CASE REPORT

A case of constrictive pericarditis during cabergoline treatment for hyperprolactinaemia

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Abstract

Objective: Treatment with dopamine agonists has been associated with cardiopulmonary fibrotic reactions, predominantly in patients treated for Parkinson's disease. To our knowledge, these reactions have previously not been associated with low-dose cabergoline treatment for hyperprolactinaemia.

Method: A case of constrictive pericarditis in a patient treated with cabergoline for hyperprolactinaemia is presented. The patient has been treated at a county hospital and a university hospital in southern Sweden.

Results: A 20-year-old woman with a 3-year history of amenorrhoea was referred to the department in 1992. From 2001 to 2005, she was given cabergoline, 0.5–1.5 mg/week. In 2005 a pericardectomy was performed due to fibrotic, constrictive pericarditis.

Conclusions: Our present case suggests that constrictive pericarditis may develop even on low-dose cabergoline, which might indicate that this reaction, as opposed to valvular fibrosis, is not mediated by a 5-HT_{2B} agonistic mechanism.

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Introduction

During the last three decades, dopamine agonists have been widely used in the treatment of various medical conditions, such as hyperprolactinaemia, Parkinson's disease and migraine prophylaxis. These drugs have been reported to be associated with valvulopathy and cardiopulmonary fibrotic adverse drug reactions (1, 2). These adverse reactions are predominantly seen in patients treated for Parkinson's disease, where the daily doses of the drug have been much higher than those used in treatment for hyperprolactinaemia (1).

We describe a case of constrictive pericarditis in a patient treated with low-dose cabergoline for hyperprolactinaemia. Possible mechanisms and a brief review of the literature are presented.

Case report

A 20-year-old woman with 3 years of amenorrhoea was referred to the Department of Endocrinology in 1992 because of hyperprolactinaemia. She did not have any other significant medical history. There was no family history of endocrine disease and she did not use any medications. Her only symptom was amenorrhoea. Clinical examination revealed no abnormalities. She had an elevated prolactin level (PRL; 179 nmol/l (ref value

<24 nmol/l)), but her pituitary function (adrenocorticotrophin, growth hormone, follicle-stimulating hormone, luteinizing hormone and thyrotrophin) was otherwise normal. Magnetic resonance imaging (MRI) showed a 22 × 18 × 12 mm large pituitary tumour.

Her prolactinoma was treated with bromocriptine, and during the first 6 months the dose was titrated to 5 mg thrice daily (Table 1). Throughout the subsequent years her PRL averaged 40 nmol/l, indicating a partially bromocriptine-resistant nature of the tumour, and her pituitary tumour volume was stable. In 1995 bromocriptine was changed to quinagolide 75 mg daily because of side effects, mainly dizziness. Her PRL initially increased to 110 nmol/l, but as the dose was successively increased to 300 mg daily her PRL once again decreased to about 40 nmol/l. However, 2 months after the last dose increment she became deeply depressed, a condition that reversed after the withdrawal of the drug. As no other drugs were available in Sweden at that time, she was referred for pituitary surgery. The procedure was performed in February 1996 using a transsphenoidal approach. After surgery, a small tumour rest was seen on MRI and her PRL was still elevated to 54 nmol/l. Her pituitary function was otherwise still normal. During the following years her PRL progressively increased, but pharmacological treatment was not given until 2000 when she once again was prescribed bromocriptine. At that time her

Table 1 Patient's use of dopamine agonists since her diagnosis of prolactinoma in 1992.

Drug	Dose	Treatment period
Bromocriptine	5 mg×2	1992-04–1995-04
Quinagolide	75 mg×1	1995-04–1995-12
Bromocriptine	5 mg×2	2000-02–2001-02
Cabergoline	0.5 mg weekly	2001-02–2001-08
Cabergoline	1.0 mg weekly	2001-08–2001-12
Cabergoline	1.5 mg weekly	2001-12–2005-09

PRL had increased to 220 nmol/l and a small increment in tumour volume was seen on MRI.

After the reappearance of side effects, bromocriptine was changed to cabergoline in February 2001, starting with a dose 0.5 mg weekly increasing to 1.5 mg weekly. Besides a slight initial dizziness, no side effects were seen. Her PRL decreased to 45 nmol/l and the tumour volume was unchanged on MRI.

In late summer of 2005, her legs and arms became swollen and during the following months her general condition declined. She had previously been in very good physical condition but now she became short of breath after minimal physical exertion.

Physical examination on admission to the hospital showed prominent jugular veins, hepatomegaly and peripheral pitting oedema. Low-voltage complexes were seen on an electrocardiogram (ECG). Findings of further investigations with ECG, cardiac catheterization and MRI were consistent with a constrictive pericardial process (Fig. 1). Cabergoline was discontinued and the patient was referred for pericardectomy. During surgery, a thick stiff pericardium was visualized and a radical pericardial excision was performed. Her central venous pressure decreased immediately from 20 cm before surgery to 5 cm H₂O after the pericardectomy. Her cardiac function was normal on a post-operative echocardiographic examination and her general condition improved rapidly after surgery. The histological

examination of the pericardium confirmed the diagnosis of fibrotic pericarditis (Fig. 1).

In this case of prolactinoma, the serum PRL continues to be around 170 nmol/l without pharmacological treatment. MRI has been done every 6 months and so far no increment in tumour volume has been seen.

Discussion

To our knowledge, constrictive pericarditis has only been reported in three cases of cabergoline treatment (2, 3). These three patients had Parkinson's disease and received considerably higher doses of the drug than the patient in this study.

Dopamine agonists with potent 5-HT_{2B} receptor agonist properties such as pergolide and cabergoline have consistently been linked to a risk of developing multivalvular heart disease similar to that seen in patients with carcinoid syndrome (1, 4, 5). Dopamine agonist without (i.e. bromocriptine, quinagolide) or with (i.e. lisuride) 5-HT_{2B} antagonistic properties has not been reported to be associated with valve disease (5, 6). In contrast to this, ergot dopamine agonists (i.e. bromocriptine, pergolide, cabergoline, lisuride) have all been shown to increase the risk for constrictive pericarditis and pleuropulmonary fibrotic reactions when used in therapeutic doses for Parkinson's disease (1, 2, 4, 7). This has, to our knowledge, not been previously reported in patients treated with low-dose cabergoline for hyperprolactinaemia. Cabergoline given in a dose < 3 mg daily has been considered to be safe with respect to valve fibrosis (1). However, our present case may indicate that constrictive pericarditis could develop even on considerably lower cabergoline doses. This might suggest that this reaction, as opposed to valvular fibrosis, is not mediated by a 5-HT_{2B} agonistic mechanism.

Figure 1 MRI showed pericardial effusion and a thickening of the pericardium by up to 6 mm width. The findings supported the clinical suspicion of a constrictive pericardial process. Histological examination confirmed the clinical diagnosis of fibrotic pericarditis, showing connective tissue infiltrated by inflammatory cells.

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