



Post-Partum Cardiomyopathy in a Duchenne Carrier: A Case Report

Sepideh Taghavi¹, Marzieh Mirtajadini^{2,1,*}, Maryam Chenaghlo¹, Nasim Naderi¹, Ahmad Amin¹, Nahid Rezaeian¹ and Mohammad Javad Alemzadeh-Ansari¹

¹Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran

²Cardiovascular Research Center, Kerman University of Medical Sciences, Kerman, Iran

*Corresponding author: Cardiovascular Research Center, Kerman University of Medical Sciences, Kerman, Iran. Email: m.mirtajadini@gmail.com

Received 2019 July 29; Revised 2019 September 07; Accepted 2019 September 14.

Abstract

Introduction: Duchenne muscular dystrophy is an X-linked disease and the carriers are almost asymptomatic but rarely, they may present with muscular and even cardiac manifestations.

Case Presentation: This report presents a 41-year-old female case as a carrier of Duchenne muscular dystrophy who presented at our centre with cardiomyopathy, 2.5 months after delivery. Three differential diagnoses including DCM, postpartum cardiomyopathy and cardiomyopathy due to Duchenne muscular dystrophy were considered for this case. According to findings of patient's CMR, cardiomyopathy due to Duchenne muscular dystrophy was recognized as the most probable disease in this case.

Conclusions: Based on the undertaken investigations, screening with cardiac MRI and echocardiography is recommended for carriers.

Keywords: Duchenne Muscular Dystrophy, Carrier, Cardiomyopathy, Delivery

1. Introduction

Duchenne muscular dystrophy is an X-linked disease and usually presents in sons of female carriers (1). The incidence of Duchenne muscular dystrophy is 1 in 3500 male newborns. This disease is characterized by weakness of leg, shoulder and pelvic girdle muscles which is presented in the early childhood (2). Cardiac involvement is common in Duchenne muscular dystrophy which is not related to the degree of skeletal presentation; it may occur dominantly, with or without muscular involvement. Cause of death in Duchenne muscular dystrophy are usually heart failure, heart block or tachyarrhythmia (3). Carriers are often asymptomatic but in rare cases they may have only muscular, muscular and cardiac manifestations (4) or even cardiac manifestations without skeletal muscle weakness (5). The possibility of cardiac presentations in Duchenne muscular dystrophy carriers depends on age (about 15% in female younger than 16 years of age while 45% in female older than 16 years of age) (6). Cardiac involvement of carriers may vary from asymptomatic cases to end stage heart failure ones (7). The main cause of cardiac presentation in carriers is unknown. In some studies, inactivation of one of the two X-chromosome has been recognized as the etiology (8-10).

2. Case Presentation

A 41-year-old female presented at our hospital because of exacerbation of dyspnea and orthopnea, 10 days before her first visit. She was suffering from dyspnea in the last 5 months. Non-exertional chest pain in this period was another symptom of the patient. She had four pregnancies that were led to two abortions and two deliveries. The latest delivery referred to 2.5 months ago. Her firstborn was 17 years old male with confirmed Duchenne muscular dystrophy, in his genetic study. The other important family history of the patient was her father's disease who died at 31 years old because of heart failure with no further investigations. It is noteworthy that her parents were not relative.

She had no history of deafness and or muscle weakness. In her physical examinations, neurologic and muscular signs were not seen. Her electrocardiogram showed sinus rhythm, interventricular conduction defect and T wave inversion in V₃-V₆ leads. Morphology of QRS complex in lead V₁ was rS. The laboratory data showed that serum Cr: 0.7mg/dL, AST: 20 IU/L, ALT: 4 IU/L, ALKP: 217 IU/L, Bilirubin: 1.1 mg/dL, TSH: 0.9 μ IU/mL, pro-BNP: 3415 pg/mL, troponin: 5.1 μ g/L (normal range) and creatine kinase (CK): 340 IU/L (normal range).

After performing echocardiography, it was revealed that left ventricle (LV) was moderately enlarged (LVEDVI:

75 cc/m²) with global hypokinesia and severely reduced systolic function (ejection fraction: 10%). Cardiac output was estimated 4600 cc/min. Mitral valve was normal with up to moderate functional regurgitation. In angiography, normal coronary arteries were observed. For further evaluation and specifying the cause of cardiomyopathy, cardiac MRI (CMR) was requested. The CMR results showed severe enlarged LV size with severely reduced systolic function (LVEDVI: 138 mL/m², LVEF: 13%), normal right ventricle size (RV) with moderate to severe systolic dysfunction (RVEDVI: 59 mL/m², RVEF: 30%), myocardial hyperemia without edema and there was also evidence of subepicardial fibrosis of lateral LV wall (Figure 1). According to CMR findings, muscular dystrophy with prominent cardiac involvement was considered.

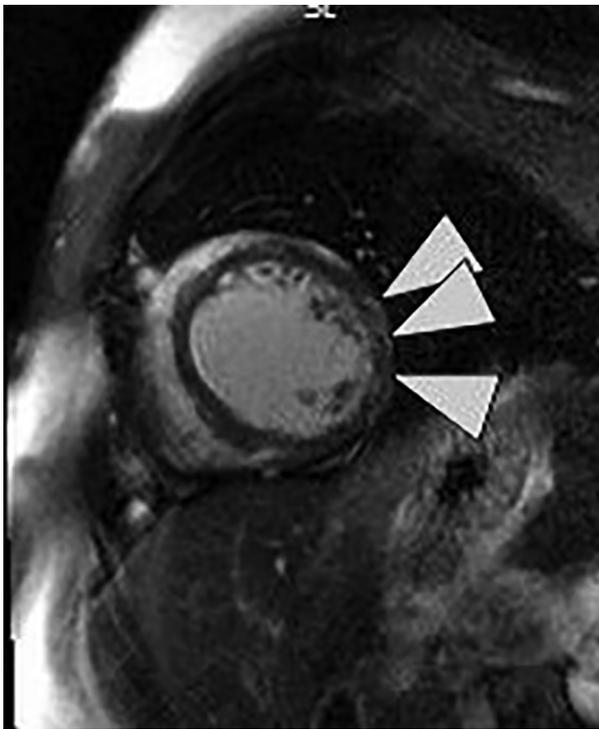


Figure 1. Late gadolinium enhancement sequences on CMR. The arrow shows subepicardial fibrosis of lateral LV wall.

The patient was subjected to treatment with Lisinopril (5 mg daily), metoprolol succinate (23.75 mg BID), spironolactone (25 mg daily), furosemide (40 mg TDS), folic acid (1 mg daily) and vitamin B₁ (300 mg daily).

3. Discussion

Cardiac and muscle involvement may be seen in female carriers of Duchenne muscular dystrophy. The age of

symptom presentation is variable but it almost occurs in adult age (11). Finsterer et al. (12) presented a case of muscular dystrophy carrier, with cardiomyopathy and a rise in serum CK while the increase of CK level is not representative of severity or progression of the disease (13). Florian et al. (14) reported a case of cardiomyopathy without muscular involvement, in a carrier of Duchenne muscular dystrophy while the serum CK level was elevated.

The case presented in this study, had cardiomyopathy without skeletal muscle weakness. Her serum CK level was normal and the disease manifested 2.5 months after delivery. Cheng and Prior also presented a case of asymptomatic Duchenne muscular dystrophy which manifested with post-partum cardiomyopathy (15). CMR, using late gadolinium enhancement is a robust tool for screening of cardiac involvement and early detection of myocardial fibrosis in Duchenne muscular dystrophy patients and carriers. The pattern of fibrosis in their CMR, is presented with subepicardial fibrosis in the inferolateral wall (16). Cardiac MRI findings were in favour of cardiomyopathy due to Duchenne muscular dystrophy. Three differential diagnoses may be considered for this case. First, the patient is a case of familial dilated cardiomyopathy (DCM) which had progression during pregnancy and delivery; second, the patient is a case of postpartum cardiomyopathy and third; the patient is a carrier of Duchenne muscular dystrophy that her disease was progressed during pregnancy and delivery. Pregnancy and delivery may aggravate muscular and cardiac manifestations of carriers (17).

Six months later at follow up, the symptoms including dyspnea and orthopnea were improved and ejection fraction was increased to 25%. To differentiate the diagnosis of this patient, genetic study was recommended but the patient refused it.

Therefore, it is recommended that mothers of sons with Duchenne muscular dystrophy should be screened with CMR and echocardiography at the time of diagnosis of disease in their children (18,19). They should also follow up using echocardiography every 5 years (20).

Footnotes

Conflict of Interests: There is no conflict of interest.

Ethical Approval: This research was approved by the local Ethical Committee of Rajaie Cardiovascular Medical and Research Center.

Funding/Support: The presented case report was conducted in the absence of any commercial or financial support. The paper was supported by Heart Failure and Transplantation departments of Rajaie Cardiovascular, Medical

and Research Center, Iran University of Medical Sciences, Tehran, Iran.

Patient Consent: Written informed consent was not available due to patient's change of residence address but oral agreement was taken for publishing the data.

References

- Lee T, Takeshima Y, Kusunoki N, Awano H, Yagi M, Matsuo M, et al. Differences in carrier frequency between mothers of Duchenne and Becker muscular dystrophy patients. *J Hum Genet.* 2014;**59**(1):46–50. doi: [10.1038/jhg.2013.119](https://doi.org/10.1038/jhg.2013.119). [PubMed: [24225992](https://pubmed.ncbi.nlm.nih.gov/24225992/)]. [PubMed Central: [PMC3970902](https://pubmed.ncbi.nlm.nih.gov/PMC3970902/)].
- Bushby K, Finkel R, Birnkrant DJ, Case LE, Clemens PR, Cripe L, et al. Diagnosis and management of Duchenne muscular dystrophy, part 2: implementation of multidisciplinary care. *Lancet Neurol.* 2010;**9**(2):177–89. doi: [10.1016/S1474-4422\(09\)70272-8](https://doi.org/10.1016/S1474-4422(09)70272-8). [PubMed: [19945914](https://pubmed.ncbi.nlm.nih.gov/19945914/)].
- Mavrogeni S, Markousis-Mavrogenis G, Papavasiliou A, Kolovou G. Cardiac involvement in Duchenne and Becker muscular dystrophy. *World J Cardiol.* 2015;**7**(7):410–4. doi: [10.4330/wjc.v7.i7.410](https://doi.org/10.4330/wjc.v7.i7.410). [PubMed: [26225202](https://pubmed.ncbi.nlm.nih.gov/26225202/)]. [PubMed Central: [PMC4513493](https://pubmed.ncbi.nlm.nih.gov/PMC4513493/)].
- Soltanzadeh P, Friez MJ, Dunn D, von Niederhausern A, Gurvich OL, Swoboda KJ, et al. Clinical and genetic characterization of manifesting carriers of DMD mutations. *Neuromuscul Disord.* 2010;**20**(8):499–504. doi: [10.1016/j.nmd.2010.05.010](https://doi.org/10.1016/j.nmd.2010.05.010). [PubMed: [20630757](https://pubmed.ncbi.nlm.nih.gov/20630757/)]. [PubMed Central: [PMC2944769](https://pubmed.ncbi.nlm.nih.gov/PMC2944769/)].
- Adachi K. Expression of symptoms in a female Duchenne muscular dystrophy carrier: skeletal muscle, cardiac muscle and central nervous system. *Medicine.* 2006;**60**:603–9.
- Nolan MA, Jones OD, Pedersen RL, Johnston HM. Cardiac assessment in childhood carriers of Duchenne and Becker muscular dystrophies. *Neuromuscul Disord.* 2003;**13**(2):129–32. [PubMed: [12565910](https://pubmed.ncbi.nlm.nih.gov/12565910/)].
- Hoogerwaard EM, van der Wouw PA, Wilde AA, Bakker E, Ippel PF, Oosterwijk JC, et al. Cardiac involvement in carriers of Duchenne and Becker muscular dystrophy. *Neuromuscul Disord.* 1999;**9**(5):347–51. doi: [10.1016/S0960-8966\(99\)00018-8](https://doi.org/10.1016/S0960-8966(99)00018-8). [PubMed: [10407858](https://pubmed.ncbi.nlm.nih.gov/10407858/)].
- Florian A, Ludwig A, Engelen M, Waltenberger J, Rosch S, Sechtem U, et al. Left ventricular systolic function and the pattern of late-gadolinium-enhancement independently and additively predict adverse cardiac events in muscular dystrophy patients. *J Cardiovasc Magn Reson.* 2014;**16**:81. doi: [10.1186/s12968-014-0081-1](https://doi.org/10.1186/s12968-014-0081-1). [PubMed: [25315351](https://pubmed.ncbi.nlm.nih.gov/25315351/)]. [PubMed Central: [PMC4176580](https://pubmed.ncbi.nlm.nih.gov/PMC4176580/)].
- Cohen N, Muntoni F. Multiple pathogenetic mechanisms in X linked dilated cardiomyopathy. *Heart.* 2004;**90**(8):835–41. doi: [10.1136/hrt.2003.023390](https://doi.org/10.1136/hrt.2003.023390). [PubMed: [15253946](https://pubmed.ncbi.nlm.nih.gov/15253946/)]. [PubMed Central: [PMC1768363](https://pubmed.ncbi.nlm.nih.gov/PMC1768363/)].
- Giliberto F, Radic CP, Luce L, Ferreiro V, de Brasi C, Szijan I. Symptomatic female carriers of Duchenne muscular dystrophy (DMD): Genetic and clinical characterization. *J Neurol Sci.* 2014;**336**(1-2):36–41. doi: [10.1016/j.jns.2013.09.036](https://doi.org/10.1016/j.jns.2013.09.036). [PubMed: [24135430](https://pubmed.ncbi.nlm.nih.gov/24135430/)].
- Politano L, Nigro V, Nigro G, Petretta VR, Passamano L, Papparella S, et al. Development of cardiomyopathy in female carriers of Duchenne and Becker muscular dystrophies. *JAMA.* 1996;**275**(17):1335–8. doi: [10.1001/jama.275.17.1335](https://doi.org/10.1001/jama.275.17.1335). [PubMed: [8614119](https://pubmed.ncbi.nlm.nih.gov/8614119/)].
- Finsterer J, Stollberger C, Freudenthaler B, Simoni D, Hofberger R, Wagner K. Muscular and cardiac manifestations in a Duchenne-carrier harboring a dystrophin deletion of exons 12-29. *Intractable Rare Dis Res.* 2018;**7**(2):120–5. doi: [10.5582/irdr.2018.01003](https://doi.org/10.5582/irdr.2018.01003). [PubMed: [29862154](https://pubmed.ncbi.nlm.nih.gov/29862154/)]. [PubMed Central: [PMC5982619](https://pubmed.ncbi.nlm.nih.gov/PMC5982619/)].
- Pegoraro E, Schimke RN, Garcia C, Stern H, Cadaldini M, Angelini C, et al. Genetic and biochemical normalization in female carriers of Duchenne muscular dystrophy: Evidence for failure of dystrophin production in dystrophin-competent myonuclei. *Neurology.* 1995;**45**(4):677–90. doi: [10.1212/wnl.45.4.677](https://doi.org/10.1212/wnl.45.4.677). [PubMed: [7723955](https://pubmed.ncbi.nlm.nih.gov/7723955/)].
- Florian A, Ludwig A, Ong P, Klingel K, Kandolf R, Bornemann A, et al. Cause of cardiac disease in a female carrier of Duchenne muscular dystrophy: Myocarditis versus genetic cardiomyopathy without skeletal myopathy? *Circulation.* 2014;**129**(18):e482–4. doi: [10.1161/CIRCULATIONAHA.113.006891](https://doi.org/10.1161/CIRCULATIONAHA.113.006891). [PubMed: [24799508](https://pubmed.ncbi.nlm.nih.gov/24799508/)].
- Cheng VE, Prior DL. Peripartum cardiomyopathy in a previously asymptomatic carrier of Duchenne muscular dystrophy. *Heart Lung Circ.* 2013;**22**(8):677–81. doi: [10.1016/j.hlc.2012.11.015](https://doi.org/10.1016/j.hlc.2012.11.015). [PubMed: [23279916](https://pubmed.ncbi.nlm.nih.gov/23279916/)].
- Mavrogeni S, Papavasiliou A, Skouteli E, Magoutas A, Dangas G. Cardiovascular magnetic resonance imaging evaluation of two families with Becker muscular dystrophy. *Neuromuscul Disord.* 2010;**20**(11):717–9. doi: [10.1016/j.nmd.2010.06.009](https://doi.org/10.1016/j.nmd.2010.06.009). [PubMed: [20630758](https://pubmed.ncbi.nlm.nih.gov/20630758/)].
- Hori H, Maeda Y, Ishizaki M, Hirahara T, Watanabe M, Yamashita S, et al. A carrier with de novo mutation in the dystrophin gene whose myopathic symptoms became seriously progressive after pregnancy and delivery. *Muscle Nerve.* 2015;**52**(5):913–4. doi: [10.1002/mus.24744](https://doi.org/10.1002/mus.24744). [PubMed: [26088440](https://pubmed.ncbi.nlm.nih.gov/26088440/)].
- Schelhorn J, Schoenecker A, Neudorf U, Schemuth H, Nensa F, Nassenstein K, et al. Cardiac pathologies in female carriers of Duchenne muscular dystrophy assessed by cardiovascular magnetic resonance imaging. *Eur Radiol.* 2015;**25**(10):3066–72. doi: [10.1007/s00330-015-3694-3](https://doi.org/10.1007/s00330-015-3694-3). [PubMed: [25791640](https://pubmed.ncbi.nlm.nih.gov/25791640/)].
- Lang SM, Shugh S, Mazur W, Sticka JJ, Rattan MS, Jefferies JL, et al. Myocardial fibrosis and left ventricular dysfunction in duchenne muscular dystrophy carriers using cardiac magnetic resonance imaging. *Pediatr Cardiol.* 2015;**36**(7):1495–501. doi: [10.1007/s00246-015-1192-7](https://doi.org/10.1007/s00246-015-1192-7). [PubMed: [25976773](https://pubmed.ncbi.nlm.nih.gov/25976773/)].
- American Academy of Pediatrics Section on C, Cardiac S. Cardiovascular health supervision for individuals affected by Duchenne or Becker muscular dystrophy. *Pediatrics.* 2005;**116**(6):1569–73. doi: [10.1542/peds.2005-2448](https://doi.org/10.1542/peds.2005-2448). [PubMed: [16322188](https://pubmed.ncbi.nlm.nih.gov/16322188/)].