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Cardiovascular Disease Associated with the Chronic Use of Ergotamine: A Case Report

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ABSTRACT

Ergotamine and its derivatives were used for multiple diseases; in the nineties, its use in association with caffeine was considered a standard treatment for migraines, although it has been in decline, due to the evidenced toxic effects related to its chronic use including vascular, cardiovascular and central nervous system manifestations. In this article is reported a case of a 59-year-old female with chronic use of caffeine plus ergotamine for more than 20 years; afterwards she develops peripheral artery disease, severe mitral and tricuspid valve regurgitation with requirement of valve replacement. In the absence of past cardiovascular history and rheumatic fever, its clinical evolution and pathology results are associated with ergotism.

Keywords: Ergotamine, caffeine, ergotamine drug combination, valvular disease, cardiovascular disease.

Conflicts of interests

The authors have no conflicts of interests to declare.

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INTRODUCTION

Migraine is a common disease with a prevalence of 4-9.5% in men and 11.2-25% in women, with a lifetime prevalence of 8%. It affects more than 10% of the worldwide population (1), and there are multiple therapeutic options such as non-specific drugs (eg. NSAIDs, etc.) and specific treatments like triptans, D2 receptor antagonists, ergotamine and its derivatives, which can double the risk of cardiovascular events, and even increase them up to 8-times-fold if are used concomitantly with other cardiovascular medications.(2) Ergotamine and its derivatives were used for multiple diseases; since 1936 there has been cases of necrosis and gangrene related to its use, (3) reason why its was progressively limited and recommended at lower doses to treat migraine. Until now cardiovascular disease due to ergotamine use is infrequent and unknown.

CLINICAL CASE

59-year-old female patient, with a long-standing pathological history of migraine (20 years), aortic arterial stenosis in the iliac bifurcation, aorto-femoral bypass surgery in 2007 in treatment with warfarin 5 mg daily and self-medicated caffeine/ergotamine, up to 8 tablets daily, since 30 years ago. Patient consulted due to progressive dyspnea, that started several weeks ago and impaired ability to exercise, with no other associated symptoms. In the physical examination was found a "murmur". Complementary studies were performed; in the transthoracic echocardiogram was documented a good bi-ventricular function with severe tricuspid and mitral valve insufficiency (Figure 1). Mitral valve was replaced and tricuspid valve plasty was made, and in the absence of a history of previous rheumatic fever and cardiovascular risk factors, the valve that was removed was taken to pathology analysis. It finally reported dense fibrous connective tissue with areas of myxoid degeneration. No vegetations, signs of malignancy or dysplasia

were observed, neither inflammation, calcifications, or necrosis (Figure 2).

DISCUSSION

Ergotamine is an ergot alkaloid, used for the prevention of vascular headaches such as migraine and cluster headache. Its prolonged or excessive use is associated with a high risk of ergotism, gangrene or drug dependence; given the decreasing use of these drugs resulting from the associated adverse effects and appearance of new therapies, the cardiovascular alterations associated with the use of ergotamine are less known.(10) As a partial agonist of tryptaminergic receptors (including 5HT₂ receptors) and several alpha adrenergic receptors in blood vessels and various types of smooth muscle, (8,11) there is more evidence of vascular events than cardiac events (valvular); (2) direct valve involvement is more common in patients with chronic exposure. (4)

In the presented case, the patient had a chronic exposure to high doses of ergotamine for partial control of headache and as a consequence she developed a vascular and cardiac complication with an interval of ten years apart. Although ergot can affect all the vessels of the body as reported by Liegl, et al., (11) the direct vasoconstrictor effect associated with ergotism is curiously directed at medium-sized vessels, particularly the external iliac artery and the femoral superficial artery, which concur with the presentation in the patient. Important to highlight that despite this event, the patient continued with the use of ergotamine, which we assume, inevitably lead to valvular heart disease, in this case a concomitance of mitral and tricuspid valve insufficiency, that has been previously described by Rasmussen VG, et al. (9) Even though there are no molecular studies, retrospective studies or long-term follow-ups with statistically significant power, the finding of dense fibrous connective tissue with areas of myxoid degeneration is described in several

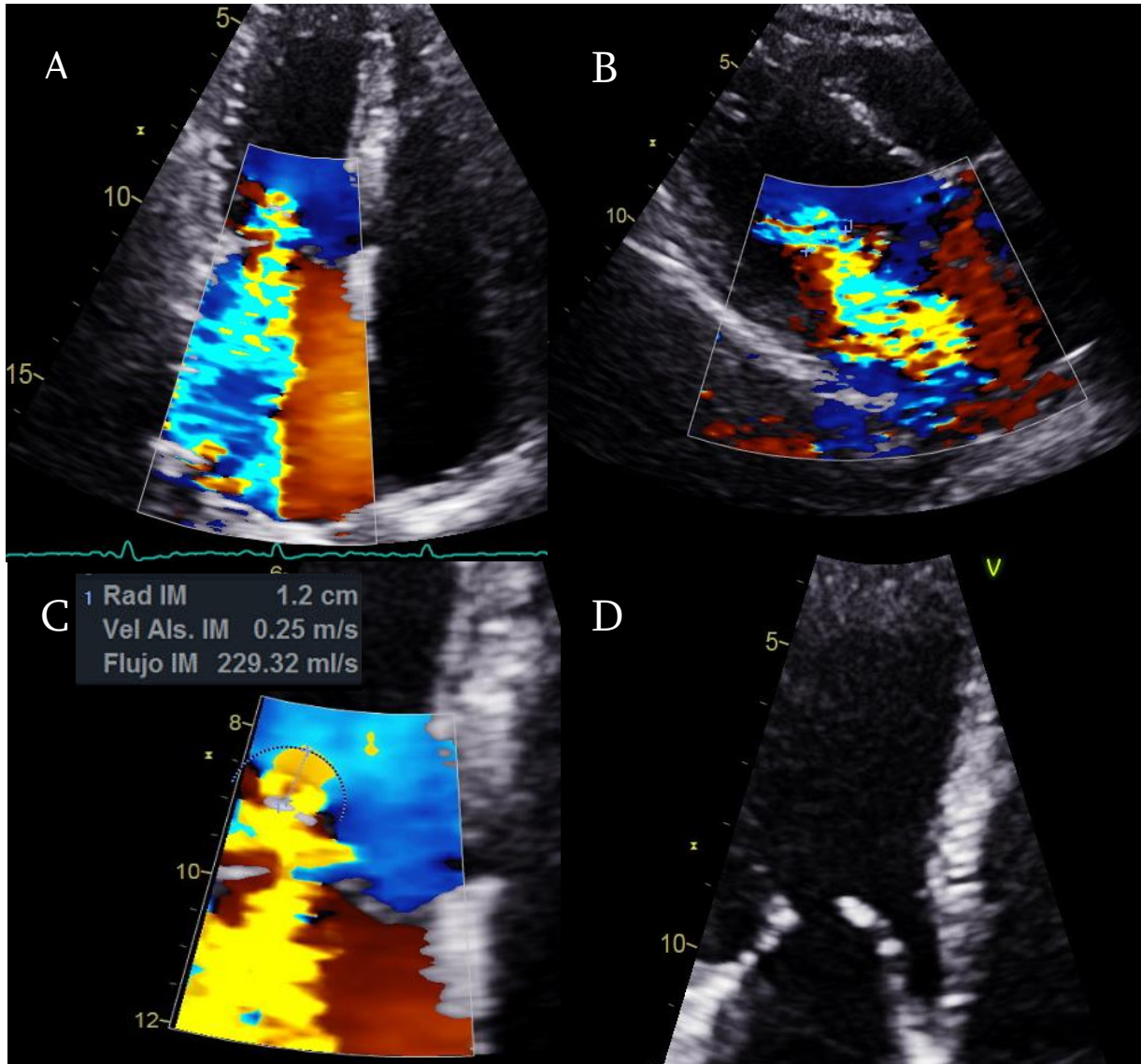


Figure. 1. Transthoracic Echocardiogram. Mitral regurgitation. In A, Doppler image that occupies more than 50% of the left atrium. In B, vena contracta of 12 mm. In C, radius of convergence zone of 12 mm, In D, appearance of the valve with opening in dome.

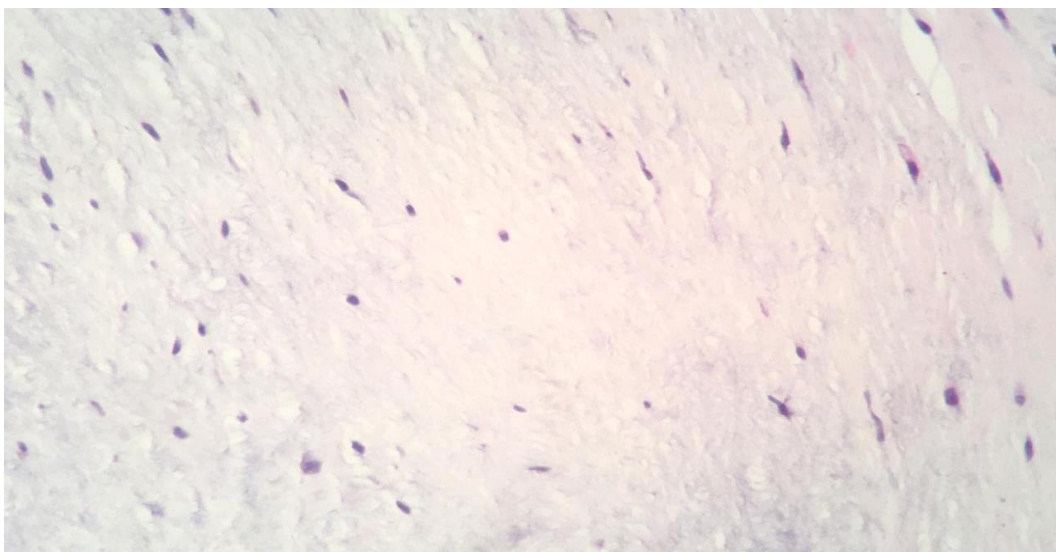


Figure 2. Cardiac valve shows marked stromal myxoid degeneration (H&E 400X)

papers (12-14) and is considerably similar to the case reported by Lazopoulos, et al. (5)

Chronic ergotamine use has been described as causing an irregular proliferation of myofibroblasts in an avascular myxoid matrix in cardiac valves due to the mitotic activity of high levels of serotonin and other vasoactive amines that affect the cardiovascular system, similar to carcinoid tumors. (4) Ergot-derived agents interfere with the serotonin metabolism and activate the 5-HT_{2B} receptors, which are found in heart valves and other structures such as the pleura, peritoneum and pericardium. (5) Valvular heart disease can also be accompanied by myocardial ischemia, pain, claudication and ischemia in upper or lower limbs or a combination of the previous ones, and sometimes symptoms related to heart failure are the ones that lead the patient to consult. (6,7) This pathophysiological event is mediated by the stimulation of alpha adrenergic receptors in the smooth muscle, leading to an important vasospasm and loss of endothelial integrity; (8) some authors have tried to screen this population, Rasmussen VG, et al. evaluated 138 patients who received treatment with ergotamine-derived agonists and described 25% of patients with some degree of valvular involvement, found severe aortic insufficiency (n = 4), moderate aortic insufficiency (n = 12), mitral (n = 3) and tricuspid valve insufficiency (n = 5). Two patients had a coexisting mitral insufficiency and moderate tricuspid valve insufficiency. (9) It has been described an important association, but until now it is not possible to determine which dose and treatment length produce these injuries and if it is possible the regression of the valvular lesions after the therapy withdrawal. Therefore, the surgical option is the viable alternative in patients with impaired functional classification and worsening of heart failure symptoms.

The purpose of this case report is to increase the awareness of the clinicians about this possible complication; in patients with this treatment it is mandatory to regularly monitor the cardiovascular system, and even more in those patients with a chronic use of ergotamine, in whom is fundamental the auscultation. If the physical exam findings include murmurs, the treatment should be discontinued, and the patient should be followed to evaluate the cardiac function with an echocardiogram; it will be necessary to switch to therapies which are now first-line options such as the triptans and the NSAIDs. (15) Until there is more available data about the true prevalence of this undetermined side effect, physicians should be aware of its impact to count with diagnostic suspicion and avoid in young patients this preventable morbidity. Given these considerations, is of vital importance to detect the patients who present an abusive use of ergot derivatives not only to initiate an adequate prophylactic management for migraine and change the crisis treatment to triptans or other kinds of drugs, but also to carry out an appropriate screening, focused on the common complications derived from the chronic use of these medications.

REFERENCES

1. Minen MT, Younger DS. Epidemiology of Migraine. *Neurol Clin.* 2016;34(4):849-861. doi:10.1016/j.ncl.2016.06.011
2. Roberto G, Raschi E, Piccinni C, et al. Adverse cardiovascular events associated with triptans and ergotamines for treatment of migraine: Systematic review of observational studies. *Cephalalgia.* 2015;35(2):118-131. doi:10.1177/0333102414550416
3. Katz AI, Massry SG. Arteriospasm After Ergotamine Tartrate in Infectious Hepatitis. *Arch Intern Med.* 1966;118(1):62-64. doi:10.1001/archinte.1966.00290130064011
4. Zanettini R, Antonini A, Gatto G, Gentile R, Tesei S, Pezzoli G. Regression of cardiac valvulopathy related to ergot-derived dopamine agonists. *Cardiovasc Ther.* 2011;29(6):404-410. doi:10.1111/j.1755-5922.2010.00169.x

5. Lazopoulos G, Papaioannou G, Kantartzis M. Cardiac surgery for ergotamine-induced multivalvular heart disease. *Thorac Cardiovasc Surg.* 2013;61(5):435-437. doi:10.1055/s-0032-1331580
6. Donnet A, Braunstein D, Pradel V, et al. Ergot Use and Overuse: A Pharmacoepidemiology Retrospective Cohort Study. *Headache.* 2016;56(3):547-554. doi:10.1111/head.12776
7. Roithinger FX, Punzengruber C, Gremmel F, Hinterreiter M, Holzner F, Pachinger O. Myocardial infarction after chronic ergotamine abuse. *Eur Heart J.* 1993;14(11):1579-1581. <http://www.ncbi.nlm.nih.gov/pubmed/8299645> . Accessed April 5, 2018.
8. Schiff PL. TEACHERS' TOPICS Ergot and Its Alkaloids HISTORY OF ERGOT. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1637017/pdf/ajpe98.pdf>. Accessed April 5, 2018.
9. Rasmussen VG, Poulsen SH, Dupont E, Østergaard K, Safikhany G, Egeblad H. Heart valve disease associated with treatment with ergot-derived dopamine agonists: A clinical and echocardiographic study of patients with Parkinson's disease. *J Intern Med.* 2008;263(1):90-98. doi:10.1111/j.1365-2796.2007.01874.x
10. Martínez Quintana E, Llorens León R, Redondo Martínez E, Nieto Lago V, Jiménez Cabrera F, Gross Kastanovitz E. Valvular Heart Disease Associated With Ergotamine. *Rev Española Cardiol (English Ed.* 2005;58(1):97-99. doi:10.1016/S1885-5857(06)60238-7
11. Claudia A. Liegl, BSc Michael A. McGrath, MD F. Ergotism: Case Report and Review of the Literature. *Int J Angio.* 2016:e8-e11. doi:10.1542/peds.113.4.e380
12. Austin SM, El-Hayek A, Comianos M, Tamulonis DJ. Mitral valve disease associated with long-term ergotamine use. *South Med J.* 1993;86(10):1179-1181. <http://www.ncbi.nlm.nih.gov/pubmed/8211344> . Accessed April 5, 2018.
13. Rothman RB, Baumann MH, Savage JE, et al. Evidence for possible involvement of 5-HT(2B) receptors in the cardiac valvulopathy associated with fenfluramine and other serotonergic medications. *Circulation.* 2000;102(23):2836-2841. <http://www.ncbi.nlm.nih.gov/pubmed/11104741>. Accessed April 5, 2018.
14. Rasmussen VG, Poulsen SH, Dupont E, Ostergaard K, Safikhany G, Egeblad H. Ergotamine-derived dopamine agonists and left ventricular function in Parkinson patients: systolic and diastolic function studied by conventional echocardiography, tissue Doppler imaging, and two-dimensional speckle tracking. *Eur J Echocardiogr.* 2008;9(6):803-808. doi:10.1093/ejehocard/jen160
15. Loder E, Burch R, Rizzoli P. The 2012 AHS / AAN Guidelines for Prevention of Episodic Migraine : A Summary and Comparison With Other Recent. 2012:930-945. doi:10.1111/j.1526-4610.2012.02185.

