



Danon Disease: A Challenging Case with Diagnosis of Hypertrophic Cardiomyopathy

Ahmad Amin¹, Meysam Khoshavi^{1*}, Sepideh Taghavi¹, Nasim Naderi¹, Nejat Mahdieh², Zahra Emkanjoo¹ and Mitra Chitsazan³

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

²Cardiogenetic Research Center, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran

³Cardiovascular Research Center, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran

*Corresponding author: Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran. Email: meysamkhoshavi@yahoo.com

Received 2018 December 09; Revised 2019 April 12; Accepted 2019 April 16.

Abstract

Danon disease is an X-linked dominant glycogen storage disease characterized by cardiomyopathy, skeletal myopathy, and intellectual disability. Danon disease has a rapidly progressive natural course, hence early diagnosis is crucial to achieve a proper management plan. This case concerns a 30-year-old male of Danon disease presenting with symptoms and signs of systolic heart failure, with no intellectual impairment and skeletal muscle involvement at presentation. Thus, he was initially misdiagnosed and managed as idiopathic sarcomeric hypertrophic cardiomyopathy. To the best of our knowledge, this is the first report of Danon disease in Iran, further implicating previous cases overlooked by local cardiologists.

Keywords: Danon Disease Cardiomyopathy, Glycogen Storage Disease, Skeletal Myopathy, Heart Failure

1. Introduction

Danon disease (or lysosomal glycogen storage disease type 2B) is a rare, X-linked dominant genetic disorder caused by mutations in the lysosomal associated membrane protein 2 (LAMP2) gene. This results in a deficiency of LAMP2 protein, a component of the lysosomal membrane, causing excessive intra-sarcomeric glycogen accumulation similar to what is observed with acid maltase deficiency; however, acid maltase activity is normal in these patients (1). Danon disease is characterized by cardiac involvement, intellectual disability and skeletal myopathy; although the clinical manifestations can vary and with other organ involvement (1, 2). Classic cardiac involvement in Danon disease is hypertrophic cardiomyopathy, with a reported prevalence of 1% to 33% of Danon disease among hypertrophic cardiomyopathy patients (3-5). Dilated and restrictive cardiomyopathies have been reported less frequently in Danon disease (6).

This case concerns a 30-year-old male presenting with recently developed exertional dyspnea, which was first diagnosed and managed as sarcomeric hypertrophic cardiomyopathy. Deteriorating clinical status, despite optimum heart failure therapy, and the development of progressive proximal muscle weakness over the course of the

disease resulted in making the diagnosis of Danon disease, which to the best of our knowledge is the first report of this rare genetic disorder in Iran.

2. Case Presentation

A 30-year-old male was referred to Heart Failure and Transplantation Clinic of Rajaie Cardiovascular Medical and Research Center, Tehran, Iran with recently developed exertional dyspnea (New York Heart Association Functional class II - III), without complaining of orthopnea or syncope. His past medical history was unremarkable, in particular for musculoskeletal complaints.

On physical examination, the patient appeared in good general health and his mental and speech status was normal. His temperature was 36.8°C, blood pressure was 100/65 mmHg and pulse rate was 65 beats/minutes and respirations were 20/minutes. On cardiovascular examination, the heart rate and rhythm were regular, and S4 sound was heard. Jugular venous pressure was distended. No peripheral edema, clubbing, or cyanosis was present. His family history was notable for the deaths of his two older brothers, his mother and his sister which were declared to be due to cardiac failure, although he did not have more de-

tailed information. Laboratory test results, including complete blood count, serum electrolytes, serum creatinine level, liver and thyroid function tests, lactate dehydrogenase, creatine phosphokinase and cardiac troponins were within normal ranges. Electrocardiography (ECG) revealed left axis deviation and left bundle branch block (LBBB) with a mild slurred QRS upstroke without short PR interval (Figure 1A). Echocardiography showed a left ventricular ejection fraction (LVEF) of 45%, normal left ventricular (LV) size, mild LV Hypertrophy, severe hypertrophied papillary muscles, and mild mitral and tricuspid regurgitation (Figure 1B). The right ventricular function was normal.

Considering all above, patient was diagnosed with hypertrophic cardiomyopathy (HCM) and carvedilol, lisinopril and furosemide was started for him. An implantable cardioverter defibrillator (ICD) device was also implanted.

A few months later, the patient presented to the Emergency Department with an ICD Shock due to an inappropriate therapy. ECG tracing revealed irregularly irregular wide QRS tachyarrhythmia (atrial tachycardia) (Figure 1C). Therefore, the patient was decided to undergo electrophysiology study (EPS) and ablation. On EPS, ventricular tachycardia (VT) was not induced and catheter ablation for atrial arrhythmia was done. Moreover, a high-grade A-V block was identified during EPS, encouraging a decision to upgrade ICD device to cardiac resynchronization therapy with defibrillator (CRT-D). Chest X-ray after CRT-D implantation showed cardiomegaly, prominent right heart border and pulmonary congestion (Figure 1D).

During the following year, despite receiving standard heart failure therapy, NYHA function class deteriorated; and peripheral edema and ascites occurred. The patient also developed hypothyroidism. Laboratory test results showed increased muscle enzymes (creatine phosphokinase), lactate dehydrogenase (LDH) and liver aminotransferases (Table 1). Due to the progressive proximal muscle weakness and laboratory findings, biopsy of the deltoid muscle and genetic study were performed. The muscle biopsy showed mild myopathic atrophy, autophagic vacuoles and no prominent glycogen excess. The genetic study and sequence analysis identified a nonsense mutation in exon 7 (c.877C > T, p.Arg293Ter) of LAMP2 gene, which showed hemizygoty for a T > G transition at position 987 resulting in a premature stop codon, a pathogenic mutation in LAMP2 gene, confirming the diagnosis of Danon disease (Table 2).

A few months later, despite using inotrope and high dose diuretics, the patient died due to cardiac pump failure and respiratory infection.

Table 1. Complete Lab Data of Patient After Beginning of Skeletal Myopathy

Lab Data	Patient Data	Normal Range
Hemoglobin, gr/dL	9.4	14 - 16
Creatinine, mg/dL	0.7	0.7 - 1.2
Sodium, mEq/L	130	135 - 145
Potassium, mEq/L	3.4	3.5 - 5.5
Thyroglobulin stimulation test (TSH), μ IU/mL	5.8	0.4 - 4
Alanine aminotransferase (ALT), U/L	311	< 32
Aspartate aminotransferase (AST), U/L	418	< 32
Lactate dehydrogenase, U/L	1773	< 190
Creatine phosphokinase, IU/L	1698	< 120
Troponin, ng/L	0.5	< 0.05
Albumin, gr/dL	2.8	3.5 - 5.5

3. Discussion

Danon disease is a rare genetic disorder due to mutations in the lysosomal associated membrane protein 2 (LAMP2) gene, causing a deficiency of LAMP2 protein. The LAMP2 deficiency, as a component of the lysosomal membrane, results in the accumulation of intracellular vacuoles that contain autophagic materials, including glycogen, degenerating mitochondria, lipids and basophilic granules within the cells (7-9). Danon disease is inherited via X-linked dominant inheritance, although the phenotypic expression of LAMP2 deficiency varies.

We described a patient presenting with symptoms and signs of heart failure, initially misdiagnosed as having idiopathic hypertrophic cardiomyopathy. Rapidly deteriorating clinical status, despite receiving standard heart failure treatment, the development of mild muscular myopathy in conjunction of elevated muscle enzymes encouraged us to re-evaluate the patient. After thorough examinations and genetic analysis, we diagnosed the first report of Danon disease in Iran. However, we assume that there might have been other affected patients previously which have not been diagnosed properly and have been managed as idiopathic causes of cardiomyopathies, such as our patient's older brothers. This highlights the necessity of careful assessment when encountering cardiomyopathy patients, in particular patients with positive family history and patients with rapidly progressive disease and those not responding adequately to standard medications.

3.1. Clinical Presentations

The classic clinical trial of Danon disease includes LV hypertrophy, mental retardation, and peripheral myopathy (10). However, a number of cases have been reported with dominant cardiac involvement and no to minimal cognitive or peripheral muscular impairment (4, 11, 12).

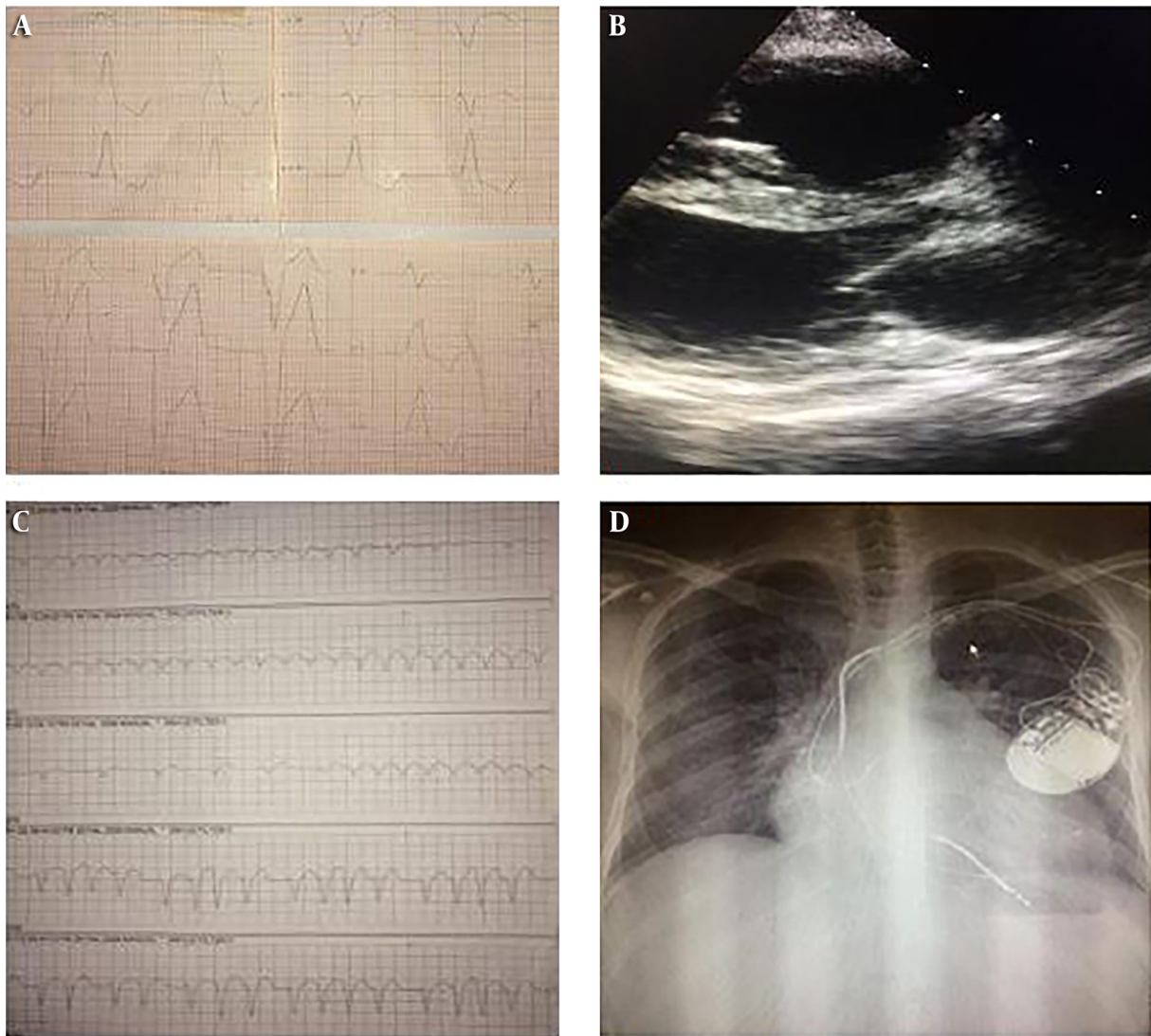


Figure 1. A, ECG revealed left bundle branch block (LBBB) and mild slurred upstroke of QRS; B, echocardiography showed left ventricular hypertrophy (LVH) and normal left ventricular size; C, atrial arrhythmia caused inappropriate ICD shock; D, chest X-ray revealed cardiomegaly and pulmonary congestion.

Table 2. Report of the Genetic Study of Patient^a

Gene	Nucleic Acid Alteration	Variant Location	Amino Acid Alteration	Genotype			Clinical Significance
				Index	Mother	Father	
LAMP2	c.877C > T	Exon7	p.Arg293Ter	Hemi	NA	NA	Pathogenic

^aDirect sequencing of the coding regions of LAMP2 gene showed a hemizygous pathogenic mutation at position c.877C > T presented at protein level as p.Arg293Ter.

Similarly, our patient presented with cardiac involvement and normal cognitive function and he had no muscular involvement at presentation; although he developed proximal myopathy later on with disease progression.

The most important prognostic factor in Danon dis-

ease is the severity of cardiac involvement (1). Characteristic cardiac manifestations include cardiomyopathy and cardiac electrical abnormality.

Male and female patients have different clinical presentation in terms of type of cardiomyopathy. Men usu-

ally present at an earlier age with predominantly hypertrophic cardiomyopathy while women are equally affected with hypertrophic or dilated cardiomyopathy (12). Overall, females have a better long-term prognosis than males; without heart transplantation, men usually die before the age of 25 (1, 13-15). The electrocardiographic abnormalities in Danon disease include voltage criteria consistent with LV hypertrophy, left bundle branch block, a slurred QRS upstroke, short or long PR interval and atrio-ventricular block (16, 17). Ventricular pre-excitation pattern is found in 68% of men and 27% of women (14). Both atrial and ventricular arrhythmias can occur. Arrhythmias account for 50% - 55% of death in Danon disease (1, 15). Considering the conspicuous prevalence of arrhythmia and cardiac arrest, ICD is usually considered for these patients (15-17). Our patient and his affected family members died from advanced heart failure, although he had experienced frequent atrial arrhythmias.

Skeletal myopathy is seen in 80% - 100% of affected males and 33% - 50% of female. Females also have lower serum creatine kinase compared to male patients (10, 15, 17, 18). The muscles in the back, upper arms, shoulders, neck, and thighs are most often involved; however, patients usually retain their ability to walk. Some studies have shown intellectual and cognitive impairment in Danon disease, in particular in men (70% - 100%) (1, 17). Other studies showed that most patients do not have overt mental and intellectual disability, but rather mild cognitive deficits and higher incidence of mood and anxiety disorders (19, 20).

Other organs can also be affected in Danon disease. Restrictive lung diseases occur due to respiratory muscle weakness. Gastrointestinal complaints are more common in men and include chronic abdominal pain, constipation, diarrhea, and esophageal dysmotility (10). Mild liver injury can occur due accumulation of autophagic vacuoles and intrahepatic cholestasis, which presents with abnormal liver function tests (21). Danon disease may cause a primary retinal pigment epitheliopathy with reduced trans-epithelium potential (22). Significant loss of retinal pigments causes central scotoma, serious color vision disturbances and a cone-rod dystrophy on the electroretinogram in male patients (69% of cases); however, affected females (64%) may show milder peripheral pigmentary retinopathy (1, 17).

3.2. Diagnosis

In patients with non-ischemic cardiomyopathy (especially HCM) and/or impaired liver function test and/or muscle weakness with elevated CK and/or pre-excitation's changes in ECG, glycogen storage diseases, in particular Danon disease should be considered (23).

Cardiac magnetic resonance imaging (MRI) may provide valuable morphological and structural information in patients with Danon disease. However, studies have not demonstrated typical late gadolinium enhancement (LGE) pattern in Danon disease, whether in HCM or in DCM phenotypes. The extent of LGE (fibrosis) may contribute to heart failure, ventricular arrhythmias and poor outcome (24, 25).

Simultaneous endomyocardial and skeletal muscle biopsy might show discordant findings. Vacuolar myopathy in skeletal muscle but not myocardial biopsy and the reciprocal situation has been described (26, 27). It is important to note that excess glycogen is not always visible on a single muscle biopsy (28). Vacuoles with undigested glycogen may be found in other glycogenosis, including protein kinase CGMP-dependent 2 (PRKG2) cardiomyopathy and Fabry's disease that can have similar presentations to Danon disease (4). The Immunofluorescence and morphometric analysis, immunoblotting and gene expression analyses on biopsy samples can be used for evaluation of LAMP2 deficiency (29). However, genetic mutation analysis of LAMP2 gene can confirm the clinical suspicion (1).

3.3. Treatment

It is not clear whether standard heart failure treatment, including beta-adrenergic receptor blockers, angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) and mineralocorticoid receptor antagonist (MRA) are effective in slowing disease progression and increasing survival in Danon disease. However, beta-blockers are used for patients presenting with HCM phenotype to control arrhythmia; and typical heart failure medication may be attenuated symptoms in DCM subtype. Diuretics can reduce pulmonary congestion and peripheral edema (1, 15). Electrophysiology studies to assess electrical conduction system are warranted in patients presenting with arrhythmias. Early implantation of cardioverter defibrillator should be considered in susceptible individuals to develop life-threatening arrhythmias. Cardiac ablation therapy might also be needed in a subset of patients. Cardiac resynchronization therapy (CRT) is suggested for patients with high grade atrioventricular block (1, 15, 30, 31). As cardiac involvement usually progresses rapidly, cardiac transplantation should be considered at an early stage, in particular in male patients. The survival after heart transplantation is similar to other causes of heart transplantation.

Proximal skeletal myopathy and mental disorder is usually mild and often does not cause serious limitations for cardiac transplantation. Physical therapy can improve muscle weakness (32, 33).

In the series of Samad and Co, 2 out of 3 transplanted patients did not have a good outcome (34) but other studies reported, better outcome was achieved after heart transplantation. This bias can be due to the phenotype-genotype variation and the small number of cases. However, considering the progressive heart failure despite treatment, the transplantation is inevitable and recommended early listing (34, 35).

Other novel therapies including gene therapy, use of human induced pluripotent stem cell-derived cardiomyocytes (iPSC-CMs) and recombinant LAMP2 protein therapy are under investigation (9, 35, 36).

3.4. Conclusions

Danon disease is a rare cause of genetic susceptibility to cardiomyopathy with progressive and eventually life-threatening natural course. This case highlights the importance of a careful and thorough assessment of unexplained cardiomyopathies, including genetic counseling, for early detection of genetic causes of cardiomyopathies, particularly in patients with positive family history and in patients with progressive disease despite standard medications. In such circumstances, early diagnosis is crucial in making an appropriate treatment plan and in pursuing proper management strategies.

Footnotes

Conflict of Interests: The authors declare that the case report was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Funding/Support: This article was supported by Heart Failure and Transplantation departments of Rajaie Cardiovascular, Medical and Research Center.

Patient Consent: Informed consent was not declared by the authors.

References

- D'Souza R S, Levandowski C, Slavov D, Graw SL, Allen LA, Adler E, et al. Danon disease: Clinical features, evaluation, and management. *Circ Heart Fail*. 2014;7(5):843-9. doi: [10.1161/CIRCHEARTFAILURE.114.001105](https://doi.org/10.1161/CIRCHEARTFAILURE.114.001105). [PubMed: [25228319](https://pubmed.ncbi.nlm.nih.gov/25228319/)]. [PubMed Central: [PMC4169002](https://pubmed.ncbi.nlm.nih.gov/PMC4169002/)].
- Kim J, Parikh P, Mahboob M, Arrighi JA, Atalay MK, Rowin EJ, et al. Asymptomatic young man with Danon disease. *Tex Heart Inst J*. 2014;41(3):332-4. doi: [10.14503/THIJ-13-3279](https://doi.org/10.14503/THIJ-13-3279). [PubMed: [24955057](https://pubmed.ncbi.nlm.nih.gov/24955057/)]. [PubMed Central: [PMC4060354](https://pubmed.ncbi.nlm.nih.gov/PMC4060354/)].
- Charron P, Villard E, Sebillon P, Laforet P, Maisonneuve T, Duboscq-Bidot L, et al. Danon's disease as a cause of hypertrophic cardiomyopathy: A systematic survey. *Heart*. 2004;90(8):842-6. doi: [10.1136/hrt.2003.029504](https://doi.org/10.1136/hrt.2003.029504). [PubMed: [15253947](https://pubmed.ncbi.nlm.nih.gov/15253947/)]. [PubMed Central: [PMC1768382](https://pubmed.ncbi.nlm.nih.gov/PMC1768382/)].
- Arad M, Maron BJ, Gorham JM, Johnson WH Jr, Saul JP, Perez-Atayde AR, et al. Glycogen storage diseases presenting as hypertrophic cardiomyopathy. *N Engl J Med*. 2005;352(4):362-72. doi: [10.1056/NEJMoa033349](https://doi.org/10.1056/NEJMoa033349). [PubMed: [15673802](https://pubmed.ncbi.nlm.nih.gov/15673802/)].
- Fanin M, Nascimbeni AC, Fulizio L, Spinazzi M, Melacini P, Angelini C. Generalized lysosome-associated membrane protein-2 defect explains multisystem clinical involvement and allows leukocyte diagnostic screening in Danon disease. *Am J Pathol*. 2006;168(4):1309-20. doi: [10.2353/ajpath.2006.050646](https://doi.org/10.2353/ajpath.2006.050646). [PubMed: [16565504](https://pubmed.ncbi.nlm.nih.gov/16565504/)]. [PubMed Central: [PMC1606547](https://pubmed.ncbi.nlm.nih.gov/PMC1606547/)].
- Sugie K, Koori T, Yamamoto A, Ogawa M, Hirano M, Inoue K, et al. Characterization of Danon disease in a male patient and his affected mother. *Neuromuscul Disord*. 2003;13(9):708-11. [PubMed: [14561493](https://pubmed.ncbi.nlm.nih.gov/14561493/)].
- Yang Z, Vatta M. Danon disease as a cause of autophagic vacuolar myopathy. *Congenit Heart Dis*. 2007;2(6):404-9. doi: [10.1111/j.1747-0803.2007.00132.x](https://doi.org/10.1111/j.1747-0803.2007.00132.x). [PubMed: [18377432](https://pubmed.ncbi.nlm.nih.gov/18377432/)].
- Bertini E, Donati MA, Broda P, Cassandrini D, Petrini S, Dionisi-Vici C, et al. Phenotypic heterogeneity in two unrelated Danon patients associated with the same LAMP-2 gene mutation. *Neuropediatrics*. 2005;36(5):309-13. doi: [10.1055/s-2005-872844](https://doi.org/10.1055/s-2005-872844). [PubMed: [16217705](https://pubmed.ncbi.nlm.nih.gov/16217705/)].
- Rowland TJ, Sweet ME, Mestroni L, Taylor MR. Danon disease - dysregulation of autophagy in a multisystem disorder with cardiomyopathy. *J Cell Sci*. 2016;129(11):2135-43. doi: [10.1242/jcs.184770](https://doi.org/10.1242/jcs.184770). [PubMed: [27165304](https://pubmed.ncbi.nlm.nih.gov/27165304/)]. [PubMed Central: [PMC4920246](https://pubmed.ncbi.nlm.nih.gov/PMC4920246/)].
- Boucek D, Jirikovic J, Taylor M. Natural history of Danon disease. *Genet Med*. 2011;13(6):563-8. doi: [10.1097/GIM.0b013e31820ad795](https://doi.org/10.1097/GIM.0b013e31820ad795). [PubMed: [21415759](https://pubmed.ncbi.nlm.nih.gov/21415759/)].
- Sugie K, Yamamoto A, Murayama K, Oh SJ, Takahashi M, Mora M, et al. Clinicopathological features of genetically confirmed Danon disease. *Neurology*. 2002;58(12):1773-8. [PubMed: [12084876](https://pubmed.ncbi.nlm.nih.gov/12084876/)].
- Maron BJ, Roberts WC, Arad M, Haas TS, Spirito P, Wright GB, et al. Clinical outcome and phenotypic expression in LAMP2 cardiomyopathy. *JAMA*. 2009;301(12):1253-9. doi: [10.1001/jama.2009.371](https://doi.org/10.1001/jama.2009.371). [PubMed: [19318653](https://pubmed.ncbi.nlm.nih.gov/19318653/)]. [PubMed Central: [PMC4106257](https://pubmed.ncbi.nlm.nih.gov/PMC4106257/)].
- Van Der Starre P, Deuse T, Pritts C, Brun C, Vogel H, Oyer P. Late profound muscle weakness following heart transplantation due to Danon disease. *Muscle Nerve*. 2013;47(1):135-7. doi: [10.1002/mus.23517](https://doi.org/10.1002/mus.23517). [PubMed: [23168931](https://pubmed.ncbi.nlm.nih.gov/23168931/)].
- Cheng Z, Fang Q. Danon disease: focusing on heart. *J Hum Genet*. 2012;57(7):407-10. doi: [10.1038/jhg.2012.72](https://doi.org/10.1038/jhg.2012.72). [PubMed: [22695892](https://pubmed.ncbi.nlm.nih.gov/22695892/)].
- D'Souza R S, Mestroni L, Taylor MRG. Danon disease for the cardiologist: Case report and review of the literature. *J Community Hosp Intern Med Perspect*. 2017;7(2):107-14. doi: [10.1080/20009666.2017.1324239](https://doi.org/10.1080/20009666.2017.1324239). [PubMed: [28638575](https://pubmed.ncbi.nlm.nih.gov/28638575/)]. [PubMed Central: [PMC5473185](https://pubmed.ncbi.nlm.nih.gov/PMC5473185/)].
- Konrad T, Sonnenschein S, Schmidt FP, Mollnau H, Bock K, Ocete BQ, et al. Cardiac arrhythmias in patients with Danon disease. *Eurpace*. 2017;19(7):1204-10. doi: [10.1093/europace/euw215](https://doi.org/10.1093/europace/euw215). [PubMed: [27742774](https://pubmed.ncbi.nlm.nih.gov/27742774/)].
- Ruiz-Guerrero L, Barriales-Villa R. Storage diseases with hypertrophic cardiomyopathy phenotype. *Glob Cardiol Sci Pract*. 2018;2018(3):28. doi: [10.21542/gcsp.2018.28](https://doi.org/10.21542/gcsp.2018.28). [PubMed: [30393640](https://pubmed.ncbi.nlm.nih.gov/30393640/)]. [PubMed Central: [PMC6209457](https://pubmed.ncbi.nlm.nih.gov/PMC6209457/)].
- Nishino I. Autophagic vacuolar myopathy. *Semin Pediatr Neurol*. 2006;13(2):90-5. doi: [10.1016/j.spenn.2006.06.004](https://doi.org/10.1016/j.spenn.2006.06.004). [PubMed: [17027858](https://pubmed.ncbi.nlm.nih.gov/17027858/)].
- Yardeni M, Weisman O, Mandel H, Weinberger R, Quarta G, Salazar-Mendiguchia J, et al. Psychiatric and cognitive characteristics of individuals with Danon disease (LAMP2 gene mutation). *Am J Med Genet A*. 2017;173(9):2461-6. doi: [10.1002/ajmg.a.38320](https://doi.org/10.1002/ajmg.a.38320). [PubMed: [28627787](https://pubmed.ncbi.nlm.nih.gov/28627787/)]. [PubMed Central: [PMC5561494](https://pubmed.ncbi.nlm.nih.gov/PMC5561494/)].
- Dickens C, Cherrington A, McGowan L. Depression and health-related quality of life in people with coronary heart disease: A systematic review. *Eur J Cardiovasc Nurs*. 2012;11(3):265-75. doi: [10.1177/1474515111430928](https://doi.org/10.1177/1474515111430928). [PubMed: [22457381](https://pubmed.ncbi.nlm.nih.gov/22457381/)].

21. Wang L, Wang J, Cai W, Shi Y, Zhou X, Guo G, et al. A critical evaluation of liver pathology in humans with Danon disease and experimental correlates in a rat model of LAMP-2 deficiency. *Clin Rev Allergy Immunol*. 2017;**53**(1):105-16. doi: [10.1007/s12016-017-8598-3](https://doi.org/10.1007/s12016-017-8598-3). [PubMed: [28124283](https://pubmed.ncbi.nlm.nih.gov/28124283/)].
22. Thompson DA, Constable PA, Liasis A, Walters B, Esteban MT. The physiology of the retinal pigment epithelium in Danon disease. *Retina*. 2016;**36**(3):629-38. doi: [10.1097/IAE.0000000000000736](https://doi.org/10.1097/IAE.0000000000000736). [PubMed: [26398689](https://pubmed.ncbi.nlm.nih.gov/26398689/)].
23. Linhart A, Cecchi F. Common presentation of rare diseases: Left ventricular hypertrophy and diastolic dysfunction. *Int J Cardiol*. 2018;**257**:344-50. doi: [10.1016/j.ijcard.2018.01.006](https://doi.org/10.1016/j.ijcard.2018.01.006). [PubMed: [29506729](https://pubmed.ncbi.nlm.nih.gov/29506729/)].
24. Nucifora G, Miani D, Piccoli G, Proclemer A. Cardiac magnetic resonance imaging in Danon disease. *Cardiology*. 2012;**121**(1):27-30. doi: [10.1159/000336448](https://doi.org/10.1159/000336448). [PubMed: [22378182](https://pubmed.ncbi.nlm.nih.gov/22378182/)].
25. Vago H, Somloi M, Toth A, Merkely B. Danon disease: a rare cause of left ventricular hypertrophy with cardiac magnetic resonance follow-up. *Eur Heart J*. 2016;**37**(21):1703. doi: [10.1093/eurheartj/ehv332](https://doi.org/10.1093/eurheartj/ehv332). [PubMed: [26206213](https://pubmed.ncbi.nlm.nih.gov/26206213/)].
26. Lines MA, Hewson S, Halliday W, Sabatini PJ, Stockley T, Dipchand AI, et al. Danon disease due to a novel LAMP2 microduplication. *JIMD Rep*. 2014;**14**:11-6. doi: [10.1007/8904_2013_277](https://doi.org/10.1007/8904_2013_277). [PubMed: [24222494](https://pubmed.ncbi.nlm.nih.gov/24222494/)]. [PubMed Central: [PMC4213339](https://pubmed.ncbi.nlm.nih.gov/PMC4213339/)].
27. Taylor MR, Ku L, Slavov D, Cavanaugh J, Boucek M, Zhu X, et al. Danon disease presenting with dilated cardiomyopathy and a complex phenotype. *J Hum Genet*. 2007;**52**(10):830-5. doi: [10.1007/s10038-007-0184-8](https://doi.org/10.1007/s10038-007-0184-8). [PubMed: [17899313](https://pubmed.ncbi.nlm.nih.gov/17899313/)].
28. Sugie K, Noguchi S, Kozuka Y, Arikawa-Hirasawa E, Tanaka M, Yan C, et al. Autophagic vacuoles with sarcolemmal features delineate Danon disease and related myopathies. *J Neuropathol Exp Neurol*. 2005;**64**(6):513-22. [PubMed: [15977643](https://pubmed.ncbi.nlm.nih.gov/15977643/)].
29. Nascimbeni AC, Fanin M, Angelini C, Sandri M. Autophagy dysregulation in Danon disease. *Cell Death Dis*. 2017;**8**(1). e2565. doi: [10.1038/cddis.2016.475](https://doi.org/10.1038/cddis.2016.475). [PubMed: [28102838](https://pubmed.ncbi.nlm.nih.gov/28102838/)]. [PubMed Central: [PMC5386379](https://pubmed.ncbi.nlm.nih.gov/PMC5386379/)].
30. Guo LY, Wang B, Shen M, Liu B, Liu LW. Cardiac resynchronization therapy-pacemaker implantation guided by three-dimensional electroanatomic mapping for a Chinese young man with Danon disease. *Chin Med J (Engl)*. 2018;**131**(22):2760-2. doi: [10.4103/0366-6999.245156](https://doi.org/10.4103/0366-6999.245156). [PubMed: [30425207](https://pubmed.ncbi.nlm.nih.gov/30425207/)]. [PubMed Central: [PMC6247605](https://pubmed.ncbi.nlm.nih.gov/PMC6247605/)].
31. Zaki A, Zaidi A, Newman WG, Garratt CJ. Advantages of a subcutaneous implantable cardioverter-defibrillator in LAMP2 hypertrophic cardiomyopathy. *J Cardiovasc Electrophysiol*. 2013;**24**(9):1051-3. doi: [10.1111/jce.12142](https://doi.org/10.1111/jce.12142). [PubMed: [23577876](https://pubmed.ncbi.nlm.nih.gov/23577876/)].
32. Poignant S, Bourguignon T, Espitalier F. Heart transplantation in Danon disease: A single family displaying diverse phenotypes. *J Heart Lung Transplant*. 2017. doi: [10.1016/j.healun.2017.10.027](https://doi.org/10.1016/j.healun.2017.10.027). [PubMed: [29153639](https://pubmed.ncbi.nlm.nih.gov/29153639/)].
33. Samad F, Jain R, Jan MF, Sulemanjee NZ, Menaria P, Calvin L, et al. Malignant cardiac phenotypic expression of Danon disease (LAMP2 cardiomyopathy). *Int J Cardiol*. 2017;**245**:201-6. doi: [10.1016/j.ijcard.2017.06.031](https://doi.org/10.1016/j.ijcard.2017.06.031). [PubMed: [28874292](https://pubmed.ncbi.nlm.nih.gov/28874292/)].
34. Sankaranarayanan R, Fleming EJ, Garratt CJ. Mimics of hypertrophic cardiomyopathy - diagnostic clues to aid early identification of phenocopies. *Arrhythm Electrophysiol Rev*. 2013;**2**(1):36-40. doi: [10.15420/aer.2013.2.1.36](https://doi.org/10.15420/aer.2013.2.1.36). [PubMed: [26835038](https://pubmed.ncbi.nlm.nih.gov/26835038/)]. [PubMed Central: [PMC4711498](https://pubmed.ncbi.nlm.nih.gov/PMC4711498/)].
35. Arad M. Cardiac Danon disease: Insights and challenges. *Int J Cardiol*. 2017;**245**:211-2. doi: [10.1016/j.ijcard.2017.07.106](https://doi.org/10.1016/j.ijcard.2017.07.106). [PubMed: [28874294](https://pubmed.ncbi.nlm.nih.gov/28874294/)].
36. Flotte TR, Daniels E, Benson J, Bevett-Rose JM, Cornetta K, Diggins M, et al. The gene therapy resource program: A decade of dedication to translational research by the national heart, lung, and blood institute. *Hum Gene Ther Clin Dev*. 2017;**28**(4):178-86. doi: [10.1089/humc.2017.170](https://doi.org/10.1089/humc.2017.170). [PubMed: [29130351](https://pubmed.ncbi.nlm.nih.gov/29130351/)]. [PubMed Central: [PMC5733658](https://pubmed.ncbi.nlm.nih.gov/PMC5733658/)].