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Case Report

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Latent Dilated Cardiomyopathy Unmasked by Pregnancy

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ABSTRACT

BACKGROUND

There are many findings support the hypothesis that Peripartum Cardiomyopathy (PPCM) might indeed be a subtype of dilated Cardiomyopathy (DCM). The mechanisms underlying PPCM remain unclear. Recently, genetic susceptibility is increasingly recognized as a risk factor of PPCM. More than 10% of women undergo PPCM with a pathogenic TTN gene (encoding giant protein titin) mutation. TTN truncation is also a mainly contributive genetic factor of DCM.

RESULTS

A female patient manifested deteriorating heart function after delivery. She received a diagnosis of PPCM. Her father experienced sudden cardiac death (SCD) due to DCM.A brand-new TTN gene heterozygous mutation c.77785G>A (p.Q25929X) was found in this patient though her medical history prior to delivery was unremarkable. This indicates the potential of pregnancy to unmask latent dilated Cardiomyopathy.

CONCLUSION

In conclusion, pregnancy is a risk factor for women with latent dilated Cardiomyopathy. For individuals with a family history of SCD, gene screening is imperative.

KEYWORDS: Peripartum Cardiomyopathy (PPCM), Dilated Cardiomyopathy (DCM), Pregnancy, TTN gene mutation

INTRODUCTION

According to the conception proposed by the European Society of Cardiology Working Group, Peripartum Cardiomyopathy (PPCM) is an idiopathic Cardiomyopathy manifesting with heart failure due to decreased left ventricular (LV) systolic function at the end period of gestation or in the months after delivery, with no other causes of heart failure, which is a diagnosis of ruling out. LV may not be obviously dilated yet the ejection fraction (EF) is almost reduced under 45% [1]. The morbidity of PPCM is particularly uneven due to the differences of race or geographical location [2]. The mechanisms underlying PPCM remain unclear. Several risk factors and possible underlying pathological processes have received attention, such as fetal micro chimerism induced maternal autoimmune response [3], infection, oxidative stress, inflammation, micronutrient deficiency, disturbance of cardiac anti angiogenic and proapoptotic factors [4]. Therefore, PPCM is probably caused by a complex interaction of more than one pathogenic mechanism. Many studies recently reported that PPCM can be an initial manifestation of familial dilated Cardiomyopathy (DCM) and more than 10% of women undergo PPCM with a pathogenic mutation, indicating that, at least in a subset of cases, genetic predisposition plays a role in the pathophysiology of pregnancy-associated heart failure [5]. The potential of mutations in DCM is well identified. Prior

reports have indicated that mutations in at least 40 genes are associated with DCM, among which TTN (titin) truncations are the mainly contributive genetic factor of DCM [6, 7]. We here report a patient with a family history of DCM related sudden cardiac death (SCD). This patient manifested deteriorating heart function after delivery and received a diagnosis of PPCM initially. A brand-new TTN gene heterozygousmutation c.77785G>A (p.Q25929X) was found in this patient though her medicine history prior to delivery was unremarkable. This indicated the potential of pregnancy to unmask latent dilated Cardiomyopathy and further support the hypothesis that PPCM may indeed be a subtype of DCM.

CASE REPORT

A 34-year-old female Han Chinese patient presented with dyspnea and chest distress over the past three years. She suffered from gestational hypertension at the early stage and complained of dyspnea, chest distress and palpation at the late stage of the pregnancy. All of these symptoms aggravated. Physical examinations showed cyanosis, jugular venous distention, blood pressure of 112/73mmHg. Laboratory testing's were unremarkable except pro-BNP of1098.00pg/ml. Electrocardiogram (ECG) showed arrhythmia accompanied by frequent ventricular premature beats (Figure 1).

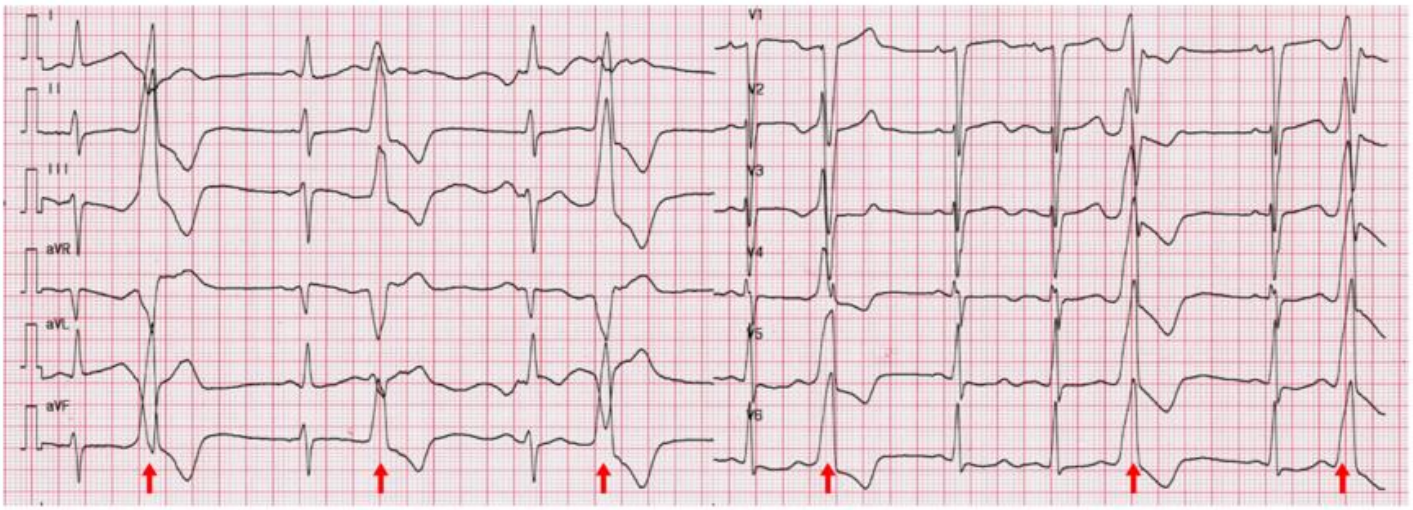

Figure 1: Abnormal ECG pattern of this patient showed arrhythmia of frequent ventricular premature beats (red arrow).

Chest radiography revealed enlarged heart shadow and increased lung markings (Figure 2).

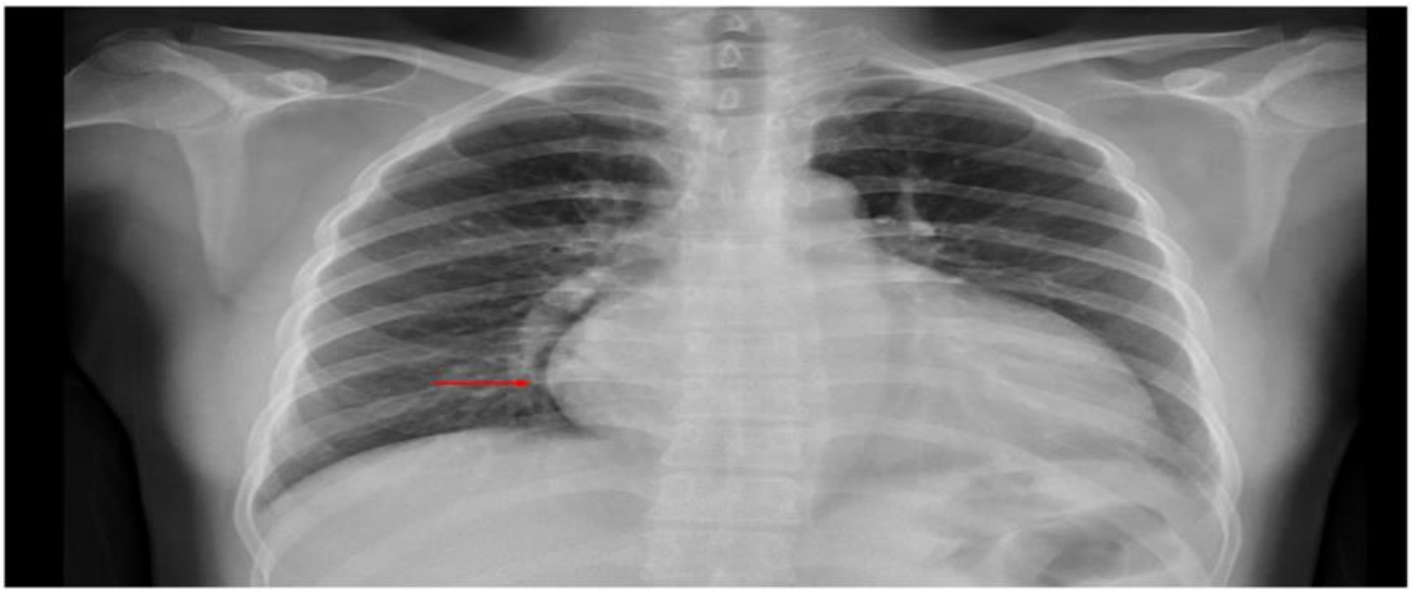

Figure 2: Chest radiography of this patient showed enlarged heart shadow (red arrow) and increased lung markings.

Echocardiography indicated left ventricular ejection fraction (LVEF) of only 27%, global dilatation, thinned-out cardiac walls and decreased systolic function of the whole LV. Standard symptomatic and supportive treatments were given including oral administration of aspirin (0.1 g/d)to anti-platelet, benazepril(10 mg/d) to inhibit cardiac remodeling, metoprolol (47.5 mg/d) to control heart rhythm and digoxin (0.125 mg/d) to improve heart function, spironolactone (20 mg/d) and surosemide (20 mg/d) to decrease cardiac load, trimetazidine (20 mg, three times a day) to alleviate angina, coenzyme Q10 (20 mg, three times a day) for cardiac nutrition, and other regimens maintaining water electrolyte balance. After standard treatments for heart failure, the patient recovered steadily with alleviated symptoms and nearly normal ECG manifestation when discharged (Figure 3).

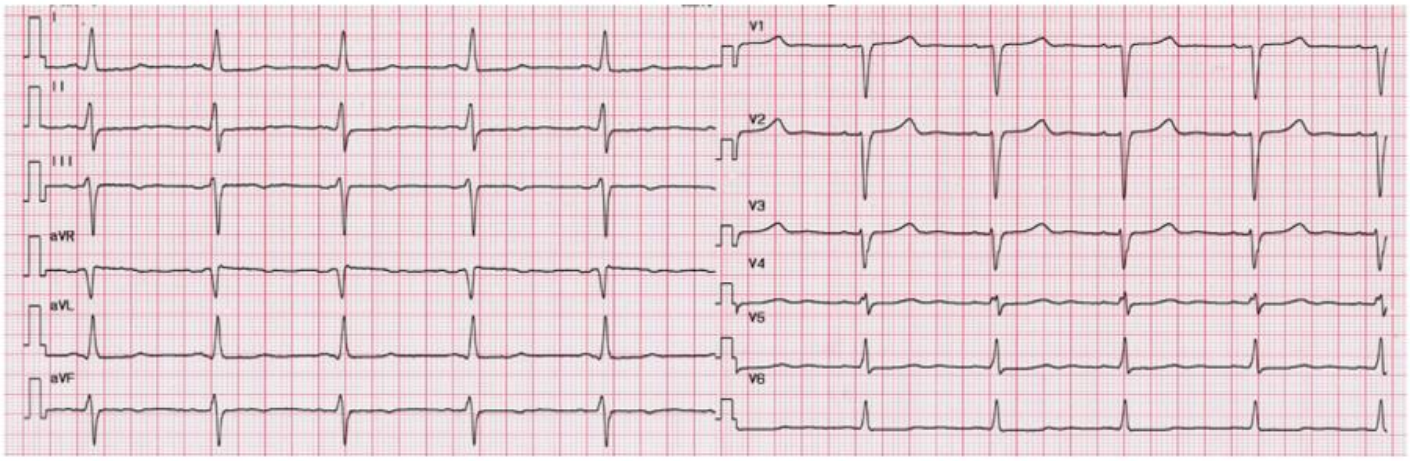

Figure 3: ECG of this patient when discharged showed nearly normal pattern of sinus rhythm, HR (heart rate) of 62.

We investigated her family medical history. Her father was diagnosed as DCM and experienced SCD. Further genetic analysis revealed a heterozygousmutationc.77785G>A (p.Q25929X) of TTNgene was found in this patient (Figure 4). This TTN mutation has not been reported in the previous literatures.

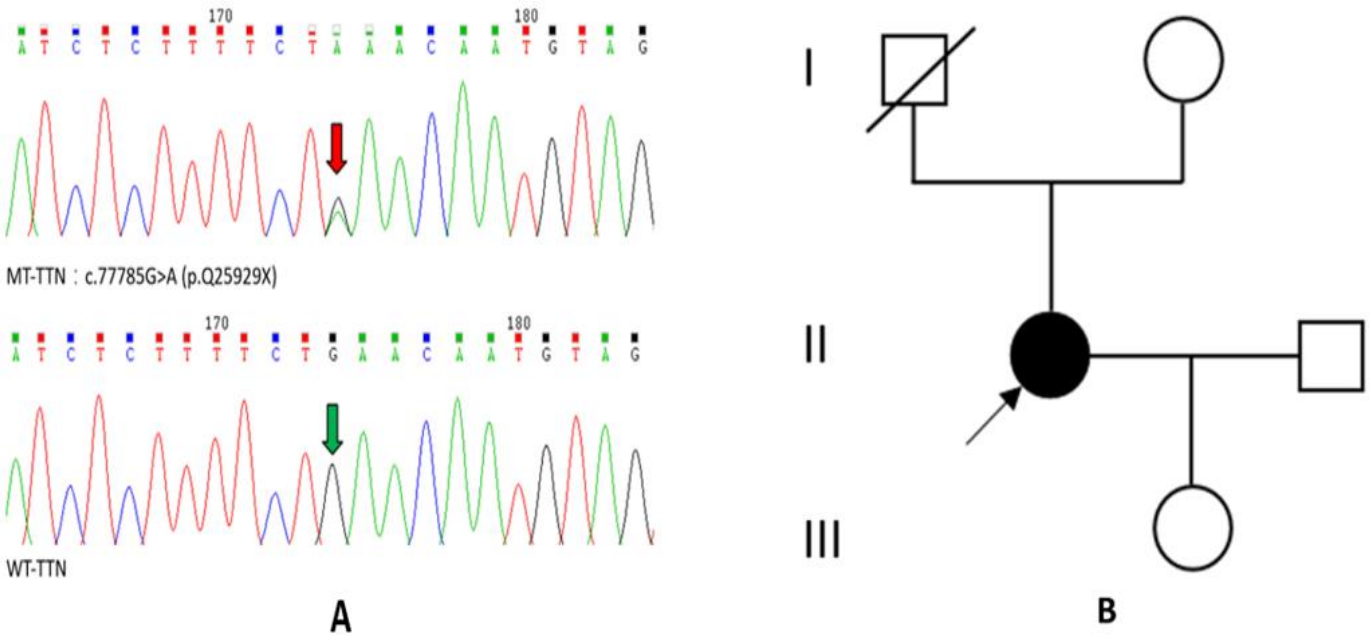

Figure 4: A new mutation c.77785G > A (p.Q25929X) of TTN gene was detected in this patient, the upper line showed the mutant TTN gene in which a guanine (G) was substituted by an adenine (A) and the lower line showed the wild type (A). Family tree of this patient (the proband was marked as black circle with arrow) (B).

DISCUSSION

A Some studies have proposed that a part of PPCM might be a portion of familial DCM. On the bases of gene susceptibility, hormonal and hemodynamic alterations during pregnancy predispose the latent DCM patients to heart failure. Changes of hemodynamic stresses during pregnancy include accelerated heart rate, increased stroke volume, increased cardiac output, increased preload via increased blood volume and reduced after load secondary to peripheral vasodilatation [8]. Majority of pregnant women experiencing the normal physiological changes does not suffer from Cardiomyopathy. But for those who possess a genetic risk factor of Cardiomyopathy, things may be different. Latent or asymptomatic DCM could be unmasked by pregnancy, which may typically present as dilated LV and impaired LV function.

Hormonal levels also play an important part in PPCM. During normal pregnancy, mild enlarged heart results from increased cardiac volume overload via progesterone elevation in the early stage [9]. On the contrary, estrogen seems to be anti hypertrophic [10]. Relax in is related to enhanced cardiac output and reduced vascular resistance [11]. Counterbalance of these hormones is important to maintain normal pregnant procedure. In latent DCM patients with mutations, however, the balance reserve may be unsettled due to the genetic susceptibility, resulting in a cardiac dysfunction during the gestation period.

TTN truncations are the most frequent genetic causes of DCM. The detection rate of TTN truncations is also high in PPCM [12, 13]. TTN gene mutations such as c.82117C>T, c.86171_86174dupAAAG, c.52795C>T, c.71867_71876delGAGTTCTGGA, c.81949dupA, c.55070G>A, c.46990_46993delAAGG have already been identified in patients manifesting PPCM with DCM family history [14]. In our case report, a brand-new pathogenic TTN gene mutation c.77785G>A (p.Q25929X) was found. The genetic contribution in this case was further supported but not determined by the evidence that her family relative died from DCM, though the genetic screening was unavailable in this relative. These further indicate the potential of genetic susceptibility in PPCM.

Several lines of evidence support a substantial role for genetic contributions to PPCM showing that at least 10–15% of women with PPCM have a pathogenic mutation. GWASs also show additional genomic associations with this condition, and murine models highlight the roles of metabolism and free radical stress [5]. In conclusion, PPCM might indeed be a subtype of DCM due to the increased genetic susceptibility and pregnancy is a risk factor for women with latent dilated Cardiomyopathy. For individuals with a family history of SCD, gene screening is imperative

REFERENCES

1. Sliwa K, Hilfiker-Kleiner D, Petrie MC, Mebazaa A, Pieske B, Buchmann E, et al. Current state of knowledge on aetiology, diagnosis, management, and therapy of peripartum cardiomyopathy: a position statement from the Heart Failure Association of the European Society of Cardiology Working Group on peripartum cardiomyopathy. Eur J Heart Fail. 2010; 12: 767-778.
2. Sliwa K, Fett J, Elkayam U. Peripartum cardiomyopathy. Lancet. 2006; 368: 687-693.
3. Ansari AA, Fett JD, Carraway RE, Mayne AE, Onlamoon N, Sundstrom JB. Autoimmune mechanisms as the basis for human peripartum cardiomyopathy. Clin Rev Allergy Immunol. 2002; 23: 301-324.
4. Ntusi NB, Mayosi BM. Aetiology and risk factors of peripartum cardiomyopathy: a systematic review. Int J Cardiol. 2009; 131: 168-179.
5. Lee YZJ, Judge DP. The Role of Genetics in Peripartum Cardiomyopathy. J Cardiovasc Transl Res. 2017; 10: 437-445.
6. Pierce JA, Price BO, Joyce JW. Familial occurrence of postpartal heart failure. Arch Intern Med. 1963; 111: 651-655.
7. Strunge P. Familial cardiomyopathy. Peripartum and primary congestive cardiomyopathy in a sister and brother. Ugeskr Laege. 1976; 138: 2567-2569.
8. Liu LX, Arany Z. Maternal cardiac metabolism in pregnancy. Cardiovascular research. 2014; 101: 545-553.
9. Chung E, Leinwand LA. Pregnancy as a cardiac stress model. Cardiovasc Res. 2014; 101: 561-570.
10. van Eickels M, Grohe C, Cleutjens JP, Janssen BJ, Wellens HJ, Doevendans PA. 17beta-estradiol attenuates the development of pressure-overload hypertrophy. Circulation. 2001; 104: 1419-1423.
11. Conrad KP. Maternal vasodilation in pregnancy: the emerging role of relaxin. Am J Physiol Regul Integr Comp Physiol. 2011; 301: R267-275.
12. van Spaendonck-Zwarts KY, Posafalvi A, van den Berg MP, Hilfiker-Kleiner D, Bollen IA, Sliwa K, et al. Titin gene mutations are common in families with both peripartum cardiomyopathy and dilated cardiomyopathy. Eur Heart J. 2014; 35: 2165-2173.
13. Ware JS, Li J, Mazaika E, Yasso CM, DeSouza T, Cappola TP, et al. Shared Genetic Predisposition in

Peripartum and Dilated Cardiomyopathies. N Engl J Med. 2016; 374: 233-241.

14. van Spaendonck-Zwarts KY, Posafalvi A, van den Berg MP, Hilfiker-Kleiner D, Bollen IAE, Sliwa K, et al. Titin gene mutations are common in families with both peripartum cardiomyopathy and dilated cardiomyopathy. Eur Heart J. 2014; 35: 2165-2173.