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LETTER TO THE EDITOR

Very long-chain acyl-CoA dehydrogenase (VLCAD) deficiency: Case Report of Hypoglycaemia and Rhabdomyolysis in a Two-Day Old Infant

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Dear Editor,

Very long-chain acyl-CoA dehydrogenase (VLCAD) deficiency is an autosomal recessive fatty-acid oxidation disorder resulting in the inability to convert and utilise C12 to C18 acylcarnitines (OMIM#201475)[1]. The clinical phenotype is heterogeneous. Recently, a baby with VLCAD deficiency had a severe clinical presentation prior to the results of Newborn Bloodspot Screening (NBS).

The baby was born full term via spontaneous vaginal delivery to non-consanguineous parents (Table 1). He was breastfed every 3-4 hours. At 57 hours-of-life, he missed a feed stretching to a 6 hour feeding interval. He was then noted to be hypothermic, pale and lethargic with a weak cry. He was also hypotonic and had hepatomegaly. He was transferred to the special care nursery. Investigations showed hypoglycaemia (1.5 mmol/L) and transaminitis (Table 1). He was treated with a 10% dextrose bolus (2ml/kg) and maintained on Solution 120 (dextrose containing fluids) at 120ml/kg/day. Within 24 hours, the patient's lethargy, hypothermia and hypoglycaemia resolved but abnormal transaminases persisted. The Metabolic Service was consulted on day 4 of life and the differential diagnosis included fatty-acid oxidation and glycogen storage disorders.

The patient was transferred to the tertiary hospital for management. Septic work-up was negative. The laboratory findings of rhabdomyolysis and transaminitis especially AST which is present in high concentrations in skeletal muscles were more in keeping with a fatty-acid oxidation disorder. The abnormal acylcarnitine species (particularly C14:1 and its ratio to C10) in the dried blood spot (DBS), increased C4:1 species on qualitative analysis of the plasma carnitine and results of the genetic and enzymatic tests supported the diagnosis of VLCAD deficiency (Table 1). With low long-chain fat diet supplemented with medium-chain fats, the CK gradually decreased.

Our patient had a severe and early clinical presentation with significant hypoglycaemia and rhabdomyolysis with no cardiac involvement. Management of the patient included a low long-chain fat diet supplemented with medium-chain fats and avoidance of prolonged fasting or dehydration to prevent complications such as hypoglycaemia and rhabdomyolysis[3]. When the patient is unwell, especially with poor oral intake, the parents have been advised to call the metabolic service and present early to an emergency department for prompt assessment and intravenous glucose therapy.

This case highlights that: 1) A fatty acid oxidation disorder should be suspected in newborns/infants with unexplained hypoglycaemia and/or acute liver disease, rhabdomyolysis and cardiac arrhythmias/cardiomyopathy; 2) Glucose containing fluids should be started; 3) Newborns with a fatty-acid oxidation disorder can become symptomatic even before NBS can be done; and 4) Prompt referral to a metabolic service is recommended.

References

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Table 1 Clinical details and laboratory investigations

Clinical Details		
Gestational age	38 weeks + 3 days	
Weight	3.225 kg (29th centile)	
Length	50.5cm (50th centile)	
Head circumference	33.5 cm (14th centile)	
Physical examination	Normal (including appropriate neurologic, cardiac and respiratory systems)	
Laboratory investigations – Day 3		
Test	**Result**	**Reference Values**
Haemoglobin	173	95-180 g/L
White cell count	22.4	(5.0 – 15.0) x 10^9/ L
Platelets	351	(150 – 500) x 10^9/ L
Neutrophils	19.3	(2.0 – 8.0) x 10^9/L
Lymphocytes	1.6	(1.5 – 8.0) x 10^9/ L
Sodium	142	133 – 145 mmol/L
Potassium	5.1	3.3 – 6.5 mmol/L
Chloride	106	95 – 110 mmol/L
Bicarbonate	21	17 – 27 mmol/L
Urea	14.3	1.0 – 7.5 mmol/L
Creatinine	68	10 – 30 umol/L
ALP	120	70 – 250 U/L
GGT	74	< 226 U/L
AST	784	20 – 80 U/L
ALT	119	<51 U/L
Ammonia	91	11 -35 umol/L
CRP	5.9	< 3.0 mg/L
pH	7.39	7.35 – 7.35
CO2	44	35 – 45 mm Hg
Base excess	+2	-2 - +3 mmol/L
Bicarbonate	26.8	21.0 – 28.0 mmol/L

Lactate	3.7	< 1.5 mmol/L
Laboratory Results Day 4 - 8		
Creatine Kinase (CK)	39,335 (Day 4) 21,320 (Day 5) 1067 (Day 8)	<301 U/L
CK-MB	277.1	<4.9 ug/L
Carnitine* Laboratory Results – Day 4		
C14:1	1.29	<0.47 umol/L
C14:1 to C10 ratio - DBS	25.2	<0.7
C12 – plasma	++	
C14:1 – plasma	+++	
C14 - plasma	+++	
C16 - plasma	++	
C18 - plasma	++	
Total carnitine - plasma	68	38 – 79 umol/L
Subsequent investigations		
VLCAD activity expressed as nmol/min/mg protein	0	1.54 – 6.24 – normal 0.02 – 0.47 – abnormal
Molecular	Heterozygous (ACADVL):c.722A>G;p.Tyr241Cys, located in exon 8 (classified as variant of uncertain significance)	

* Total plasma carnitine is calculated from the sum of the individual carnitine (C) species identified in the profile i.e. C0 (free), C2, C3, C4, C5:1, C5, hydroxy C4 + C3 DC, C6, hydroxy C5 + C4DC, C5DC + hydroxy C6, C8, C10, C12, C14:1, C14, C16, hydroxy C16, C18:1. C18, and hydroxy C18:1. Individual plasma carnitine specifies are only reported semi-quantitatively as: + (1 - 3 times cut-off); ++ (3 - 10 times cut-off);and +++ (>10 times cut-off). The individual plasma carnitine species greater than the cut off are shown in the table, the other species were all within the reference cut-off.

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