Rare disease

Reversible cushing dilated cardiomyopathy mimicking peripartum cardiomyopathy with successful subsequent pregnancy

Rashed Al Banna,¹ Aysha Husain,² Jalila Al Aali,³ Khalid Ebrahim,³ AbdulAziz Mohammed⁴

¹Medical Department, Salmaniya Medical Complex, Manama, Bahrain;

²Cardiology Unit, Internal Medicine Department, Salmaniya Medical Complex, Manama, Bahrain;

³Internal Medicine Department, Salmaniya Medical Complex, Manama, Bahrain;

⁴Orthopedics Department, Salmaniya Medical Complex, Manama, Bahrain

Correspondence to Dr Rashed Al Banna, abdullarashed@yahoo.com

Summary

A 29-year-old lady G4P3A0 has been admitted in her last trimester with features of peripartum cardiomyopathy. She was treated accordingly with comprehensive antifailure therapy. She lost follow-up but reappeared 12 weeks later with further deterioration of her heart failure, severe depression and osteoporotic multiple lumbar fractures. She turned to be having Cushing syndrome secondary to adrenal adenoma. Post adrenalectomy all her symptoms subsided and her cardiac function fully recovered as shown by stress echocardiography. She reconceived with uneventful pregnancy and delivery.

BACKGROUND

Peripartum cardiomyopathy is an idiopathic disease confined to the last trimester of pregnancy or 5 months of puerperium. It is a diagnosis of exclusion. In this patient, her cardiomyopathy turned to be Cushing syndrome related rather than idiopathic peripartum cardiomyopathy. The diagnostic dilemma together with full recovery of her myocardium adding to her subsequent well-tolerated pregnancy are unique features of this case.

CASE PRESENTATION

A 29-year-old Bahraini woman at 35 weeks of pregnancy was admitted to the antenatal clinic for pregnancy-induced hypertension and an absence of foetal heart sounds.

Upon direct questioning, she was found to have shortness of breath, which was initially provoked by moderate exertion, progressed to paroxysmal nocturnal dyspnoea. This symptom was also associated with palpitation and mild ankle swelling. The patient denied any history of chest pain, syncope, jaundice or convulsions. A few days prior to this evaluation, she could not feel the movements of her foetus.

The patient was the mother of three children; her last pregnancy was 1.5 years ago and was uneventful. There was no history of abortion, and she had not been prescribed any medication other than folate and iron supplements.

On examination, the patient looked depressed, was mildly dyspneic, and had a blood pressure of 145/95 mm Hg and a heart rate of 98 beats/min.

Her oxygen saturation was maintained at 96% with a 4 l/min nasal cannula. Multiple small, ecchymotic patches were evident on her forearms, which were attributed to multiple venous cannulations. She had signs of congestive heart failure, a raised jugular venous pressure, a laterally displaced apex, an apical S3 and bi-basilar rales. Fetal heartbeats were absent.

INVESTIGATIONS

The relevant evaluations are shown in (table 1). An electrocardiogram showed a sinus tachycardia with no ischaemic changes. Her vasculitic screen was negative for autoimmune diseases. Her first echocardiogram documented findings (table 2).

The fetal ultrasound documented intrauterine foetal death, and the patient underwent augmented labour after a spontaneous rupture of the amniotic membrane.

TREATMENT

The gestational time of the patient's presentation (during the last trimester of pregnancy) and the lack of any surrogate cause hinted at a diagnosis of peripartum cardiomyopathy. She was treated accordingly with 2.5 mg bisoprolol, 40 mg furosemide, 12.5 mg spironolactone and perindopril 2.5 mg once daily. She was discharged and scheduled for follow-up at the cardiology clinic 2 weeks later.

Table 1 Investigation results

Investigation	Reference range	Presentation	12 weeks	Post surgery
Sodium	140–148 mmol/l	148	147	140
Potassium	3.6–5.2 mmol/l	2.9	3.2	4.0
Chloride	100–107 mmol/l	106	104	100
Bicarbonate	21–30 mmol/l	30	30	24
Creatinine kinase	<67 u/l	36	50	55
CKMB	0–10 u/l	8	9	10
Troponin	0–1.5 ug/l	0.00	0.03	0.45
Hormones				
44 h-urine free cortisol	131–451 nmol/l	-	1457	120
8 a m cortisol	193–690 nmol/l	-	1073	432
ACTH	0–10 pmol/l	-	<0.2	1.1

ACTH, adrenocorticotropin; CKMB creatinine kinase muscle and brain fraction.

Figure 1 A homogenous right adrenal mass with low attenuation on CT abdomen.

Table 2 Serial measurements on echocardiography

Parameters	At presentation	12 weeks	Post adrenalectomy
LVIDd (cm)	6.8	7.2	5.0
LVIDs (cm)	5.6	6.3	3.3
IVSd (cm)	0.85	0.87	0.87
IVSs (cm)	1.0	1.2	1.2
EF	30%	23%	60%
E/E'	16	21	8.2

E velocity, early mitral inflow velocity; E' peak tissue Doppler early diastolic velocity of the septal mitral annulus; EF, ejection fraction; IVSd, interventricular septal wall thickness at end-diastole; IVSs, interventricular septal wall thickness at end-systole; LVIDd, left ventricular internal diameter end-diastole; LVIDs, left ventricular internal diameter at end-systole.

OUTCOME AND FOLLOW-UP

She missed the initial follow-up appointment but reappeared at the clinic 12 weeks later. Her husband was very concerned about her poor adherence to medication as well as the severe backache that disturbed her sleep. He also did not comprehend her recent persistent, unprovoked crying. Her clinical signs of overt congestive heart failure were persistent, and her forearm ecchymotic patches were alarming. Her severe depression along with her tendency to bruise easily remained unexplained. In addition, the further deterioration of her myocardium, as documented by echocardiography, was unusual for a case of uncomplicated peripartum cardiomyopathy. Her poor compliance to treatment, however, could have partially explained persistent systolic dysfunction but not her further deterioration (table 2). We decided to readmit this patient to control her heart failure and perform a related investigation.

The repeat investigation was negative for myocardial ischemia, collagenosis and myocarditis. However, the endocrinology screening revealed frank Cushing syndrome (CS) which we did not screen her for at her initial presentation (table 1). The cause of the CS was determined to be an autonomous right adrenal adenoma (figure 1). In addition to causing her heart failure, the CS was complicated by multiple wedge fractures in her lumbar spine that required corrective surgery (figures 2 and 3).

After stabilising her heart failure, she underwent laparoscopic resection for her right adrenal adenoma. She was discharged and given 5 mg bisoprolol once daily and 2.5 mg perindopril once daily.

Her subsequent follow-up at the cardiology clinic documented progressive improvement in her functional capacity and in the normalisation of her mood. Her cardiac systolic dysfunction normalised, as shown by a repeated echocardiogram at 4 months postadrenalectomy.

From our perspective, it was challenging when she asked for advice concerning her desire to conceive. We were unable to provide a confident answer due to the lack of published data in the literature. The two major concerns regarding the patient's desire to conceive were the risk of relapse and the degree of myocardial recovery. Additionally, data addressing the persistent harmful effect of CS on myocardium even after treatment started to accumulate.¹

We subjected the patient to a dobutamine stress echocardiogram to monitor the systolic performance of her left ventricle upon stress exposure. Her stress echocardiogram showed a normal hyperkinetic response.

We told the patient that future pregnancy would carry a risk, although the prognosis of future pregnancies was more favourable due to the result of her stress echocardiogram.

The patient chose to conceive, so her cardiac medications were discontinued. The pregnancy was well tolerated, and her systolic function was normal upon subsequent serial echocardiogram studies. She delivered a healthy baby girl weighing 3.2 kg and having an Apgar score of nine at 1 min and 10 at 5 min. She has remained asymptomatic since this time and was discharged from the cardiology services.

DISCUSSION

Peripartum cardiomyopathy is an idiopathic disease of the myocardium that is generally confined to the last trimester of pregnancy or the first 5 months of the puerperium. Being

a diagnosis of exclusion, other rare aetiologies mimicking peripartum cardiomyopathy have to be ruled out.²

The existence of CS during pregnancy has been well documented in the literature,³ although the reported cases of reversible cardiomyopathy secondary to CS are limited.⁴⁻⁷

This is the first reported case of a clinical scenario of a patient who was pregnant and diagnosed with CS, who presented with dilated cardiomyopathy, recovered post treatment and subsequently conceived successfully (table 3). Most cases of CS in pregnancy have been attributed to autonomous, cortisol-producing adrenal adenomas.^{8 9}

Both normal and complicated pregnancies share common clinical features with CS, such as depression, abdominal striae, weight gain, diabetes and hypertension. As a result, the clinical suspicion of their coexistence is relatively low.¹⁰

Figure 2 T1 weighted MRI of the lumbar spine showing multiple fractures.

Figure 3 X-ray lateral view of lumbar spine post surgery.

Table 3 Cases of reversible cardiomyopathy in Cushing syndrome

No of case	Case description	Reference number
1	51 year old male with biventricular failure (EF 19%) improved to (EF 40%) after treatment of Cushing disease.	4
2	48 year old female with CS due to unilateral adenoma, LV function recovered after adrenalectomy (EF from 27% to 69%).	5
3	28 year old female with CS due to unilateral adrenal adenoma with biventricular failure, reversed after surgery.	6
4	28 year old female with CS due to adrenal adenoma with biventricular failure (LV EF 34%), recovered after adrenalectomy.	7
5	(current case)-29 year old pregnant with CS due to adrenal adenoma presenting with heart failure (LV EF 30%) mimicking peripartum cardiomyopathy, recovered after adrenalectomy (LV EF 60%).	Our case

EF, ejection fraction; LV, left ventricle.

However, the clustering of clinical signs, such as severe striae, moon face, marked weight gain, proximal muscle wasting, poor wound healing and a reduced stature due to spinal fractures and hypokalemia, should raise the clinical suspicion of this coexistence.¹⁰

In addition to the materno-fetal risks of CS, other complications and morbidities can also be anticipated, such as spinal fractures, poor wound healing and increased susceptibility to infections.¹¹

Treatment of choice is surgery by resection of the adrenal adenoma if it turns to be the aetiology. Surgery can be performed safely during the second trimester, although parenteral steroid administration is required to prevent an Addisonian crisis during the perioperative period.¹¹

Cardiac manifestations of CS have received a significant level of recognition.¹² Most investigators believe that heart failure in CS is secondary to systemic hypertension. By echocardiogram, the patient in this report harboured features of dilated cardiomyopathy rather than left ventricular hypertrophy. This observation led us to endorse the opinion of others, which was that cortisol may have an independent myocardial remodeling effect.⁷ Further evidence in support of the independent myocardial action of excess cortisol is the finding that was published by Lindsay *et al.* Of the 135 pregnant patients with CS, 68% were found to have hypertension, while only 3% developed congestive heart failure.¹³

The patient in this report is the fifth reported case of the total remission of a congestive heart failure following treatment for CS. The most recent similar case was reported in 2010. Interestingly, both of these cases had the common features of dilated cardiomyopathy and a unilateral, right adrenal adenoma as the underlying cause of CS⁷ (table 3).

An informed decision regarding the patient's desire to reconceive was elusive, as future pregnancies carry some level of risk that is not quantifiable. We chose to proceed with a dobutamine stress echocardiogram to estimate her contractile reserve, as this procedure can help to stratify the risk of future pregnancies in patients with peripartum cardiomyopathy.¹⁴

The rational for this evaluation was to differentiate a true recovery from an apparent but false recovery. Normal resting systolic function will turn hyperkinetic in patients with full recovery. On the contrary, those with unrecovered myocardium will fail to augment (or depress) the ejection fraction upon stress exposure. Women with normal stress echocardiograms have much lower myocardial relapsing risk for future pregnancies. It was difficult to extrapolate such a conclusion for patients with non-peripartum cardiomyopathy. A consensus regarding the complete recovery of the myocardium after treatment for CS is lacking. Moreover, some investigators believe that the effect of CS on both the heart and the vasculature may partially remain

after treatment.¹ Therefore, the estimation of the contractile reserve upon stress exposure appears to be a rational method for this type of evaluation, and this should unmask any systolic dysfunction that could be dormant under resting conditions.

Learning points

- Peripartum cardiomyopathy is a diagnosis of exclusion.
- Cushing cardiomyopathy is reversible once the primary disease is treated.
- Females with Cushing syndrome secondary to cortical adenoma can conceive if got the disease during childbearing age.

Competing interests None.

Patient consent Obtained.

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