Case Report: Intravenous Thrombolysis for Acute Ischemic Stroke Due to Cardiac Myxoma

Sara Esmaeili\textsuperscript{1}, Seyyedeh Fahimeh Shojaei\textsuperscript{1}, Maryam Bahadori\textsuperscript{2}, Mohammad Mojtahed\textsuperscript{3}, Masoud Mehrpour\textsuperscript{4*}

1. Department of Neurology, Cellular and Molecular Research Center, Firoozgar Hospital, Student Research Committee, Iran University of Medical Sciences, Tehran, Iran.
2. Firoozgar Clinical Research and Development Center (FCRDC), Iran University of Medical Sciences, Tehran, Iran.
3. Department of Neurology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran.
4. Department of Neurology, School of Medicine, Firoozgar Hospital, Iran University of Medical Sciences, Tehran, Iran.

* Corresponding Author:
Masoud Mehrpour, MD. MPH.
Address: Department of Neurology, School of Medicine, Firoozgar Hospital, Iran University of Medical Sciences, Tehran, Iran.
Tel: +98 (937) 9874678
E-mail: dr.masoudmehrpour@gmail.com

Background: Myxoma may cause systemic embolization and frequently presents as ischemic stroke.

Case Presentation: There have been debates about whether it is safe to use recombinant tissue plasminogen activator (rt-PA) in patients with cardiac myxoma who referred with ischemic stroke to the hospital's emergency.

Results: The patient was a young case of atrial myxoma with initial presentation of acute cerebral infarction symptoms who was treated with ischemic stroke to the hospital's emergency.

Conclusion: The case provides an evidence of the efficacy and safety of intravenous rt-PA in cases of cardiac myxoma. However, we cannot always expect thrombolytic therapy to be effective, especially in tumor emboli.
1. Introduction

Myxoma, as the most common primary cardiac tumor, may cause systemic embolization and frequently is presented as ischemic stroke (Ekinci & Donnan, 2004). We believe that the administration of recombinant tissue plasminogen activator (rt-PA) for stroke is still controversial in cases of cardiac myxoma, although it is generally recognized as safe for early treatment of acute brain infarction in the emergency rooms. It is still debatable among neurologists in cases of cardiac myxoma with concerning the helpfulness and safety of rt-TPA. In this report, we described a young male who was later found to be a case of atrial myxoma with initial presentation of brain infarction. He was treated with intravenous rt-PA as the first-line therapy. No bleeding or any other complications occurred afterward. On the fourth day of admission, the patient underwent cardiac surgery for the removal of cardiac myxoma and on the tenth day, the patient was discharged in good general condition. After being discharged, he continued using aspirin. One and a half year follow-ups revealed no further brain events or any other complications. Our case provides another evidence of the effectiveness and safety of using intravenous rt-PA in case of cardiac myxoma.

2. Case Presentation

We present a 31-year-old man with no significant past medical history with left-sided sudden hemiparesis which started 2 hours before admission. On admission, his National Institutes of Health Stroke Scale (NIHSS) score was 10. Initial physical examination revealed a body temperature of 37.1°C, pulse rate of 76 bpm, and blood pressure of 125/80 mm Hg. The electrocardiogram showed sinus rhythm. A spiral brain CT scan without contrast was done immediately which was normal. All criteria for intravenous thrombolysis were met. Finding no contraindications, we decided to start thrombolysis. The patient received 0.9 mg/kg rt-PA (a total dose of 58 mg) based on a standard protocol. Door-to-needle time and symptom-to-needle time were 50 and 170 min, respectively after he became stable. Later, brain MRI was performed disclosing hyperintensity of periventricular, centrum semi-oval, and subcortical areas of both sides. Diffusion-weighted MR imaging (DWI) showed restriction of right centrum semi-oval in parietal lobe which confirmed acute infarction (Figure 1). He was admitted to the stroke unit. After 24 hours of thrombolytic therapy, his NIHSS score was 1 due to slight dysarthria. His mo-
tor forces however, recovered completely. The control CT scan was obtained revealing an acute infarction over the left Middle Cerebral Artery (MCA) territory with no evidence of hemorrhage. Aspirin 80 mg/d, clopidogrel 75 mg/d, and prevention of deep venous thrombosis with heparin were started. Transthoracic echocardiogram discovered a large, mobile, ovoid, and heterogeneous mass in the left atrium, attached with a long narrow stalk to the interatrial septum protruding to the left ventricle during diastole, with normal size cardiac chambers and normal ejection fraction (55%) (Figure 2). According to cardiothoracic surgery consultation, dual antplatelet therapy was discontinued and the dose of heparin increased to 900 U/h. On the fourth day of admission, the patient underwent cardiac surgery. The size of the tumor was 5 in 4.5 cm and histologic examination confirmed the diagnosis of myxoma. There were no complications, including bleeding. On the tenth day of admission, the patient was discharged in good general condition while his NIHSS score and Modified Ranking Scale (MRS) score were both zero. After being discharged, he continued using aspirin 80 mg/d. His one and a half year follow-ups were both zero. After being discharged, he continued using aspirin 80 mg/d. His one and a half year follow-ups until now have revealed no further embolic events or any other complications.

3. Discussion

Cardiac myxoma, detected by echocardiography, accounts for 50% of all primary heart tumors and the reason for 0.5% of strokes, mainly in the territory of MCA (Thyagarajan, Kumar, Patel, & Agrawal, 2017; Yuan, & Humuruola, 2015). Cardiac myxoma mainly develops in the left atrium and leads to 35% embolization which frequently affects the central nervous system in ischemic stroke as well as retinal arteries (Iyer, Aung, Awan, Kososky, & Barn, 2016). It has been claimed that compared to the tumor itself, it is the adherent thrombus to the tumor which embolizes more (Herbst et al., 2005; Abascal, Kasznica, Aldea, & Davidoff, 1996; Demaerschalk et al., 2016). We could not determine whether the adherent thrombus or a portion of the tumor itself was the source of cardiac emboli in our case. However, since the intravenous rt-PA was successful in treating this patient, it can be assumed that the blood clot might have been the source of emboli rather than tumoral particles.

Although cardiac mass is not considered as an exclusion criterion in the guidelines and is not a warning in the current FDA labels (Sato, Saji, Kobayashi, Shibazaki, & Kimura, 2016), there have been debates whether it is safe to use rt-PA in patients with underlying cardiac myxoma who are admitted with acute ischemic stroke at emergency rooms. Some reports had stated the risk of intracerebellar hemorrhage after using rt-PA in patients with cardiac myxoma. It is argued that one-third of patients with left atrial myxoma has been diagnosed with cerebral aneurysm (Viganò et al., 2013). These aneurysms are probably caused by tumoral invasion to arterial walls. It is said that these microaneurysms make patients prone to bleeding (Al-Said, Al-Rached, Baesa, Kurdi, Zabani, & Hassan, 2013).

Some authors have reported thrombolysis in ischemic stroke without any intracranial hemorrhage in cases with myxoma so far (Sun, Tai, & Lee, 2011; Chutinet, Roongphiboonsopit, & Suwanwela, 2014; Gassanov et al., 2011) while some others have reported intracranial hemorrhage after using rt-PA in myxoma cases (Kohno et al., 2012; Hatayama et al., 2012; Kulkarni, Yadav, Mustare, & Modi, 2014). One study suggested that using IV rt-PA leads to less intra-cerebellar hemorrhage in young patients and it may cause more hemorrhage in those who are older than 65 years (Kulkarni et al., 2014). To our knowledge, all myxoma cases who experienced intracranial bleeding after IV rt-PA were older than 65 years (Gassanov et al., 2011; Kohno et al., 2012; Hatayama et al., 2012; Kulkarni et al., 2014). Accordingly, our patient was young, 31 years old, and markedly recovered within 24 hours of thrombolysis without any intracerebral hemorrhage. In our case, however, since we did not want to lose time, the injection was performed before the echocardiography, so we did not know about the cardiac myxoma at the time of thrombolysis.

Another fact is that earlier thrombolysis is associated with a lesser chance of symptomatic hemorrhage (Demaerschalk et al., 2016; Gassanov et al., 2011). This was true for our patient since we started thrombolysis within 2 hours of stroke onset which might have reduced the risk.

Intra-atrial injection as an alternative approach has also been suggested in some reports. This invasive approach has the merit of envisioning the vessels directly, thus focal injection can be performed directly only on the occluded vessels. Furthermore, those arteries which aneurysmal are easily visible. This therapy might reduce the hemorrhage risk of thrombolytic therapy in strokes associated with myxoma (Kohno et al., 2012; Chong, Vraaniak, Etienne, Sherman, & Elkind, 2005). This strategy has been successfully reported in some reports in similar cases (Bekavac et al., 1997).

Another significant point in ischemic stroke due to cardiac myxoma is the safe interval between recent stroke and cardiac surgery. Generally, since there is a risk of
recurrent emboli, it seems critical to remove cardiac myxoma as soon as possible. On the other hand, the therapeutic dose of antiocoagulants which is required before cardiac surgery is a matter of concern due to the increased risk of intracerebral hemorrhage in an ischemic brain with vascular dysregulation, especially in patients who have received thrombolytic therapy recently. There have been no clear guidelines in this regard. However, in one study it was recommended to perform open-heart surgery at least 4 weeks after ischemic stroke to reduce the mortality rate (Eishi, Kawazoe, Kuriyama, Kitoh, Kawashima, & Omae, 1995). A recent study suggested early surgery if the territory of the infarct is not too large (Yuan & Humuruola, 2015).

Our case underwent cardiac surgery 90 hours after stroke onset and there were no complications such as massive bleeding. After 10 days of hospitalization, he was completely recovered and was discharged with an MRS of 0.

4. Conclusion

Our case provides another evidence of the efficacy and safety of intravenous rt-PA in cases of cardiac myxoma. However, we cannot always expect thrombolytic therapy to be effective, especially in tumor emboli. Therefore, further research is needed in a larger population to determine safe and effective therapies for brain infarction associated with cardiac myxomas.

Ethical Considerations

Compliance with ethical guidelines

All ethical principles are considered in this article.

Funding

This research did not receive any grant from funding agencies in the public, commercial, or non-profit sectors.

Authors' contributions

Writing – original draft and writing – review & editing: Sara Esmaeili, and Maryam Bahadori; Data curation, investigation, and data analysis: Seyedeh Fahimeh Shojaei; Resources: Mohammad Mojtahae and Masoud Mehrpour.

Conflict of interest

The authors declare no conflict of interest in this study.

References

Abascal, V. M., Kasznica, J., Aldea, G., & Davidoff, R. (1996). Left atrial myxoma and acute myocardial infarction: A dangerous duo in the thrombolytic agent era. Chest, 109(4), 1106-8. [DOI:10.1378/chest.109.4.1106] [PMID]

Al-Said, Y., Al-Rached, H., Baeesa, S., Kurdi, K., Zabani, I., & Hassoan, A. (2013). Emergency excision of cardiac myxoma and endovascular coiling of intracranial aneurysm after cerebral infarction. Case Reports in Neurological Medicine, 2013, 839270. [DOI:10.1155/2013/839270] [PMID] [PMCID]

Bekavac, I., Hanna, J. P., Wallace, R. C., Powers, J., Ratliff, N. B., & Furlan, A. J. (1997). Intra-arterial thrombolysis of embolic proximal middle cerebral artery occlusion from presumed atrial myxoma. Neurology, 49(2), 618-20. [DOI:10.1212/WNL.49.2.618] [PMID]

Chong, J. Y., Vranik, P., Etienne, M., Sherman, D., & Elkind, M. S. V. (2005). Intravenous thrombolytic treatment of acute ischemic stroke associated with left atrial myxoma: A case report. Journal of Stroke and Cerebrovascular Diseases, 14(1), 39-41. [DOI:10.1016/j.jstrokecerebrovasdis.2004.09.002] [PMID]

Chutinet, A., Roongpiboonsopit, D., & Suwanwela, N. C. (2014). Intracerebral hemorrhage after intravenous thrombolysis in patients with cerebral microbleeds and cardiac myxoma. Frontiers in Neurology, 5, 252. [DOI:10.3389/fneur.2014.00252] [PMID] [PMCID]

Demaerschalk, B. M., Kleindorfer, D. O., Adeoye, O. M., Demchuk, A. M., Fugate, J. E., & Grotta, J. C., et al. (2016). Scientific rationale for the inclusion and exclusion criteria for intravenous alteplase in acute ischemic stroke: A statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke, 47(2), 581-641. [DOI:10.1161/STR.0000000000000866] [PMID]

Dong, M., Ge, Y., Li, J., Fu, K., Zhang, L., & Teng, W., et al. (2020). Intravenous thrombolysis for pure pontine infarcts caused by cardiac myxoma: A case report and literature review. International Journal of Neuroscience, 130(6), 635-41. [DOI:10.1080/00207454.2019.1702537] [PMID]

Eishi, K., Kawazoe, K., Kuriyama, Y., Kitoh, Y., Kawashima, Y., & Omae, T. (1995). Surgical management of infective endocarditis associated with cerebral complications: Multi-center retrospective study in Japan. The Journal of Thoracic and Cardiovascular Surgery, 110(6), 1745-55. [DOI:10.1016/S0022-5223(95)70838-2]

Ekinci, E. I., & Donnan, G. A. (2004). Neurological manifestations of cardiac myxoma: A review of the literature and report of cases. Internal Medicine Journal, 34(5), 243-9. [DOI:10.1111/j.1445-0903.2004.00563.x] [PMID]

Gassanov, N., Nia, A. M., Dahir, K. M., Ederer, S., Wedemeyer, I., & Caglayan, E., et al. (2011). Local thrombolysis for successful treatment of acute stroke in an adolescent with cardiac myxoma. The Scientific World Journal, 11, 574530. [DOI:10.1100/tsw.2011.90] [PMID] [PMCID]

Hatayama, S., Ogata, T., Okawa, M., Higashi, T., Inoue, T., & Takanou, K., et al. (2012). [Ischemic stroke induced by a left atrial myxoma (Japanese)]. Brain and Nerve, 64(10), 1175-9. [PMID]

Horbst, M., Wattjes, M. P., Urbach, H., Inhetvin-Hutter, C., Becker, D., & Klockgether, T., et al. (2005). Cerebral embolism from left atrial myxoma leading to cerebral and retinal aneurysms: A case report. American Journal of Neuroradiology, 26(3), 666-9. [PMID]
Iyer, P., Aung, M. M., Awan, M. U., Kososky, C., & Barn, K. (2016). A case of large atrial myxoma presenting as an acute stroke. *Journal of Community Hospital Internal Medicine Perspectives, 6*(1), 29604. [DOI:10.3402/jchimp.v6.29604] [PMID] [PMCID]

Kohno, N., Kawakami, Y., Hamada, C., Toyoda, G., Bokura, H., & Yamaguchi, S. (2012). Cerebral embolism associated with left atrial myxoma that was treated with thrombolytic therapy. *Case Reports in Neurology, 4*(1), 38-42. [DOI:10.1159/000336179] [PMID] [PMCID]

Kulkarni, G. B., Yadav, R., Mustare, V., & Modi, S. (2014). Intravenous thrombolysis in a patient with left atrial myxoma with acute ischemic stroke. *Annals of Indian Academy of Neurology, 17*(4), 455-8. [DOI:10.4103/0972-2327.144038] [PMID] [PMCID]

Sato, T., Saji, N., Kobayashi, K., Shihazaki, K., & Kimura, K. (2016). [A case of cerebral embolism due to cardiac myxoma presenting with multiple cerebral microaneurysms detected on first MRI scans (Japanese)]. *Clinical Neurology, 56*(2), 98-103. [DOI:10.5692/clinicalneurol.cn-000821] [PMID] [PMCID]

Sun, M. C., Tai, H. C., & Lee, C. H. (2011). Intravenous thrombolysis for embolic stroke due to cardiac myxoma. *Case Reports in Neurology, 3*(1), 21-6. [DOI:10.1159/000324095] [PMID] [PMCID]

Thyagarajan, B., Kumar, M. P., Patel, Sh., & Agrawal, A. (2017). Extracardiac manifestations of atrial myxomas. *Journal of the Saudi Heart Association, 29*(1), 37-43. [DOI:10.1016/j.jsha.2016.07.003] [PMID] [PMCID]

Viganò, S., Papini, G. D. E., Cotticelli, B., Valvassori, L., Frigiola, A., & Menicanti, L., et al. (2013). Prevalence of cerebral aneurysms in patients treated for left cardiac myxoma: A prospective study. *Clinical Radiology, 68*(11), E624-8. [DOI:10.1016/j.crad.2013.06.010] [PMID]

Yuan, S. M., & Humuruola, G. (2015). Stroke of a cardiac myxoma origin. *Revista Brasileira de Cirurgia Cardiovascular, 30*(2), 225-34. [DOI:10.5935/1678-9741.20150022] [PMID] [PMCID]
