

LEFT ATRIAL THROMBUS RESOLUTION WITH RIVAROXABAN IN ATRIAL  
FIBRILLATION: A CASE REPORTSergio Agosti<sup>\*1</sup>, MD, PhD, Laura Casalino<sup>2</sup>, MD, PhD, MD, Eugenia Rota<sup>3</sup>, MD, Lorella Pisano<sup>4</sup>, MD, Gabriele Zaccone<sup>1</sup>, MD and Cuzzo Enrico<sup>5</sup>, MD<sup>1</sup>Cardiology Unit, San Giacomo Hospital, Novi Ligure, Alessandria, Italy.<sup>2</sup>Cardiology Unit, ASL 3, Genoa, Italy.<sup>3</sup>Neurology Unit, San Giacomo Hospital, Novi Ligure, Alessandria, Italy.<sup>4</sup>Cardiac Surgery Unit, Brotzu Hospital, Cagliari, Italy.<sup>5</sup>Cardiologist, SCC, Oristano, Italy.**\*Corresponding Author: Dr. Sergio Agosti, MD, PhD**

Cardiology Unit, San Giacomo Hospital, Novi Ligure, Alessandria, Italy.

Article Received on 04/09/2018

Article Revised on 25/09/2018

Article Accepted on 16/10/2018

## ABSTRACT

**Background:** atrial fibrillation is a major cause of thrombus formation within the left atrium (LA) and left atrial appendage (LAA). In patients with LA/LAA thrombus by transesophageal echocardiography, current guidelines recommend vitamin K antagonist treatment. At present, data on the efficacy of direct oral anticoagulants in the resolution of LA/LAA thrombi are scarce. **Case presentation:** we here describe a case of LA thrombus resolution in a patient treated with rivaroxaban. **Conclusions:** our case report adds to the evidence that rivaroxaban is effective in LA thrombus resolution.

**KEYWORDS:** Rivaroxaban; Left atrial thrombus; Direct oral anticoagulants; Non-vitamin K antagonist oral anticoagulants; Transesophageal echocardiography.

## BACKGROUND

It has consistently been demonstrated that direct oral anticoagulants (DOACs) are noninferior to warfarin for the prevention of stroke or systemic embolism in patients with nonvalvular atrial fibrillation (AF).<sup>[1]</sup> However, data on the efficacy of DOACs in the resolution of left atrial/left atrial appendage (LA/LAA) thrombi are scarce, with only a few case reports describing successful LAA thrombus resolution.<sup>[2-5]</sup> Up to date, only rivaroxaban has been evaluated in a prospective, multicenter study in this setting, suggesting that it could be a potential option for the treatment of LA/LAA thrombi.<sup>[6]</sup>

## CASE PRESENTATION

An 82-year-old male patient presented for a follow-up cardiology visit. He had a history of previous tuberculosis, smoking, mild hypercholesterolemia, and was recently diagnosed with AF on ECG. He was on atorvastatin 10 mg.

He was in good general condition, with blood pressure of 110/80 mmHg. Blood testing was normal with a hemoglobin level of 13.2 g/dL (normal range: 12-16 g/dL), and normal renal function with a creatinine level of 0.82 mg/dL (normal range: 0.51-0.95 mg/dL) and a creatinine clearance of 76 mL/min.

The ECG showed AF with a heart rate of 93 bpm.

Transthoracic echocardiography (TTE) revealed no left ventricular dilation, no regional wall motion abnormalities with good global left ventricular systolic function (ejection fraction 62%), moderate mitral regurgitation with some degree of left atrial enlargement (46x55 mm in apical 4-chamber view). A mobile, hyperechoic, pedunculated rounded mass of  $\approx 3$  cm<sup>2</sup> attached to the interventricular septum was observed (Figure 1).

Treatment with rivaroxaban 20 mg daily and bisoprolol 5 mg twice daily was initiated.

The patient was scheduled for transesophageal echocardiography (TEE) and cardiac magnetic resonance (CMR) imaging. CMR was immediately performed and identified the LA mass as a thrombus. After 20 days, repeat TTE pre-TEE showed complete resolution of the LA thrombus, with the patient being asymptomatic and hemodynamically stable. At three-month follow-up, he is in good clinical condition with negative TTE, and on anticoagulation therapy with rivaroxaban.

## DISCUSSION AND CONCLUSION

Nonvalvular AF is known to increase the risk of ischemic stroke and systemic embolism by five-fold, and LA/LAA thrombi are identified on TEE in approximately

10% of patients with nonvalvular AF.<sup>[7]</sup> TEE is currently considered the gold standard diagnostic method for the detection of even small LA/LAA thrombi.<sup>[8]</sup>

DOACs have been shown to be noninferior to vitamin K antagonists in reducing the rate of ischemic stroke and systemic embolism, as a result of their efficacy in preventing LA thrombus formation, which is an important source of embolic events. However, literature data on the efficacy of DOACs in the resolution of thrombi in the left atrium are scarce, and current guidelines still recommend vitamin K antagonist treatment in patients with LA/LAA thrombi.<sup>[9]</sup>

Up to date, only rivaroxaban has been evaluated in a prospective, multicenter study in this setting, suggesting that it could be a potential option for the treatment of LA/LAA thrombi.<sup>[6]</sup> In the X-TRA study, patients most often showed thrombi in the LAA ( $n = 50$ ), whereas LA thrombi were present only in three patients. To the best of our knowledge, this is the first case report describing successful resolution of a LA thrombus with a non-vitamin K antagonist oral anticoagulant.

In our patient, TTE revealed a LA mass attached to the interventricular septum, raising the suspicion of an LA thrombus or atrial myxoma. The patient was scheduled to undergo TEE, which remains the gold standard for visualizing a LAA/LA thrombus, and CMR for better tissue characterization of the mass. However, TEE was not performed because CMR identified the LA mass as a thrombus and repeat TTE pre-TEE documented complete disappearance of the LA thrombus. No evidence of systemic embolization was found and the patient was asymptomatic despite the large thrombus size ( $2.5 \text{ cm}^2$ ), suggesting that rivaroxaban is effective in resolving LA thrombi.

In the context of embolic stroke, two types of thrombus can form, which differ in composition: white thrombus, typically composed of platelet aggregates as occurs in artery-to-artery embolism, or red thrombus, largely consisting of red blood cells and most often developing in the heart. However, platelets may play a critical role in the formation of intracardiac thrombi in patients with nonvalvular AF, similarly to what already documented for AF patients with valvular heart disease. In our patient, it is reasonable to assume that the thrombus had, at least in part, a platelet composition, given the rounded appearance of the mass attached to the endocardial surface.

DOACs do not interfere directly with activation of clotting factor VII, resulting in lower bleeding risk compared with warfarin. However, this may account for the limited efficacy in intracardiac thrombus resolution, though laboratory evidence from animal models suggests that DOACs may prevent platelet activation and aggregation.<sup>[10,11]</sup> In this respect, Li *et al.* described a case of large LAA thrombus resolution with rivaroxaban

in a patient with severe mitral stenosis and AF, lending support to the hypothesis that DOACs may affect platelet aggregation.<sup>[12]</sup>

The effects of rivaroxaban on both red and white thrombi may account for its efficacy in dissolving the LA thrombus in our patient and for the favorable results of the X-TRA study.

In conclusion, our case suggests that rivaroxaban could be a potential option for the treatment of LA/LAA thrombi in AF patients.



**Figure 1: Transthoracic echocardiogram showing a mass attached to the interventricular septum.**

## ABBREVIATIONS

LA: left atrium; LAA: left atrial appendage; DOACs: direct oral anticoagulants; AF: atrial fibrillation; TTE: transthoracic echocardiography; TEE: transesophageal echocardiography; CMR: cardiac magnetic resonance.

## ACKNOWLEDGEMENTS

We thank Paola Luciolli, independent medical writer, who provided editorial assistance and journal styling services prior to submission.

## Funding

No funding was received for this study.

## Availability of data and materials

All data generated or analyzed during this study are included in this published article.

## Authors' contributions

LP was the physician who handled the case, SA was a major contributor in writing the manuscript. All authors read and approved the final manuscript.

**Ethics approval and consent to participate**

Not applicable.

**Consent for publication**

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-in-Chief of this journal.

**Competing interests**

SA has received speaker honoraria from Boehringer Ingelheim, Pfizer, Bayer, Bristol-Myers Squibb, and Daiichi Sankyo. LC has received speaker honoraria from Boehringer Ingelheim, Pfizer, and Bristol-Myers Squibb. GZ has received a speaker honorarium from Boehringer Ingelheim, and Bayer. LP and EC declare that they have no conflict of interest.

**Author details**

1Cardiology Department, San Giacomo Hospital, Novi Ligure, Alessandria, Italy. 2Cardiology Unit, ASL 3, Genoa, Italy. 3Neurology Unit, San Giacomo Hospital, Novi Ligure, Alessandria, Italy. 4Cardiac Surgery Unit, Brotzu Hospital, Cagliari, Italy. 5Cardiologist, SCC, Oristano, Italy

**REFERENCES**

1. Ruff CT, Giugliano RP, Braunwald E, Hoffman EB, Deenadayalu N, Ezekowitz MD, Camm AJ, Weitz JI, Lewis BS, Parkhomenko A, Yamashita T, Antman EM. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. *Lancet*, 2014; 383: 955-62.
2. Ghalyoun BA, Lempel M, Shaaban H, Shamooun F. Successful resolution with apixaban of a massive left atrial appendage thrombus due to nonrheumatic atrial fibrillation: a case report and review. *Ann Card Anaesth*, 2018; 21: 76-77.
3. Vidal A, Vanerio G. Dabigatran and left atrial appendage thrombus. *J Thromb Thrombolysis*, 2012; 34: 545-7.
4. Kawano H, Kohno Y, Izumida S, Tsuneto A, Fukae S, Takeno M, Koide Y, Maemura K. Rivaroxaban therapy resulting in the resolution of right atrial thrombosis resistant to ordinary control with warfarin in a patient with atrial fibrillation. *Intern Med.*, 2015; 54: 601-4.
5. Murakawa Y, Nogami A, Shoda M, Inoue K, Naito S, Kumagai K, Miyauchi Y, Yamane T, Morita N, Mitamura H, Okumura K. Nationwide survey of catheter ablation for atrial fibrillation: the Japanese catheter ablation registry of atrial fibrillation (J-CARAF). A report on periprocedural oral anticoagulants. *J Arrhythm*, 2015; 31: 29-32.
6. Lip GY, Hammerstingl C, Marin F, Cappato R, Meng IL, Kirsch B, van Eickels M, Cohen A. Left atrial thrombus resolution in atrial fibrillation or flutter: Results of a prospective study with rivaroxaban (X-TRA) and a retrospective observational registry providing baseline data (CLOT-AF). *Am Heart J.*, 2016; 178: 126-34.
7. Al Saady NM, Obel OA, Camm AJ. Left atrial appendage: structure, function, and role in thromboembolism. *Heart*, 1999; 82: 547-54.
8. Manning WJ, Weintraub RM, Waksmonski CA. Accuracy of transesophageal echocardiography for identifying left atrial thrombi. A prospective, intraoperative study. *Ann Intern Med.*, 1995; 123: 817-22.
9. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, Castella M, Diener HC, Heidbuchel H, Hendriks J, Hindricks G, Manolis AS, Oldgren J, Popescu BA, Schotten U, Van Putte B, Vardas P; ESC Scientific Document Group. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Eur Heart J.*, 2016; 37: 2893-962.
10. Perzborn E, Heitmeier S, Laux V. Effects of rivaroxaban on platelet activation and platelet-coagulation pathway interaction: in vitro and in vivo studies. *J Cardiovasc Pharmacol Ther*, 2015; 20: 554-62.
11. Solbeck S, Meyer MA, Johansson PI, Meyer AS, Cotton BA, Stensballe J, Schött U, Ostrowski SR. Monitoring of dabigatran anticoagulation and its reversal in vitro by thrombelastography. *Int J Cardiol*, 2014; 176: 794-9.
12. Li Y, Lin J, Peng C. Resolution of massive left atrial appendage thrombi with rivaroxaban before balloon mitral commissurotomy in severe mitral stenosis: a case report and literature review. *Medicine (Baltimore)*, 2016; 95: e5577.