Conclusion

Clinical presentation of this anomaly shows great variability and it is difficult to estimate the anatomical progression. Therefore, the treatment of the disease should be personalized and risk score should be formulated for the objective treatment decision but further studies are needed for this.

Video 1. Echocardiography showed that excessive right atrial dilatation without any tricuspid valve and cardiac anomalies
Video 2. During the injection of opaque matter to innominate vein, we detected that enlarged right atrium had became larger than right ventricle as a stomach shape

References

1. Sumner RG, Phillips JH, Jacoby WJ Jr, Tucker DH. Idiopathic enlargement of the right atrium. Circulation 1965; 32: 985-91. [CrossRef]
2. Forbes K, Kantoch MJ, Divekar A, Ross D, Rebeyka IM. Management of infants with idiopathic dilatation of the right atrium and atrial tachycardia. Pediatr Cardiol 2007; 28: 289-96. [CrossRef]
3. Blaysat G, Villain E, Maron F, Rey C, Lipka J, Lefevre M, et al. Prognosis and outcome of idiopathic dilatation of the right atrium in children. A cooperative study of 15 cases. Arch Mal Coeur Vaiss 1997; 90: 645-8.
4. Divekar A, Soni R, Ross D. Rapidly progressive idiopathic dilation of the right atrium in infancy associated with dynamic obstruction of the airways. Cardiol Young 2002; 12: 491-3. [CrossRef]
5. Kalangos A, Ouaknine R, Hulin S, Cohen L, Lecompte Y. Pericardial reinforcement after partial atrial resection in idiopathic enlargement of the right atrium. Ann Thorac Surg 2001; 71: 737-8. [CrossRef]
6. Blondheim DS, Klein R, Plich M, Marmor AT. Familial idopathic dilatation of the right atrium with complete atrio-ventricular block: a new syndrome? Cardiology 2000; 94: 224-6. [CrossRef]
7. Hofmann SR, Heilmann A, Häusler HJ, Dähnert I, Kamin G, Lachmann R. Congenital idiopathic dilatation of the right atrium: antenatal appearance, postnatal management, long-term follow-up and possible pathomechanism. Fetal Diagn Ther 2012; 32: 256-61. [CrossRef]
8. İmren Y, Halit V, Kula S, Olguntürk R. Giant right atrial aneurysm: case report. Int J Cardiol 2006; 112: 66-8. [CrossRef]
9. Zaqout M, De Wolf D. Congenital giant aneurysm of the right atrium. Anadolu Kardiyol Derg 2011; 11: E34.
10. Binder TM, Rosenhek R, Frank H, Gwechenberger M, Maurer G, Baumgartner H. Congenital malformations of the right atrium and the coronary sinus: an analysis based on 103 cases reported in the literature and two additional cases. Chest 2000; 117: 1740-8. [CrossRef]

This case was presented as a poster in the 11th National Pediatric Cardiology and Pediatric Cardiovascular Surgery Congres, May 2012, Izmir-Türkiye

Address for Correspondence: Dr. Abdullah Özyurt,
Erciyes Üniversitesi Tıp Fakültesi, Pediyatrik Kardiyoloji Bölümü, Kayseri-*Türkiye*
Phone: +90 352 207 66 66-25036
Fax: +90 352 437 58 25
E-mail: duruozyurt@yahoo.com.tr
Available Online Date: 18.12.2013

doi:10.5152/akd.2013.5086

A child with L-2 hydroxyglutaric aciduria presenting with dilated cardiomyopathy: Coincidence or a new syndrome?

Sedat Işıkay, Serdar Ceylaner[1], Mehmet Karacan*
Clinics of Pediatric Neurology and *Pediatric Cardiology, Gaziantep Children's Hospital; Gaziantep-*Turkey*
[1]Intergen Genetics Centre; Ankara-*Turkey*

Introduction

The etiology of dilated cardiomyopathy (DCM) is generally undetectable; its main feature is dilated ventricles of the heart. While metabolic disorders are among the etiologic factors (1), no patient with L-2 hydroxyglutaric aciduria (L2HGA) and DCM has been reported. We present a 16-year-old male under follow-up with DCM, who was subsequently diagnosed as L2HGA.

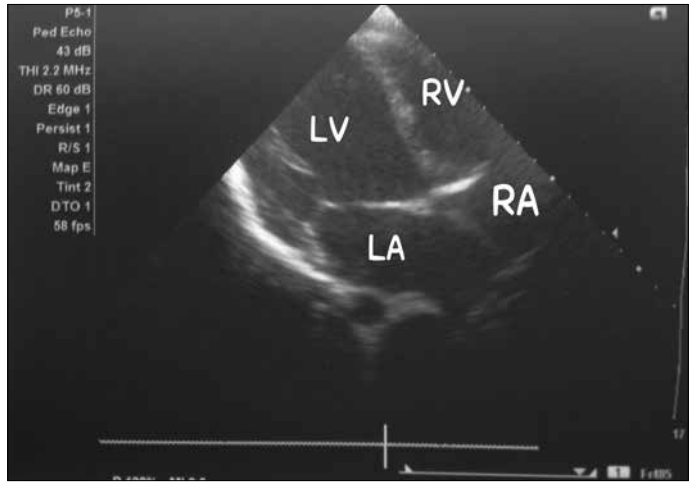

Figure 1. Two-dimensional echocardiogram showing a four-chamber view of the heart in a patient with systolic dysfunction. Note: dilated LV
LA - left atrium; LV - left ventricle; RA - right atrium; RV - right ventricle

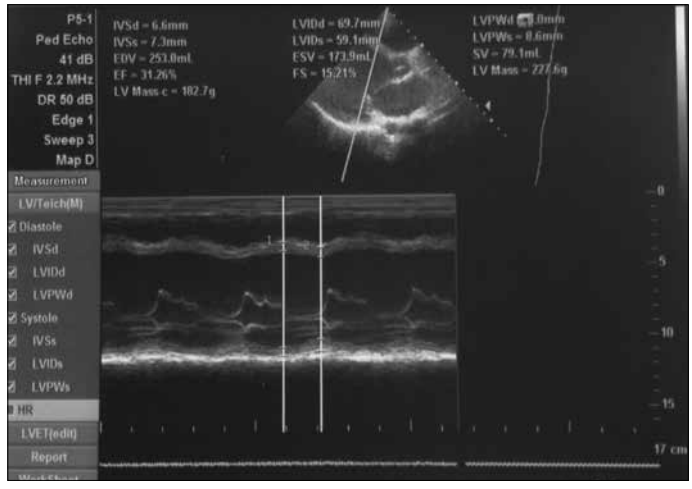

Figure 2. M-mode echocardiogram showing dilated left ventricle and decreased left ventricular contractility.

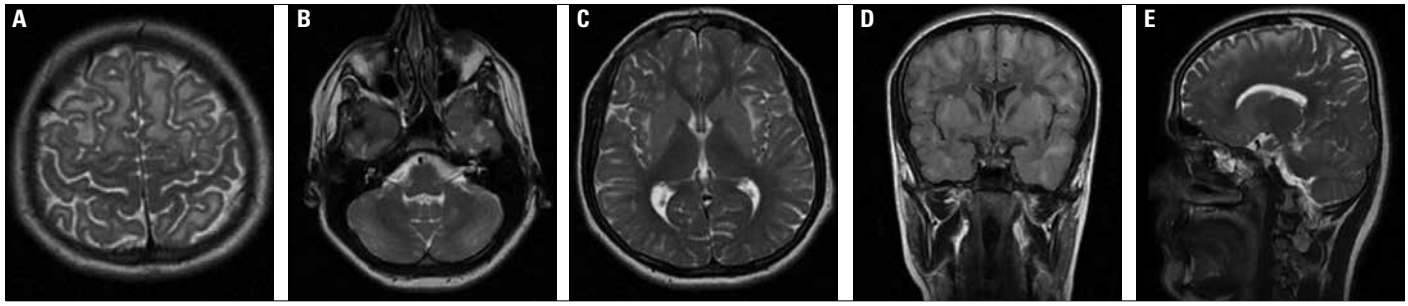

Figure 3. T_2-weighted axial slices (A-C), T_2-FLAİR coronal (D) sagital (E) slices in subkortikal deep white matter (A-D), globus pallidus (C, D) dentat nucleus (B, E) hyperintense lesions on MRİ

Case Report

The patient presented with fatigue, respiratory distress, chest pain, and 10 kg weight loss in the last 20 days. Vomiting developed five days before admission. His weight was 35 kg (<3rd percentile), height 175 cm (50-75th percentile), head circumference 57.5 cm (>98th percentile), body mass index 9.7 kg/m^2 (<5th percentile), heart rate 146/min, arterial blood pressure 70/40 mm Hg, and respiratory rate 32/min, and he had a cachectic appearance. Echocardiography revealed severe dilatation of the left ventricle, widespread decrease in contractility, and mild mitral insufficiency (Figs. 1, 2). The left ventricle end-diastolic diameter was 69 mm, ejection fraction 31%, and ventricular shortening fraction 15%. Neurological examination showed cerebellar dysfunction and mild mental retardation.

Complete blood count, sedimentation rate, electrolytes, liver function tests, creatinine kinase, troponin T, thyroid functions, arterial blood gases, serum thiamine, B_{12}, folate, total-free carnitine and acylcarnitine profile were normal. Viral serologic tests *(Coxsackie, adenovirus, Epstein-Barr, cytomegalovirus*, and *parvovirus B19)* were negative. MRI revealed bilateral hyperintense lesions in the frontal cerebral white matter, globus pallidus, and dentate nuclei (Fig. 3).

He was diagnosed with heart failure secondary to DCM. Dobutamine, dopamine, furosemide, and captopril therapy was initiated. L-carnitine (100 mg/kg/day) was instituted. During the follow-up, an increase in urine output and decrease in respiratory distress were observed. In the second week, dobutamine and dopamine were discontinued, and digoxin was added. Urine organic acid analysis demonstrated increased levels of 2-hydroxyglutaric acid (1039 mg/g creatinine, reference:<10 mg/g) and 3-hydroxyglutaric acid (35.6 mg/g creatinine, reference: <5 mg/g). Oral riboflavin (200 mg/day) was prescribed. He showed significant improvement with a good clinical response. In the third week, his clinical status was stable, and echocardiography revealed a 42% ejection fraction. Sequence analysis of the L-2 hydroxyglutarate dehydrogenase *(L2HGDH)* gene revealed the p.P302L (c.905C>T) mutation.

Discussion

Dilated cardiomyopathy, a myocardial disorder characterized by a dilated left ventricular chamber and systolic dysfunction that commonly results in congestive heart failure is the most common form of cardiomyopathy. However, understanding the cause of DCM remains difficult, with only 34% of pediatric patients having an identifiable cause. The secondary causes of dilated cardiomyopathy can result from infections, endocrine disorders, neuromuscular diseases and metabolic diseases (1).

L-2 hydroxyglutaric aciduria is an autosomal recessive metabolic disorder characterized by psychomotor delay and cerebellar signs, often associated with macrocephaly. Characteristic MRI findings include subcortical leukoencephalopathy, and bilateral nucleus dentatus lesions. Definitive diagnosis depends on detection of L-2 hydroxyglutaric acid in the urine, blood, and cerebrospinal fluid (2). Topçu et al. (3) mapped the L2HGA to chromosome 14q22.1 by homozygosity mapping. These researchers found nine mutations in the L-2 hydroxyglutarate dehydrogenase gene. The gene encodes a putative mitochondrial protein, which the authors dubbed "duranin", with homology to FAD-dependent oxidoreductases. In our case, sequence analysis of the L-2 hydroxyglutarate dehydrogenase gene revealed the p.P302L (c.905C>T) mutation, previously described by Topçu et al (3). This mutation is common in Turkish L2HGA patients. Our patient had macrocephaly. Increased urinary excretion of L-2 hydroxyglutaric acid, typical MRI findings, and *L2HGDH* gen mutation established the L2HGA diagnosis. To our knowledge, there are no previous reports of a patient with DCM and L2HGA; however, patients with DCM and D-2 hydroxyglutaric aciduria (D2HGA) have been discussed (4, 5).

Conclusion

This new feature may be secondary to L2HGA or coincidental. Patients with L2HGA must be monitored for any signs of DCM to investigate the relation between these disorders, and L2HGA must be kept in mind in DCM patients.

References

1. Hsu DT, Canter CE. Dilated cardiomyopathy and heart failure in children. Heart Fail Clin 2010; 6: 415-32. [CrossRef]
2. Işıkay S, Carman KB. Contribution of brain MRI in a patient diagnosed with 2-hydroxyglutaric aciduria. BMJ Case Rep 2013; 19: 2013.
3. Topçu M, Jobard F, Halliez S, Coşkun T, Yalçınkaya C, Gerçeker FO, et al. L-2-Hydroxyglutaric aciduria: identification of a mutant gene C14orf160, localized on chromosome 14q22.1. Hum Mol Genet 2004; 13: 2803-11. [CrossRef]
4. van der Knaap MS, Jakobs C, Hoffmann GF, Nyhan WL, Renier WO, Smeitink JA, et al. D-2-Hydroxyglutaric aciduria: Biochemical marker or clinical disease entity? Ann Neurol 1999; 45: 111-9. [CrossRef]
5. Kranendijk M, Struys EA, Salomons GS, Van der Knaap MS, Jakobs C. Progress in understanding 2-hydroxyglutaric acidurias. J Inherit Metab Dis 2012; 35: 571-87. [CrossRef]

Address for Correspondence: Dr. Sedat Işıkay,
Gaziantep Çocuk Hastanesi, Pediyatrik Nöroloji Kliniği, 27500, Gaziantep-*Türkiye*
Phone: +90 546 848 19 77
E-mail: dr.sedatisikay@mynet.com, dr.sedatisikay@hotmail.com

Available Online Date: 18.12.2013

doi:10.5152/akd.2013.5079