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Data Article

Data highlighting effects of Ketogenic diet on cardiomyopathy and hepatopathy in Glycogen storage disease Type IIIA

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ABSTRACT

Datasets highlighting effects of ketogenic diet (KD) in a glycogen storage disease type IIIa patient is presented with the longest patient follow up report to date. Now a 15-year old girl with GSD type IIIa, diagnosed at 1 year of age, had initially introduced treatment with diet high carbohydrates, according to the recommendations. Progressively she developed left ventricular obstructive hypertrophy, hepatomegaly and skeletal myopathy. At the age of 11 years, she was introduced KD and continuous ketosis has been maintained for over 4 years providing longest reported follow up to date. KD introduction lead to a normalization of left ventricular parameters and ventricular mass and to an improvement in hepatic injury markers and decrease in liver size.

We provided a table with biochemical parameters, a table providing detailed diet composition, tables with cardiac and hepatic measures and figures depicting cardiac NMR images; all the tables/figures are provided referring to the KD introduction (values prior/after). Interpretation of this data can be found in a case report article titled "Normalization of obstructive cardiomyopathy and improvement of hepatopathy on ketogenic diet in patient with glycogen storage disease (GSD) type IIIa".

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Specifications Table

Subject	Endocrinology, Diabetes and Metabolism
Specific subject area	Inborn errors of metabolism; Glycogen storage diseases
Type of data	Table Image
How data were acquired	NMR, Ultrasound, Laboratory, Dietary plans.
Data format	Raw
Parameters for data collection	Blood samplings were periodically taken in fasting state. Cardiac NMR was made at the 11 years old and repeated at the age of 15 with a high definition MRI machine. Abdominal ultrasound was developed by a image specialist. Dieticians calculated and constituted the diet therapy, indicated the dietary plan to the patient and checked her adherence.
Description of data collection	All the data were provided at the UMC - University Children's Hospital Ljubljana, Slovenia. The blood sampling, ultrasounds and dietary counselling were performed at the UMC - University Children's Hospital Ljubljana, Slovenia at the regular visits of patient. The NMR was performed in the UMC - Clinical Institute of Radiology Ljubljana, Slovenia. All the data (biochemical, imaging) have been recorded and obtained from the electronic medical record.
Data source location	UMC - University Children's Hospital Ljubljana. Ljubljana Slovenia 3G3C+MM Ljubljana, Slovenia
Data accessibility	Repository name: Mendeley Data Direct URL to data: DOI: 10.17632/6xxrvndt2m.2 https://data.mendeley.com/datasets/6xxrvndt2m/2
Related research article [1]	T. Marusic, M. Zerjav Tansek, A. Sirca Campa, A. Mezek, P. Berden, T. Battelino; U. Groselj. Normalization of obstructive cardiomyopathy and improvement of hepatopathy on ketogenic diet in patient with glycogen storage disease (GSD) type IIIa. Molecular Genetics and Metabolism Reports. (2020)24:100628. https://doi.org/10.1016/j.ymgmr.2020.100628

Value of the Data

- The data could be important in the process of gaining evidence about ketogenic diet (KD) as a treatment for patients with GSD type IIIa.
- The data might inform clinicians in prospective cases, it can add to the scientific reviews gaining evidence on KD in GSD type IIIa and could also be instrumental in designing the research protocols in the issue.
- Laboratory findings and cardiac MRI results could be used for a cases series publication or for designing a prospective clinical trial. Dietitians and clinicians could also apply the dietary plan provided as a tool for other comparable GSD patients.
- The data about KD in patients with GSD type IIIa might be encompassed into the recommendations on GSD type IIIa management strategies or updated guidelines for prospective patients and also to inform future research.
- As a very rare disease, each new case report brings value to the global medical community.
- It is worth mentioning that our reported study has the longest follow-up to date.

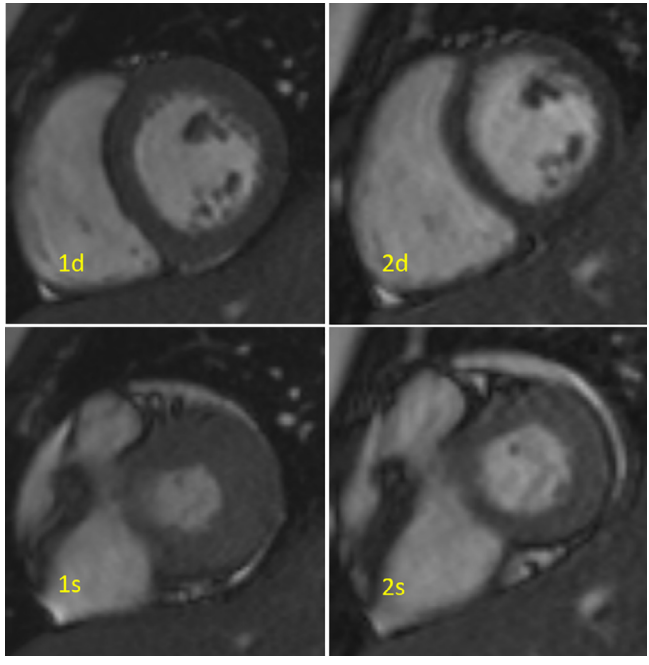

Fig. 1. Cardiac MRI, cine short axis view at mid-segment level. 1- before treatment, 2- after treatment. Myocardial thickening before treatment, normal myocardium after treatment. d = diastolic phase, s = systolic phase.

2. Data Description

We observed the impact of ketogenic diet (KD) on a 15- years old female patient with GSD IIIA. First, we presented a timeline, showing laboratory values before and after the KD onset (setting 0 months as the KD introduction) and focused on selected cardiac and hepatic-metabolic biochemical biomarkers (Table 1). Alkaline phosphatase and LDH, as non-specific cellular injury markers, sharply decreased within two months of KD onset. AST and ALT, hepatic injury markers, decreased more than twice soon after KD introduction. CK and myoglobin -muscle injury markers- and CK-MB and ProBNP -related to cardiac injury- decreased soon after KD introduction. Triglycerides and LDL-C decreased at the beginning, with a slight later increase, related to a high fat diet. Finally, Hydroxybutyrate, a measurable ketonic body for KD monitoring, fluctuated over time but remained elevated throughout the follow-up.

On the other hand, we observed the effect of the KD in cardiac MRI at the onset of the KD and after 16 months of maintaining ketosis (Table 2 and Images 1–2). It shows a decrease of total left ventricular mass index (LVMI) (from 58 g/m2 to 37 g/m2) and thickness of left ventricular walls (lateral wall from 10 to 5 cm, septal wall from 9 to 5 cm and inferosental wall from 10 to 7 cm). The end systolic and diastolic volume, and the ejection fraction were calculated, showing no residual outflow obstruction. Finally, no fibrosis was observed in cardiac tissue, but a normalization of obstructive cardiomyopathy. In addition, the 17- segment plots proposed by AHA (American Heart Association) -representing the myocardium in diastole from cardiac short axis cine MRI- shows a decrease in thickness of left ventricle walls 3 years after the onset of KD (Image 3).

Furthermore, liver sizes at the onset of KD and after 6 months of maintaining ketosis were calculated on ultrasound (Table 3). The standard liver measures sharply decreased in 6 months after the incorporation of KD (sternal line 129 to 110 mm; medioclavicular line 162 to 137 mm; anterior axillary line 167 to 146 mm) and sustained in normal range after 4 years.

Table 1
The impact of ketosis on selected cardiac and hepatic-metabolic biochemical biomarkers, setting 0 months as the KD introduction. S-LDH = Serum Lactate dehydrogenase. AST = Aspartate transaminase. ALT = alanine aminotransferase. CK = creatine kinase. CK-MB = creatine kinase myocardial band. ProBNP = Prohormone of brain natriuretic peptide. LDL-C = low-density lipoprotein cholesterol.

Months	-1	-1	-1	0	0	2	3	4	5	7	9	12	15	17	25	28	33	36	39	42	47
AGE	11.3	11.3	11.4	11.4	11.4	11.6	11.7	11.7	11.8	12.0	12.2	12.4	12.6	12.9	13.5	13.7	14.2	14.4	14.6	14.9	15.4
DATE	3/6/2015	15/6/2015	22/6/2015	23/6/2015	22/7/2015	3/9/2015	8/10/2015	10/11/2015	11/12/2015	11/2/2016	6/4/2016	28/6/2016	29/9/2016	22/12/2016	26/7/2017	9/11/2017	18/4/2018	26/6/2018	25/9/2018	15/1/2019	21/6/2019
Alkaline phosphatase (ukat/L)		11.64		ketonic diet	6.19	4.58	5.02	5.76	6.11	6.51	6.51	5.17	5.48	5.91	5.25	6.95	6.15	5.59	6.34	3.97	6.14
S-LDH (ukat/L)		13.61	14.22	ketonic diet	8.73		5.36	5.62	5.41	4.54	5.18	4.99	4.49	4.11	3.91	4.92	4.09	4.66	4.73	5.53	5.77
AST (ukat/L)	4.97	4.74	6.78	ketonic diet	4.3	3.23	2.11	3.01	2.69	1.5	2.47	2.49	2.26	2.64	2.56	3.95	2.8	2.42	3.15	3.4	2.48
ALT (ukat/L)	5.44	4.15	6.6	ketonic diet	3.85	2.69	2.03	2.92	2.43	1.69	2.57	2.52	2.37	3	3.52	4.03	3.15	2.95	2.99	3.44	4.19
GGT (ukat/L)		0.97	0.77	ketonic diet	0.6	0.34	0.3	0.4	0.42	0.62	0.64	0.61	0.65	0.92	1.15	1.24	0.93	0.73	0.81	0.67	1.06
CK (ukat/L)	53.10	65.70	64.70	ketonic diet	41.60	32.90	16.60	13.60	16.00	7.60	14.20	7.10	12.29	8.82	9.54	25.66	13.66	13.24	14.48	17.93	26.46
CK-MB (ukat/L)		2.17	2.50	ketonic diet	1.09	0.73	0.42	0.27	0.25	0.11	0.16	0.10	0.13	0.08	0.10	0.17	0.18	0.17	0.16	0.20	0.35
Mioglobin (nmol/L)		22.35	21.42	ketonic diet		10.51	9.91	6.87	8.39	4.21	4.62	4.76	4.29	2.97	5.18	5.44	6.25	7.87	5.77	6.80	8.31
Triglicerid (mmol/L)		2.6	4.1	ketonic diet	2	1.3	2.4	2.1	1.4	1.4	2.5	1.9	1.3	1.6	1.6	2.6	1.3	1.7	2.7	2.7	4.5
LDL (mmol/L)	3.3	1.5	2.4	ketonic diet	1.7	1.9	1.6	2	2.1	2.2	2.5	2.4	1.9	2.7	2.5	4.2	2.9	2.7	4	5.1	4.6
ProBNP (pmol/L)		36.2		ketonic diet			10.0	13.4	12.9	14.0	10.0	4.3	5.6	6.3	3.1	6.9	11.0	7.7	2.9		5.8
β-hydroxy-butyrate (µmol/L)				ketonic diet	2439		2043				1470	3033	1099	1155	1204	1305	212	1135	1190		616

Table 2
Cardiac MRI results at the onset of ketogenic diet (KD), after 16 months and after 40 months of maintaining ketosis. LVMI = Left ventricular mass index.

Cardiac MRI parameters	At onset of KD	After 16 months	After 40 months
Lateral wall	9 mm	4–5 mm	4–5 mm
Septum wall	8–9 mm	5–6 mm	5–6 mm
Inferoseptal wall	10 mm	6 mm	7 mm
Myocardial mass	70 g (58 g/m2)	35 r (30 g/m2)	50 g (37 g/m2)
End diastolic volume	75 ml (63 ml/m2)	64 ml (52 ml/m2)	80 ml (62 ml/m2)
End systolic volume	10 ml (8,4 ml/m2)	15 ml (12 ml/m2)	25 ml (19 ml/m2)
Ejection fraction	87%	76%	69%
Fibrosis signs	none	none	none
Myocardial hypertrophy	obstructive	none	none

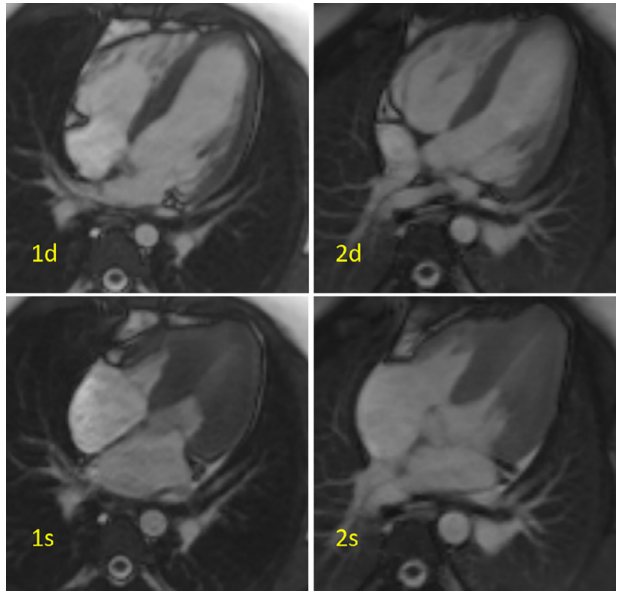

Fig. 2. Cardiac MRI, cine four chamber view. 1- before treatment, 2- after treatment. Myocardial thickening before treatment, normal myocardium after treatment. d = diastolic phase, s = systolic phase.

Table 3
Liver measures at the onset of ketogenic diet (KD) and after 6 months of maintaining ketosis.

Liver measures	At the onset of KD	After 6 months
Sternal line	129 mm	110 mm
Medioclavicular line	162 mm	137 mm
Anterior axillary line	167 mm	146 mm

Finally, we present a diet therapy timeline, registered from 2004 to 2019 at the dietician visits and in the food diary (Table 4). In 2015 the patient started with the KD. The timeline shows anthropometric characteristics, the diet composition, total and relative energy intakes, and notes showing the patient's adherence.

All the data was also added to the Mendeley repository (http://dx.doi.org/10.17632/6xxrvndt2m.2).

Table 4
Diet therapy over time, from 2004 to 2019. In 2015 the patient started with the ketogenic diet (KD). BMI = body mass index.

Year	Age	Height	Weight	BMI		Diet basic	Meals	Energy	Carb	Proteins	Fat	Cornstarch	Notes
2009/04	5 years				Diet therapy	Classic diet GSD IIIa	5 meals (interval 3 h) -all meals energy and nutritional equal- + 1 night meal 20 g oatmeal + 200 ml Prosure drink	1370 kcal	178.0 g (53%)	78.1 g (23%)	35.0 g (23%)		
2009/11					Food diary analysis		8-10 meals (interval 1–3 h) + 1 night meal 20 g oatmeal + 100 ml Prosure drink	1580 kcal	244.9 g (62%)	79.0 g (20%)	31.6% (18%)	20 g oatmeal + 100 ml Prosure at 23:00	Lot of simple sugars
2010/03	6 years				Diet therapy	Classic diet GSD IIIa	5 meals (interval 3 h) -all meals energy and nutritional equal- + 1 night meal 20 g oatmeal + 200 ml Prosure drink	1500 kcal	200.0 g (53%)	86.2 g (23%)	38.3 g (23%)		
2010/11					Food diary analysis		8–10 meals (interval 1–3 h) + 40 g cornstarch at 23:00	1842 kcal	303 g (66%)	50.6 g (11%)	47.1 g (23%)	30 g corn starch + 100 ml Supportan dink at 23:00	Lot of simple sugars. Supplement Supportan drink 200 ml / day
2011/04	7 years	117.1 cm (5p)	23.4 kg (30p)	17 (66p)	Diet therapy	Classic diet GSD IIIa	5 meals (interval 3 h) -all meals energy and nutritional equal- + 1 night meal 30 g corn starch	1600 kcal	210 g (53%)	92 g (23%)	41 g (23%)		
2011/11					Food diary analysis		8–10 meals (interval 1–3 h) + 40 g corn starch at 23:00	1932 kcal	313.9 g (65%)	72.4 g (15%)	43.0 g (20%)	30 g corn-starch + 100 ml Supported dink at 23:00	Lot of simple sugars. Supplement Supportan drink 200 ml / day
2012–2013	8–9 years	118.3 cm (3p)	23.7 kg (23p)	16.9 (66p)	no data								

(*continued on next page*)

Table 4 (*continued*)

Year	Age	Height	Weight	BMI		Diet basic	Meals	Energy	Carb	Proteins	Fat	Cornstarch	Notes
2014/4	10 years	129.9 cm (3p)	34.15 kg (46p)	20.4 (87p)	Food diary analysis		8–10 meals (interval 1–3 h) + 40 g corn starch at 23:00	2408 kcal	363 g (61%)	97.0 g (15%)	59.1 g 22%)	40 g corn starch + 100 ml Fresubin protein drink at 23:00	Lot of simple sugars. Supplement Supportan drink 200 ml / day
2014/04					Diet therapy	Classic diet GSD IIIa	5 meals (interval 3 h) -all meals energy and nutritional equal- + 1 night meal 30 g corn starch	1800 kcal	178.0 g (53%)	78.1 g (23%)	35.0 g (23%)		
2015/5	11 years	135 cm	39.1 kg	21.4 (91p)	Food diary analysis		11–14 meals (interval 1–1.5 h) + 40 g corn starch at 23:00	2549 kcal	347 g (55%)	114.0 g (18%)	75.3 g (27%)	40 g corn starch at 23:00 + 100 ml Fresubin protein drink	Lot of simple sugars. Supplement Supportan drink 200 ml / day + Fresubin Energy 200 ml / day
2015/05	11 years	135 cm	39.1 kg	21.4 (91p)	Diet therapy	Transition to ketogenic diet	6 meals (interval 3.5 h), last meal at 23:00 in the ratio 4: 1	2000 kcal	11.7 g (2%)	61.0 g (11%)	204.2 g (87%)	Ketocal 4: 1 for night meal	
2016/6	12 years	138.5 cm (3p)	36.4 kg (20p))	19.0 (59p)	Food diary analysis	Ketogenic diet 2.5: 1	6 meals (interval 3.5 h), last meal at 23:00 in a ratio of 4: 1	2123 kcal	11.7 g (2%)	61.0 g (11%)	204, 2 g (87%)	Ketocal 4: 1 for a night meal	Follows the diet
2016/09					Diet therapy	Ketogenic diet 2.5: 1	6 meals (interval 3.5 h) last meal at 23:00 in a ratio of 4: 1	2000 kcal	10.0 g (2%)	60,0 g (12%)	190,0 g (86%)	Ketocal 4: 1, for a night meal	
2018/9	14	145,3 cm (1p)	43.3 kg (12p)	20.4 (59p)	Food diary analysis	Ketogenic diet 2.8: 1	6 meals (interval 3.5 h) last meal at 23:00 in a ratio of 4: 1	1800 kcal	10.0 g (2%)	51.9 g (12%)	175.0 g (86%)	Ketocal 4: 1 for night meal	Follows the diet
2018/09					Diet therapy	Ketogenic diet 2.5: 1	6 meals (interval 3.5 h) last meal at 23:00 in a ratio of 4: 1	2000 kcal	10.0 g (2%)	60.0 g (12%)	190 0g (86%)	Ketocal 4: 1 for night meal	
2019/6	15 years	147.7 cm (1p)	43.8 kg (5p)	19.8 (44p)	Food diary analysis *	Ketogenic diet 1.5: 1 * desserts	4–5 meals (interval 3.5 h) last meal at 23:00 in a ratio of 4: 1	1700 kcal *	148 g (35%) *	63.7 g (15%) *	94.4 g (50%) *	Ketocal 4: 1 for a night meal	Tired of the diet
2019/06					Diet therapy	Ketogenic diet 2.5: 1	6 meals (interval 3.5 h) last meal at 23:00 in a ratio of 4: 1	2000 kcal	10.0 g (2%)	60.0 g (12%)	190.0 g (86%)	Ketocal 4: 1 for night meal	

* Does not reflect the real situation (elevated TG, fallen ketone bodies)

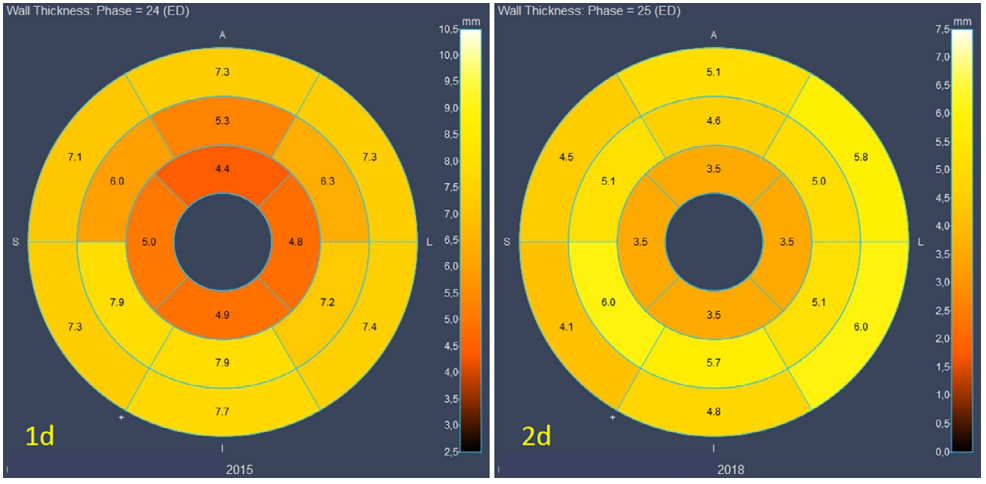

Fig. 3. AHA (American Heart Association) 17- segment plots of myocardial thickness in diastole from cardiac short axis cine MRI, 1d- before treatment, 2d- after treatment. ED = end diastole. A = anterior. L = lateral. I = inferior. S = septal.

3. Experimental Design, Materials and Methods

This is a case report of a now 15-year old girl with GSD type IIIa diagnosed at 1 year of age. At that time she was introduced a high carbohydrates diet (frequent diurnal and nocturnal cornstarch meals); carbohydrates (9 g/kg per day (g/kg/d)) contributed 53% daily calories, proteins (4 g/kg/d) contributed 23% and fats (1.8 g/kg/d) contributed another 23%, according to the recommendations [2]. Progressively she developed left ventricular obstructive hypertrophy, hepatomegaly and skeletal myopathy with highly elevated liver and muscle enzymes, as previously reported [3–6]. She also presented recurrent hypoglycemic events despite treatment with frequent diurnal and nocturnal meals with cornstarch supplements. Due to progressive obstructive cardiomyopathy, she was introduced to a ketogenic diet at the age of 11. The diet consisted of ketogenic ratios of 2.5:1; fats (5.2 g/kg/d) contributed 87% daily calories, proteins (1.6 g/kg/d) contributed 11% and carbohydrates (0.3 g/kg/d) contributed 2%. Continuous ketosis was maintained for over 4 years. Clinical support by attending physicians and experienced clinical dietitians was provided (e.g. helping with practical dilemmas via e-mail/phone soon after they arise). Periodic abdominal ultrasounds and cardiac MRI were performed. The blood sampling at regular outpatient visits was performed in a fasting state, as recommended [2,7]. For home monitoring, she daily measured the ketones in urine using a semiquantitative test.

4. Ethics Statement

Written informed consent for publication of their clinical details and/or clinical images was obtained from the patient/parent/guardian/relative of the patient.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships which have, or could be perceived to have, influenced the work reported in this article.

Acknowledgments

We would like to thank clinical dietitian Helena Kobe MSc, for her consultations with the family. Study was partly funded by the Slovenian Research Agency project V3-1505 and program P3-0343.

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