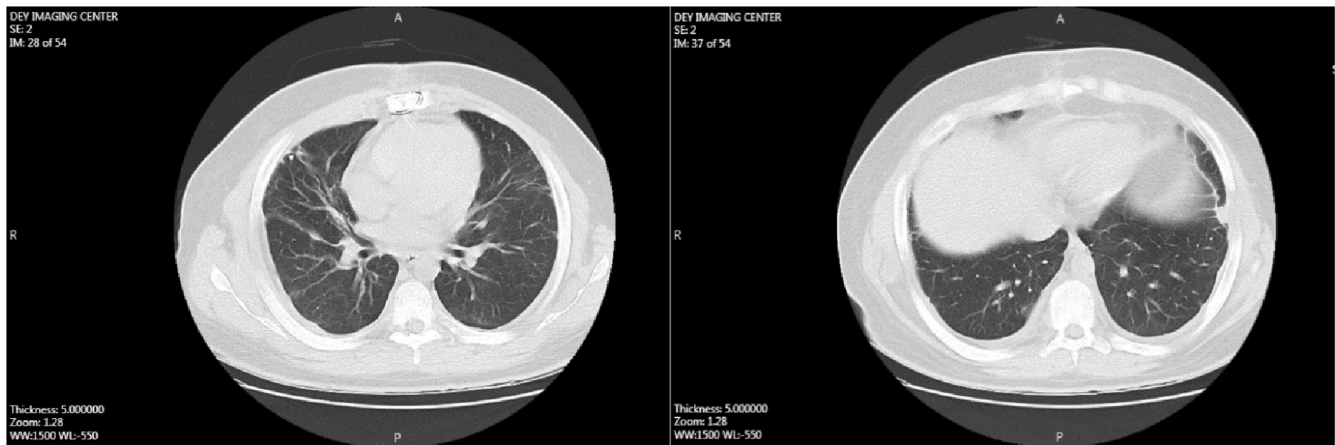


FIGURE 4 Changes in peripherals of both lungs due to bilateral nodular lesions with necrotic areas in a cut of HRCT on the 30th day of hospitalization.

in comparison to the right atrial thrombus in the development of thrombus and Covid-19 has precipitated this problem.

In this case, the emergence of an infectious thrombus on the right atrial myxoma made its diagnosis difficult; however, some cases of thrombus mimicking myxoma are also reported.^{30,45–47} It is important to differentiate these two cases due to the use of different treatment methods.⁴⁸ Despite the lack of collective expert consensus on the most appropriate diagnostic method for cardiac masses (tumors, clots, and vegetations), Table 2 presents the clinical differentiation and imaging of myxoma, as well as intra-cardiac thrombi based on a study by Aggeli et al.⁴⁹

As a suitable diagnostic method for myxoma, TEE is preferable to TTE.²⁰ In this case, TTE was first performed, but the mass characteristics and location were not precisely identified; hence, three-dimensional transthoracic echocardiography (3DTTE) was performed and the mass

size, location, and characteristics were clearly identified and reported. Thus, 3DTTE can be recommended to determine the characteristics, size, and tumor attachment point. Even though TEE is a reliable method for the diagnosis of mobile intra-cardiac thrombi, microscopic examination of tissue specimens is still the gold diagnostic standard.⁵⁰

Alrifae et al.⁴³ described a 21-year-old female who suffered from right ventricular and atrial thrombus a few months after infection with COVID-19 and eventually atrial myxoma was diagnosed after surgery and histopathological examination. Like our case patient, the myxoma was diagnosed after surgery because it was covered by a thrombus.

Even though right atrial masses cause hemodynamic changes similar to those with right heart failure,¹³ there was no evidence of right heart failure, edema (generalized or lower limb), murmur, or diastolic disorder in our patient. A total of 90% of myxoma cases occur without a

TABLE 2 Clinical, echocardiographic, and cardiac magnetic resonance (CMR) characteristics of cardiac masses.⁴⁹

	Common age at presentation	Common location at heart	Clinical manifestation	Echocardiography	CT	CMR
Myxoma	Early (familial) or middle adulthood	LA, atrial septum, any other site	Emboli, flow obstruction, systemic symptoms	Mildly lobar, heterogeneous echo density, usually mobile (with or without stalk)	Heterogeneous, low attenuation, may be calcified	Isointense T1w, High T2w, heterogeneous LGE
Clots	Adulthood	LAA, LV apex	Emboli	Acute: Low echo density Chronic: High echo density No perfusion with contrast agents	No contrast enhancement, may be calcified	No EGE/LGE Acute: Isointense to high T1w, T2w Subacute: High T1w, Low T2w Chronic: Low T1w, T2w

Abbreviations: CMR, cardiac magnetic resonance; CT, computed tomography; EGE, early gadolinium enhancement; LA, left atrium; LAA, left atrium appendage; LGE, late gadolinium enhancement; LV, left ventricle.

family history.¹³ In our case, there was no history of myxoma in the patient's family. Myxoma attachment points can be wide, attached (sessile), narrow, or stalked, and macroscopic, gelatinous with a smooth, fluffy, and fragile surface that can embolize in 35% of cases.⁵¹ In our patient, the attachment point of the myxoma to the right atrium wall was narrow, stalked, and fragile and thus it could be easily fragmented during resection and surgery (Figure 3).

According to our findings, the reported case was the first case of right atrial myxoma and thrombosis in acute phase of COVID-19. Interestingly, there was a possible association between the treatment of COVID-19 and the central venous catheter insertion for plasmapheresis in this patient. Therefore, special attention should be paid to detecting intravascular and even intra-cardiac thrombi in COVID-19 patients with central and peripheral venous catheters in addition to conducting preventive anti-inflammatory and anticoagulant therapy.

AUTHOR CONTRIBUTIONS

Mohsen Gholinataj Jelodar: Conceptualization; investigation; project administration; supervision; writing – original draft; writing – review and editing. **Samaneh Mirzaei:** Data curation; methodology; project administration; resources; software; writing – original draft; writing – review and editing. **Haniyeh Dehghan Chenari:** Data curation; investigation; writing – review and editing. **Mahdiyeh Tabkhi:** Investigation; methodology; writing – review and editing.

ACKNOWLEDGMENTS

We are grateful to all participants who contributed to the collection and compilation of the present manuscript. All

necessary ethical issues were observed, including observing fiduciary and respecting the patient's rights.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no competing interests.

DATA AVAILABILITY STATEMENT

The authors confirm that the data supporting the findings of this study are available within the article.

ETHICS STATEMENT

The Ethics Code for the study was IR.SSU.SRH.REC.1401.029 in Research Ethics Committee of Yazd Shahid Dr. Rahnemoun Hospital.

PATIENT CONSENT STATEMENT

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

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How to cite this article: Gholinataj Jelodar M, Mirzaei S, Dehghan Chenari H, Tabkhi M. Diagnosis of the right atrial myxoma after treatment of COVID-19: A case report. *Clin Case Rep*. 2023;11:e7216. doi:[10.1002/ccr3.7216](https://doi.org/10.1002/ccr3.7216)