

Supplementary material

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Supplementary Table 1. Characteristics of women with genetic testing for peripartum cardiomyopathy

	Case 1	Case 2	Case 3
Age at delivery, y	36	41	37
Past medical history	HBV carrier	HBV carrier; history of breast cancer with chemotherapy completed 8 years ago	Gout; mild renal impairment
Family history of cardiac disease	Mother had repeated admissions for congestive heart failure and arrhythmia; died at 59 years old	No	No
Hypertensive disorders of pregnancy	No	Yes	Yes
Gestational age at delivery, wk	36	38	35
Mode of delivery	Normal vaginal delivery	Instrumental delivery	Normal vaginal delivery
Timing of symptom onset	45 days after delivery	37 weeks of pregnancy	32 days after delivery
Timing of PPCM diagnosis	5 days after symptom onset	1 day after delivery	30 days after symptom onset
PPCM clinical presentation	SOB, orthopnoea, PND	SOB, orthopnoea	Cough, SOB, tachypnoea
Echocardiogram at presentation	LVEF 34%; severe MR; moderate TR; no RV dysfunction; dilated LA and LV; severe global	LVEF 20%; moderate to severe MR; dilated LA, RA, LV, and RV; global hypokinaemia	LVEF 17%; severe MR; impaired RV function; dilated heart chambers

hypokinesia

Follow-up echocardiograms/interventions	1st-year echo: LVEF 43% 2nd-year echo: LVEF 41% Daily oral cardiac medications (captopril and metoprolol)	9 months after delivery: decompensated congestive heart failure with LV thrombosis; required anticoagulation, IABP, and LVAD 15 months after delivery: heart transplantation 2 years 8 months post-transplant: stable graft function on regular oral immunosuppressants	1st-year echo: LVEF 34% 2nd-year echo: LVEF 35% 3rd-year echo: LVEF 33% 4th-year echo: LVEF 35% 3 years after PPCM diagnosis: ICD implanted Daily oral cardiac medications (bisoprolol, Entresto, and frusemide)
Dilated cardiomyopathy sequencing panel test	Heterozygous <i>FLNC</i> NM_001458.5: c.850+1G>T (likely pathogenic)*	1. Heterozygous <i>TTN</i> NM_001267550.1: c.47391_47392delAA (likely pathogenic)* 2. Heterozygous <i>MYBPC3</i> NM_000256.3: c.3653delG (likely pathogenic)*	Heterozygous <i>NEXN</i> NM_144573.3: c.1426G>C (variant of uncertain significance)*
Subsequent pregnancies	No	No	4 years after delivery: TOP
Length of follow-up, mo	51	47	48
Clinical condition at latest follow-up	NYHA functional class I	NYHA functional class I	NYHA functional class II

Abbreviations: echo = echocardiogram; HBV = hepatitis B virus; IABP = intra-aortic balloon pump; ICD = implantable cardioverter-defibrillator; LA = left atrium; LV = left ventricle; LVAD = left ventricular assist device; LVEF = left ventricular ejection fraction; MR = mitral regurgitation; NYHA = New York Heart Association; PND = paroxysmal nocturnal dyspnoea; PPCM = peripartum cardiomyopathy; RA = right atrium; RV = right ventricle; RVEF = right ventricular

ejection fraction; SOB = shortness of breath; TOP = termination of pregnancy; TR = tricuspid regurgitation

* According to the American College of Medical Genetics and Genomics recommendations on sequence variant classification, See reference 1

Supplementary Table 2. Univariable and multivariable logistic regression analyses concerning maternal risk factors for peripartum cardiomyopathy*

	Univariable analysis				Multivariable analysis [†]	
	Cases (n=30)	Controls (n=120)	OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Maternal age (≥40 y)	5 (16.7%)	4 (3.3%)	5.80 (1.45-23.15)	0.016	4.05 (0.49-33.30)	0.193
Ethnicity			4.33 (0.83-22.66)	0.095		
Chinese	27 (90%)	117 (97.5%)				
Non-Chinese	3 (10%)	3 (2.5%)				
Marital status			0.48 (0.08-2.77)	0.345		
Unmarried	2 (6.7%)	4 (3.3%)				
Married	28 (93.3%)	116 (96.7%)				
Education level			0.40 (0.16-1.00)	0.060		
Secondary and lower	23 (76.7%)	68 (56.7%)				
Tertiary or above	7 (23.3%)	52 (43.3%)				
Smoking	6 (20%)	4 (3.3%)	7.25 (1.90-27.67)	0.005	2.92 (0.44-19.39)	0.266
Multiparity	16 (53.3%)	59 (49.2%)	1.18 (0.53-2.63)	0.683		
Multiple pregnancy	4 (13.3%)	5 (4.2%)	3.54 (0.89-14.09)	0.079		
Obesity (BMI ≥25 kg/m ² at first antenatal visit)	8 (26.7%)	28 (23.3%)	1.20 (0.48-2.98)	0.811		
Hypertensive disorders of	17 (56.7%)	5 (4.2%)	30.08 (9.52-95.02)	<0.001	38.00 (9.66-149.52)	<0.001

pregnancy [‡]						
Pre-existing diabetes	0	1 (0.8%)	N/A	>0.99		
Gestational diabetes	4 (13.3%)	15 (12.5%)	1.08 (0.33-3.52)	>0.99		
Pre-existing thyroid disease	1 (3.3%)	4 (3.3%)	1.00 (0.11-9.29)	>0.99		
Asthma	1 (3.3%)	5 (4.2%)	0.79 (0.09-7.05)	>0.99		
Psychiatric disorder	5 (16.7%)	8 (6.7%)	2.80 (0.85-9.28)	0.137		
Antenatal anaemia (Hb <10.5 g/dL)	15 (50%)	13 (10.8%)	8.23 (3.29-20.62)	<0.001	13.04 (3.72-45.70)	<0.001

Abbreviations: 95% CI = 95% confidence interval; BMI = body mass index; Hb = haemoglobin; N/A = not applicable; OR = odds ratio

* Data are shown as No. (%), unless otherwise specified

† Variables with P<0.05 in univariable analyses were included in multivariable analysis

‡ Hypertensive disorders of pregnancy include chronic hypertension, gestational hypertension, pre-eclampsia, and chronic hypertension with superimposed pre-eclampsia

Reference

1. Richards S, Aziz N, Bale S, et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. *Genet Med* 2015;17:405-24.