

**Case Report**

# Treating the Brain But Forgetting the Heart: Mitral Valvular Disease Cabergoline Induced

**Randa Tabbah<sup>\*</sup>, Hamid Bayeh, Raffy Karaminassian**

Department of Cardiology, Holy Spirit University, Kaslik, Lebanon

**Email address:**

randa\_22tabbah@hotmail.com (R. Tabbah), bayehmd@gmail.com (H. Bayeh), raffykmd@yahoo.fr (R. Karaminassian)

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**Abstract:** Drug induced valvular heart disease is a forgotten entity of valvular disease, sometimes underdiagnosed or even misdiagnosed. The majority of drugs found to induce this kind of disease have a common pharmacological action on a specific serotonin receptor-the 5HT<sub>2B</sub> receptor. The typical echocardiographic features in these cases are mild to moderate thickening and restriction of the valve with no commissural fusion nor calcification which is the main cause of valvular regurgitation. These findings are not coherent with rheumatic valvular disease. We described a case of a 36years old female with a past medical history of hyperprolactinemia treated with low dose of cabergoline for 9 months, presenting for dyspnea on minimal exertion and palpitation. She consulted a cardiologist that discovered a systodiastolic loud murmur on apical area. A cardiac ultrasound was done revealing a mitral valve disease with moderate leaflet thickening and restriction with no commissural fusion nor calcification with a severe eccentric mitral regurgitation grade 3+ due to tenting and malcoaptation of the valve during diastole. Rheumatic and degenerative valve disease were ruled out. The final diagnosis was a drug induced valvular heart disease and more specifically a cabergoline induced mitral valve disease acting on the serotonin receptors 5HT<sub>2B</sub>. Patient was sent for surgery. Early diagnosis with a good physical examination and current echocardiographic follow up in patient with hyperprolactinemia with even low dose of cabergoline and short term treatment is suggested.

**Keywords:** Cabergoline, Drug Induced, Mitral Valve, Hyperprolactinemia, Leaflet Thickening, Tenting

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## 1. Introduction

Drug induced valvular heart disease is a forgotten entity of valvular disease, sometimes underdiagnosed or even misdiagnosed. The majority of drugs found to induce this kind of disease have a common pharmacological action on a specific serotonin receptor the 5HT<sub>2B</sub> receptor [1]. Indeed, these drugs have a high affinity for these receptors commonly present on valves, leading to valvular thickening and restriction due to abundant extracellular matrix of glycosaminoglycans and collagen, which increase mitogenesis and fibroblast proliferation. [2, 3]

Echocardiography is the golden standard for the diagnosis of this type of valvular disease. [4]

Drugs causing this described entity are: migraine drugs as Methysergide and ergotamine, anti-obesity drugs as

fenfluramine and dexfenfluramine, benfluorex for obesity, diabetes and hypertriglyceridemia, treatment for Parkinson disease the ergot-derived dopaminergic agonists [5], ecstasy and cabergoline for hyperprolactinemia [6, 7].

## 2. Clinical Case

A 36 year old female patient with no past medical history only pituitary disease, hyperprolactinemia treated with low dose Cabergoline (dostinex) for 9 months and she was started lately on oral contraceptive pills for birth control.

Patient presented to the emergency department with dyspnea on minimal exertion, intermittent palpitations and atypical chest pain for several times. Every time EKG was done revealing sinus rhythm with no ischemic changes and normal cardiac enzymes and the patient was always

discharged home diagnosed as a panic attack.

Patient was referred to a cardiologist for further investigation. Physical exam revealed a systolodiastolic loud murmur in the apical area.

Cardiac ultrasound was done revealing: (Figure 1).

Mitral valve disease with moderate leaflet thickening and restriction with no commissural fusion nor calcification with a severe eccentric mitral regurgitation grade 3+ due to tenting and malcoaptation of the valve during diastole. Let's notice also a shortening of the chordae tendineae. Mean mitral valve gradient was at 18 mmHg overestimated due severe mitral regurgitation and tachycardia and a maximum gradient of 38 mmHg.

PISA radius > 1cm, a regurgitant fraction >50%, and a regurgitant volume >60ml. Let's notice also a reversal systolic pulmonary venous flow specific in severe mitral regurgitation.

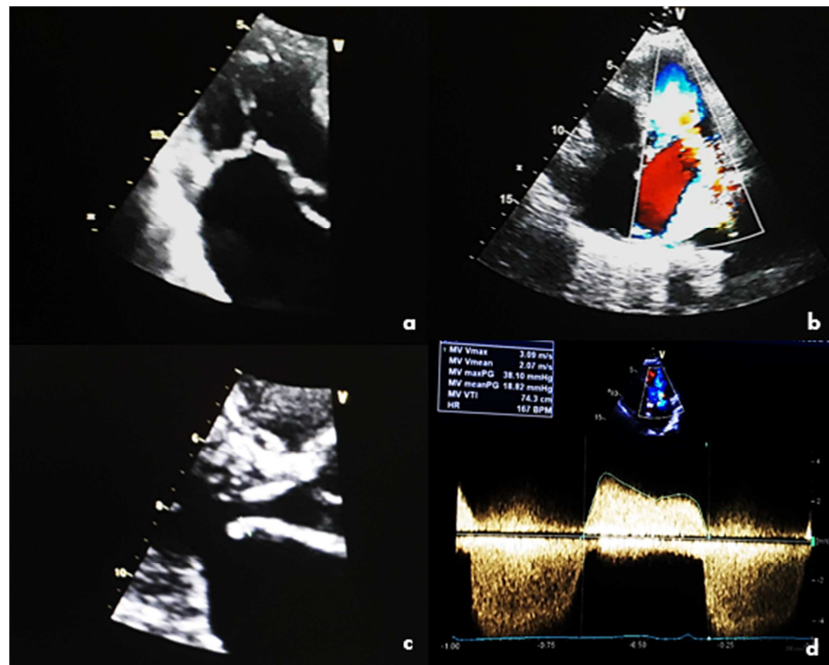
The left ventricular function is preserved with diastolic dysfunction and increased left ventricular end diastolic

pressure with signs of pulmonary hypertension. Let's also notice a tricuspid regurgitation grade 2 with a systolic pulmonary artery pressure > 60mmHg. In addition, a moderate left atrium enlargement is noticed.

Patient denied any rheumatic causes since infancy and even the echocardiographic features didn't match a rheumatic disease: no commissural fusion was noticed nor any other valvular involvement. Furthermore, no signs of degenerative disease because patient is mainly young with no calcification on valves. No systemic nor infiltrative disease were seen. So a final diagnosis was drug induced valvular disease described in rare cases after long courses of cabergoline treatment for hyperprolactinemia.

Furthermore, patient had an echocardiography 1 year ago with no severe valvular disease, so it's a rapidly progressive disease.

Patient was sent for surgery.



**Figure 1.** Echocardiographic findings.

- a. Four chambers: Thickening and restriction of the mitral valve leaflets
- b. Four chambers: Doppler indicated a severe eccentric mitral regurgitation
- c. Parasternal long axis: (PLAX): Thickening and restriction of the mitral valve leaflets
- d. Mitral valve gradient and regurgitation indicating a severe mitral disease

### 3. Discussion

The typical echocardiographic features in these cases are mild to moderate thickening and restriction of the valve with no commissural fusion nor calcification which is the main cause of valvular regurgitation. These findings are not coherent with rheumatic valvular disease [2, 7].

These findings are similar to our described case.

The cabergoline induced valvular disease is a described entity. After a long course of the drug with high doses, these findings can be more prominent and devastating especially in

Parkinson disease patients due to the need of higher doses. A meta-analysis in 2007 detected severe grade of valvular heart disease in about 1% of cabergoline-treated patients for Parkinson disease [8]. Let's notice that our patient was treated for 9 months for hyperprolactinemia with low dose of this agent. A cross-sectional study done in 2008 concluded that Cabergoline at doses sufficient to suppress hyperprolactinaemia for a period of 3-4years was not associated with an increased risk of clinically significant valvular regurgitation causing symptoms [9].

However, our patient had been treated with cabergoline for

a short term with low doses but have a devastating valvular disease.

A prospective study in 2013 [10], noted that cabergoline is not associated with an increase in valvular heart disease, no relationship to the treatment dose or duration.

The mitral valve tenting area could be a useful parameter for predicting the development of valve disease. It could be wise to perform echocardiography before initiating the treatment and no need to perform ultrasound after year because severe disease will need time to be established. It is more reasonable to switch to another drug in case of severe disease.

In 2011 Endocrine Society guidelines added as a remark for the management of hyperprolactinaemia with cabergoline that echo cardiograms might be necessary for individuals on high-dose cabergoline treatment, but those on low doses will probably not need regular echocardiographic workup. A cross-sectional study in the UK in 2014 demonstrated the same results concerning the association between the drug and valvular disease. [11]

Recently, the need for a specific protocol to identify patients at risk of valvular disease after treatment with cabergoline is important. A 2015 review of the literature and a prospective study demonstrated that the incidence of clinically significant valvular heart disease is low in the absence of a murmur in these category of patients, so in this review they suggest to screen these patients only by physical examination and echocardiogram should be reserved to patients with audible murmur as in our case and those treated for more than 5 years at high doses of cabergoline. [12]

Moreover, drug induced valvulopathy is a condition that includes changes in the functionality and morphology of the valves with thickening and restriction [13, 14]. The differential diagnosis is difficult, but specific echocardiographic pattern are needed to lead the way. Many drugs causes this condition, one of them is cabergoline described in this case. [15, 16]

## 4. Conclusion

We described a case of a severe mitral valve disease gabergoline induced in a young patient with hyperprolactinemia. Early diagnosis with physical examination and close follow up with cardiac ultrasound is mandatory even with low dose of cabergoline and short term treatment. The need to think about this diagnosis is important when having patients with atypical presentation with thickening and restriction of the valves.

## References

- [1] Fielden MR, Hassani M, Uppal H, Day-Lollini P et al. Mechanism of subendocardial cell proliferation in the rat and relevance for understanding drug-induced valvular heart disease in humans. *Exp Toxicol Pathol.* 2010 Nov; 62 (6): 607-13.
- [2] Andrejak M1, Tribouilloy C. Drug-induced valvular heart disease: an update. *Arch Cardiovasc Dis.* 2013 May; 106 (5): 333-9.
- [3] Hofmann C1, Penner U, Dorow R, Pertz HH et al. Lisuride, a dopamine receptor agonist with 5-HT2B receptor antagonist properties: absence of cardiac valvulopathy adverse drug reaction reports supports the concept of a crucial role for 5-HT2B receptor agonism in cardiac valvular fibrosis. *Clin Neuropharmacol.* 2006 Mar-Apr; 29 (2): 80-6.
- [4] Bhattacharyya S1, Schapira AH, Mikhailidis DP, Davar J. Drug-induced fibrotic valvular heart disease. *Lancet.* 2009 Aug 15; 374 (9689): 577-85.
- [5] Fietzek UM, Riedl L, Ceballos-Baumann AO. Risk assessment and follow-up of valvular regurgitation in Parkinson patients treated with cabergoline. *Parkinsonism Relat Disord.* 2012 Jun; 18 (5): 654-6.
- [6] Elangbam CS. Drug-induced valvulopathy: an update. *Toxicol Pathol.* 2010 Oct; 38 (6): 837-48.
- [7] Vallette S1, Serri K, Serri O. Cabergoline therapy for prolactinomas: is valvular heart disease a real safety concern? *Expert Rev Cardiovasc Ther.* 2010 Jan; 8 (1): 49-54.
- [8] Simonis G, Fuhrmann JT, Strasser RH. Meta-analysis of heart valve abnormalities in Parkinson's disease patients treated with dopamine agonists. *Mov Disord* 2007; 22: 1936-42.
- [9] Wakil A, Rigby AS, Clark AL, Kallvikbacka-Bennett A, Atkin SL. Low dose cabergoline for hyperprolactinaemia is not associated with clinically significant valvular heart disease. *Eur J Endocrinol.* 2008 Oct; 159 (4): R11-4.
- [10] Cordoba-Soriano JG, Lamas-Oliveira C, Hidalgo-Olivares VM, Tercero-Martinez A et al. Valvular heart disease in hyperprolactinemic patients treated with low doses of cabergoline. *Rev Esp Cardiol (Engl Ed).* 2013 May; 66 (5): 410-2.
- [11] Drake WM, Stiles CE, Howlett TA, Toogood AA et al. A cross-sectional study of the prevalence of cardiac valvular abnormalities in hyperprolactinemic patients treated with ergot-derived dopamine agonists. *J Clin Endocrinol Metab.* 2014 Jan; 99 (1): 90-6.
- [12] Caputo C, Prior D, Inder WJ. The need for annual echocardiography to detect cabergoline-associated valvulopathy in patients with prolactinoma: a systematic review and additional clinical data. *Lancet Diabetes Endocrinol.* 2015 Nov; 3 (11): 906-13.
- [13] Manolis AA, Manolis TA, Mikhailidis DP, Manolis AS. Cardiovascular safety of oncologic agents: A double-edged sword even in the era of targeted therapies - part 1. *Expert Opin Drug Saf.* 2018 Sep; 17 (9): 875-892.
- [14] Tselios K, Deeb M, Gladman DD, Harvey P, Urowitz MB. Antimalarial-induced cardiomyopathy: a systematic review of the literature. *Lupus.* 2018 Apr; 27 (4): 591-599.
- [15] Koshkelashvili N, Kohli P, Linefsky J. Fifty-seven-year-old man with progressive dyspnoea. *Heart.* 2018 Nov 22.
- [16] Bohula EA, Wiviott SD, McGuire DK, Inzucchi SE, Kuder J et al, CAMELLIA-TIMI 61 Steering Committee and Investigators. Cardiovascular Safety of Lorcaserin in Overweight or Obese Patients. *N. Engl. J. Med.* 2018 Sep 20; 379 (12): 1107-1117.