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Recovery From Postpartum Cardiomyopathy in 2 Patients by Blocking Prolactin Release With Bromocriptine

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To the Editor: Postpartum cardiomyopathy (PPCM) is a disease of unknown origin and exposes women to a high risk of mortality after delivery despite optimal medical therapy (1).

Prolactin is up-regulated postpartally where it induces lactation and promotes reshaping of the uterus. Prolactin exists in at least 2 biologically active forms with opposing effects. The physiological full-length 23 kDa prolactin promotes angiogenesis and protects endothelial cells whereas the cleaved 16 kDa derivate induces endothelial cell apoptosis and disrupts capillary structures (2). Recent data showed that oxidative stress promotes the postpartum generation of 16 kDa prolactin, which is causally related to PPCM. In turn, prolactin blockade with bromocriptine was successful in preventing onset of PPCM in mice and in patients at high risk for the disease (3). Here, we evaluated the efficacy of bromocriptine for recovery in 2 patients with acute PPCM.

Case 1

A 32-year-old woman was admitted to a peripheral hospital with heart failure (New York Heart Association [NYHA] functional class III) 3 weeks after giving birth to a healthy child. She had no pre-existing cardiac disease, exposure to cardiotoxic agents, or positive family history of pregnancy-related heart disease. Echocardiography revealed severe left ventricular (LV) dysfunction. Postpartum cardiomyopathy was diagnosed, whereupon heart failure therapy was initiated. However, the patient's condition did not improve, and she was transferred to our clinic 1 week later. N-terminal pro-brain natriuretic peptide (NT-proBNP) was markedly elevated (Table 1); creatine kinase (204 U/l), C-reactive protein (11 mg/l), and S-creatinine (109 μmol/l) were mildly elevated while troponin T was within normal range. The patient was breast feeding and displayed increased levels of total prolactin (128 ng/ml; reference: <30 ng/ml). Sixteen kDa prolactin was readily detectable by Western blot and was increased by 5- to 10-fold compared with that seen in 3 healthy nursing women. Electrocardiography showed sinus tachycardia but was otherwise normal. Echocardiography showed reduced LV function, LV dilation (Table 1), and mitral valve regurgitation grade II to III confirmed by cardiac magnetic resonance imaging.

Lactation was stopped by treatment with bromocriptine (5 mg/day, 2 weeks), which was followed by a rapid decrease of serum prolactin levels (to 2.3 ng/ml after 2 weeks) and resulted in a reduction of 16 kDa prolactin below detectable levels. In parallel, LV function and heart failure symptoms improved, accompanied by a decrease of NT-proBNP (Table 1). Bromocriptine was continued for 6 weeks at 2.5 mg/day. Four months postpartum, LV function and dimensions had further improved (Table 1), and after 6 months, LV function had completely recovered (ejection fraction: 60%, LV end-diastolic diameter 51 mm, LV end-systolic diameter 34 mm) and mitral valve regurgitation was only mild. At 12 months' follow-up, the patient was in NYHA functional class I with normal LV systolic and diastolic function.

Case 2

The second patient (41 years old) collapsed after elective cesarian section delivering twins. She was taken to the intensive care unit with NYHA functional class IV, the diagnosis of PPCM was made, and heart failure therapy and bromocriptine treatment were initiated. Thereafter, her condition improved rapidly (Table 1).

Discussion

Experimental data implicate a causal role of the 16 kDa prolactin for the development of PPCM in mice, which was prevented by suppression of prolactin secretion with bromocriptine before the onset of the disease (3). Similarly, in a small pilot study, bromocriptine prevented the recurrence of PPCM in a subsequent pregnancy in women who survived PPCM in the previous pregnancy (3).

The present study reports 2 patients with acute PPCM in whom bromocriptine treatment in addition to standard heart failure therapy was associated with recovery and prevention of chronic heart failure. This observation supports the notion that prolactin, specifically its 16 kDa derivate, seems to play a crucial role not only for the initiation but also for the progression of PPCM.

Experimental data suggest a major protective effect of bromocriptine in PPCM by eliminating 16 kDa prolactin (3).

Previous reports attribute positive effects to bromocriptine treatment in heart failure patients independent from PPCM (4). These 16 kDa prolactin-independent effects of bromocriptine may include the elimination of the vasoconstrictive 23 kDa prolactin as well as direct agonistic effects of bromocriptine on the dopamine DA2 receptors, which may lower norepinephrine release, antagonize aldosterone, and down-regulate type 1 angiotensin receptors (5,6). Therefore, beneficial effects of bromocriptine on the sympathetic nervous system and on hemodynamics may combine to assist recovery of PPCM patients.

However, both patients described here obtained beta-blockers and angiotensin-converting enzyme inhibitors before and during bromocriptine therapy, which may limit the mentioned effects of bromocriptine on sympathetic tone and hemodynamics. Nevertheless, it is possible that a multifactorial role of bromocriptine might ultimately account for its beneficial effects.

Table 1: *Time Course of NYHA Functional Class, NT-proBNP Levels, and Echocardiographic Data of Cases 1 and 2*

	Case 1			**Case 2**		
	Baseline	**2 Weeks**	**4 Months**	**Baseline**	**2 Weeks**	**4 Months**
NYHA functional class	III	II	II	IV	III	I
NT-proBNP (ng/l)	10,611	3,142	n.d.	14,933	462	97
LVEDD (mm)	60	59	51	55	53	43
LVESD (mm)	53	49	34	39	39	32
Fractional shortening (%)	12	17	33	19	26	25
Ejection fraction (%)	17	29	57	30	50	49
Heart rate (beats/min)	123	79	71	119	94	48

LVEDD = left ventricular end-diastolic diameter; LVESD = left ventricular end-systolic diameter; n.d. = not determined; NT-proBNP = N-terminal pro-brain natriuretic peptide; NYHA = New York Heart Association.

As a limitation to the present observation, it should be noted that some PPCM patients recover spontaneously (1). Therefore, a controlled randomized study is needed in order to determine the true value of bromocriptine as a specific novel therapy for PPCM.

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