OLGU SUNUMU

Non-valvuler atrial fibrilasyonlu bir hastada azaltılmış doz apiksaban tedavisi altında gelişen kardiyak trombüs olgusu

A case of cardiac thrombosis developed under reduced dose apixaban therapy in a patient with non-valvular atrial fibrillation

Mukadder Levent Çelik[1]
[1] Tuzla Devlet Hastanesi, İç Hastalıkları Kliniği, İstanbul, Türkiye
İletişim: drleventcelik32@gmail.com

ÖZET

Amaç: Atrial fibrilasyon (AF), en sık görülen aritmidir ve sıklığı yaşla birlikte artmaktadır. Kalp kaynaklı pıhtı formasyonuna neden olup inme gibi iskemik komplikasyonlarla sonuçlanabilen, morbidite ve mortalitesi oldukça yüksek irregüler bir kalp ritm bozukluğudur. Tedavisinde ilk etapta hız ve ritm kontrolü sağlanır. Daha sonra tromboemboli ve kanama riski açısından hastalar değerlendirilir ve uygun antikoagülan tedavi düzenlenir. Bu çalışmada apiksaban tedavisi altında iken doz azaltılması gereken bir hastada gelişen kardiyak trombüs vakasını sunmayı amaçladık.

Olgu sunumu: Atrial flutter nedeniyle ablasyon ve geçirilmiş coroner arter bypass grefting öyküsü olan 80 yaşında hipertansif erkek hasta, paroksismal atrial fibrilasyon (PAF) saptanması üzerine sotalol ve apiksaban tedavisi başlanarak takibe alınmış. Tedavi sürecinde gastrointestinal kanaması olması üzerine apiksaban dozu düşürülen hastanın takiplerinde kardiyak trombüs gelişmesi üzerine doz artışı yapıldı fakat trombüsün devam etmesi üzerine apiksaban tedavisi kesilerek varfarin tedavisi başlandı. Kontrol Transözefagial Ekokardiyografik (TEE) incelemede trombüsün kaybolduğu görülen hasta mevcut varfarin tedavisi ile takip edilmek üzere taburcu edildi.

Sonuç: Atrial fibrilasyonlu hastaların antikoagülan tedavisinde, doz ayarlaması ve ilaç değişimi durumlarında tromboemboli gelişimi açısından dikkatli olunmalıdır.

Anahtar Kelimeler: Apiksaban, Atrial fibrilasyon, Kardiyak Trombüs

SUMMARY

Aim: Atrial fibrillation (AF) is the most common arrhythmia and the frequency increases with age. It is an irregular heart rhythm disorder with high morbidity and mortality, which can result in ischemic complications such as stroke resulting from heart-induced clot formation. In treatment, speed and rhythm control is provided in the first step. Patients are then evaluated for thromboembolism and risk of bleeding and appropriate anticoagulant therapy is regulated. In this study, we aimed to present a case of cardiac thrombus developing in a patient whose dose had to be reduced while under apixaban therapy.

Case report: An 80-year-old hypertensive male patient with a history of atrial flutter ablation and coronary artery bypass grafting was diagnosed with paroxysmal atrial fibrillation (PAF), and sotalol and apixaban treatment was initiated. A dose increase was made due to the development of cardiac thrombus in patient whose apixaban dose had to be reduced because of gastrointestinal bleeding, low weight and age progression. Because of the continuation of the thrombus, apixaban therapy was stopped and warfarin treatment was started. Control transesophageal echocardiographic (TEE) examination revealed that the thrombus had disappeared and the patient was discharged to follow up with the current warfarin treatment.

Conclusion: In anticoagulant therapy of patients with atrial fibrillation, thromboembolic complications should be kept in mind while dose adjustment and drug exchange.

Keywords: Apixaban, Atrial Fibrillation, Cardiac Trombus

INTRODUCTION

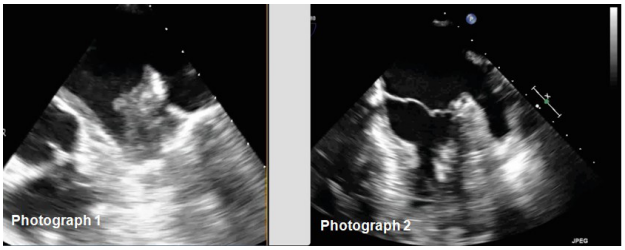
Atrial fibrillation (AF) is the most common cardiac rhythm disturbance seen in 1-2% of the general population. Atrial fibrillation causes cardiac thrombosis and thromboembolic events and is clinically important because of causing serious morbidity and mortality. In atrial fibrillation, anticoagulation is recommended for the patients who are at mid or high risk for thromboembolic complications [1,2]. Cardiac thrombus due to atrial fibrillation develops most commonly in the left atrium, transesophageal echocardiography (TEE), a method with high specificity and sensitivity, is used for diagnosis [3]. Novel oral anticoagulant agents (NOACs) are preferred in non-valvular AF patients [4], because of the lower risks of bleeding, easier dose adjustment, and no need for laboratory follow-up. Currently, four agents have been used frequently in the treatment of non-valvular AF; dabigatran, apixaban, rivaroxaban and edoksaban. But; in the usage of these medicines, antidote to be used in emergencies (except rivaroxaban) is a problem.

In this study, we will discuss the occurrence of a cardiac thrombosis in a patient who was undergone a dose reduction due to hemorrhage, age and weight, while taking apixaban therapy with the diagnosis of non-valvular AF.

CASE REPORT

An 80-year-old male patient was admitted to our clinic due to fatigue and palpitation. It was learnt that 10 years ago he was undergone coronary artery bypass grafting operation, 2 years ago undergone atrial flutter classic ablation and had a diagnosis of non-valvuler paroxysmal atrial fibrillation. It was learnt that sotalol 20 mg twice daily and apixaban 5 mg twice daily treatment was initiated when AF was diagnosed and was determined that the dose of apixaban was reduced to 2.5 mg twice daily because of weight loss, elder age and gastrointestinal hemorrhage 6 months ago.

On physical examination; blood pressure: 145/80 mm/Hg, pulse: 145 bpm, fever: 36,5°C, Sat02: 98%, pulse deficit (+) was detected, no additional sound was heard in cardiac auscultation and other systemic examination was found normal. Tests including complete blood count, electrolytes, HbA1c and liver function to eliminate potential causes of fatigue were within normal limits. An electrocardiogram confirms the diagnosis of atrial fibrillation with a rapid ventricular response of 135 bpm. Cardioversion is planned for the patient. The patient underwent TEE examination before cardioversion. TEE showed a disorganized, partially mobile and hypoechogenic mass that compatible with trombus in the left atrial appendix (Photograph 1). The patient's apixaban dose was increased to 2x5 mg. After 1 week of therapy, we performed a second TEE which showed that the atrial thrombus remained unchanged. Because of the continuation of thrombus in control TEE examination after 4 weeks, apixaban therapy was switched to warfarin. A third TEE performed at the 6 week follow-up visit revealed no thrombotic mass (Photograph 2).



The patient was discharged with suggestions to be monitored under warfarin therapy with frequent INR control.

EEG de sol fronto parietal bölgelerde periodik lateralizan epileptiform deşajların varlığı izlenmiştir. Valproat tedavisine rağmen nöbeti devam etme eğiliminde olan hastaya lacosamide 200mg/gün eklenmiş ve nöbet kontrol altında alınmıştır. Hastanın rutin beyin omurilik sıvısı (BOS) parametreleri normal sınırlarda bulundu. BOS otoimmün ensefalit paneli (VGCC, VGKC NMDA, GABA, LGI1 reseptör antikorları) ve Plazma paraneoplastik panel anti-Hu, anti-Yo, anti-Ri, anti-Ma2, CV2, amfifizin antikorları ile antinükleer antikor ve ENA (extractable nuclear antigen antibody) profili negatif bulundu. Bir ay sonra çekilen MRG sinde lezyonlarda belirgin gerileme izlendi (Resim 4). Hasta minimal bilinç düzeyinde, quadriparezik olarak ve ventilatör desteğinde, birbuçuk yıl yaşamını devam ettirebilmiş, sanrasında pnömoni ve komplikasyonlarına bağlı olarak kaybedilmiştir.

DISCUSSION

AF is the most common persistent arrhythmia and is closely related to ischemic stroke and mortality. This dysrhythmia can trigger heart failure, also causes intracardiac thrombosis formation and causes ischemic events such as paralysis [5]. In addition to speed and rhythm control, inhibition of clot formation is the main goal in AF treatment. NOACs can be used in non-valvular AF treatment. In a meta-analysis, NOACs agents were also reported to have a similar effect on warfarin in non-valvular AF and safer in risk of bleeding [6].

However, as in warfarin, dosing may be necessary in

NOACs depending on factors such as age, weight, and renal function. According to the current guidelines, the recommended dose for apixaban is 5 mg twice daily; it is recommended to administer 2,5 mg twice daily by reducing the daily dose if two of followings are positive; the patient's age is 80 years and over, the weight is 60 kg or less, and creatinine level is 1.5 mg/dl and above [7,8].

In a cohort study conducted between 2011 and 2016, non-valvular AF patients under low-dose NOACs treatment were followed, reported to have higher ischemic stroke and systemic embolic events in patients using apixaban, but this was not statistically significant [9]. In an another cohort study; it has been reported that there is no significant difference in the risk of stroke and thromboembolism in patients using standard and reduced dose NOACs [10].

In our patient, dose reduction (2.5 mg twice daily) was performed due to age, weight and gastrointestinal bleeding and then complicated with cardiac thrombus in follow-up. However, it has been reported in the literature that thrombus resolution was provided with reduced dose apixaban therapy in a cardiac thrombus patient [11]. As seen in the studies, it has been reported that apixaban is an effective anticoagulant in routine and reduced doses, to reduce intracranial hemorrhage and thromboembolism risk.It is also a good option in the treatment of venous thromboembolism.

In our case, a reduced dose of apixaban therapy resulted in cardiac thrombosis, and even though the dose was increased (routine dose), there was no resolution in thrombus. However, in our case, warfarin was effective not only for preventing thrombus formation but also for favoring thrombus resolution when apixaban treatment had failed. By reporting this unexpected situation; we want to note that thromboembolic events are multifactorial and that there is a need for customized treatments for patients. There is a need for detailed, extended studies of NOACs treatments and risks-complications.

CONCLUSION

It should be kept in mind that patients who have begun to undergo apixaban treatment due to non-valvular AF may experience undesirable events such as cardiac thrombosis due to dose reduction and drug exchange..

KAYNAKLAR

1. Gage BF, Waterman AD, Shannon W, et al. Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. JAMA. 2001;285:2864–2870.
2. Furie KL, Goldstein LB, Albers GW, et al. Oral antithrombotic agents for the prevention of stroke in nonvalvular atrial fibrillation: a science advisory for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2012;43:3442–3453.
3. Vahanian A, Baumgartner H, Bax J, et al. Guidelines on the management of valvular heart disease: The Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology. Eur. Heart J. 2007;28:230–268.
4. Agnelli G, Buller HR, Cohen A, et al. Oral apixaban for the treatment of acute venous thromboembolism. N. Engl. J. Med. 2013;369:799–808.
5. Ezzeldin M, Sáez-Peñataro J, Carné X. Positioning the New oral Anticoagulants for prevention of stroke in patients with non-valvular atrial fibrilation. Clin. Ther. 2015;37:e116.
6. Ruff CT, Giugliano RP, Braunwald E, et al. 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;383:955–962.
7. Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Europace. 2016;18:1609–1678.
8. Cohen AT, Hamilton M, Bird A, et al. Comparison of the Non-VKA Oral Anticoagulants Apixaban, Dabigatran, and Rivaroxaban in the Extended Treatment and Prevention of Venous Thromboembolism: Systematic Review and Network Meta-Analysis. PLoS One. 2016;11:e0160064.
9. Nielsen PB, Skjøth F, Søgaard M, et al. Effectiveness and safety of reduced dose non-vitamin K antagonist oral anticoagulants and warfarin in patients with atrial fibrillation: propensity weighted nationwide cohort study. BMJ. 2017;356:j510.
10. Staerk L, Gerds TA, Lip GYH, et al. Standard and reduced doses of dabigatran, rivaroxaban and apixaban for stroke prevention in atrial fibrillation: a nationwide cohort study. J. Intern. Med. [Internet]. 2017; Available from: http://dx.doi.org/10.1111/joim.12683.
11. Abubakar H, Shokr M, Subahi A, et al. Reduced dose apixaban resolving dual cardiac chamber thrombi in a patient with ischaemic cardiomyopathy in sinus rhythm. BMJ Case Rep. [Internet]. 2017;2017. Available from: http://dx.doi.org/10.1136/bcr-2017-220922.