ERNDIM Qualitative Blood Spot Acylcarnitine Scheme

Annual Report London 2012

Two circulations (19 & 20) were sent out to the 60 laboratories assigned to the London centre of the ERNDIM dried blood spot acylcarnitine scheme. The first was sent out in August, with a return date of 28th September 2012 and the second in February 2013 with a return date of 19th April 2013. The extreme delay to the second circulation, for which the scheme organisers apologise, was due to problems of sample supply. This qualitative scheme depends on the goodwill of patients donating "spare" blood for QA purposes to allow the distribution of real clinical blood samples. This may also mean that blood spots distributed may be of sub-optimal size & quality.

Returns for circulation 19 were received from 50 (83%); all but three of these arrived by the initial due date. One laboratory indicated that they had not received the samples for circulation 19 and alternative shipment arrangements were made for circulation 20. For circulation 20 valid returns were received from 52 (87%); all of these arrived before the due date.

There were 7 laboratories who failed to make a return on either circulation. Three of these did not submit results in 2010 or 2011. Two laboratories reported on Circulation 20 only, and one on circulation 19 only.

Participants were asked to respond via email using a supplied report template, and to send a scan and/or table of quantitative results if possible. All laboratories responded by email. All laboratories provided a suggested/differential diagnosis. Most suggested some form of appropriate follow-up testing to confirm a putative diagnosis. A summary of the samples sent and the number of respondents suggesting the definitive diagnosis as part of their differential diagnosis is given in the table below.

Sample	Enzyme/transporter defect	Diagnostic Acylcarnitine	Respondents
19a	Long chain hydroxyacyl CoA dehydrogenase deficiency (LCHADD, MIM 609016)	C14OH-C18OH, C14:1OH-C18:1OH	49/50
19b	Very long chain acyl CoA dehydrogenase deficiency (VLCADD, MIM 201475)	C14:1	20/50
19c	Normal		47/50
20a	Medium chain acyl CoA dehydrogenase deficiency (MCADD, MIM 201450)	C8, C6, C10:1	52/52
20b	Propionyl CoA carboxylase deficiency (MIM 606054)	C3	52/52
20c	glutaryl CoA dehydrogenase deficiency (MIM 231670)	C5DC	48/52

The profiles from patients with LCHADD (19a), MCADD (20a) and propionic acidaemia (20b) were very characteristic of the disorders and were correctly characterized by almost all laboratories. The sample from the patient with GA-1 provided difficulties for a few laboratories due to the high free carnitine concentration, secondary to supplementation, which was not referred to in the clinical details given, and was clearly distracting for a minority of respondents.

Sample 19b proved particularly difficult to interpret. This was from an adult patient, currently well, with VLCADD originally diagnosed in childhood. She was not on carnitine supplementation as there are concerns about mitochondrial toxicity of longer chain acylcarnitines. Her free carnitine was significantly depleted with a median reported concentration of 6.2 μmol/l. On this basis a majority of laboratories suggested carnitine uptake disorder as the most likely diagnosis, despite a C14:1 concentration above the upper reference interval for 18/20 of the laboratories who correctly identified VLCADD (the other two made the diagnosis on the basis of ratios). It is a concern that so many respondents failed to look closely enough at a low carnitine profile to identify a case of secondary carnitine depletion. Similar problems have occurred before (sample 2c VLCADD & 13a propionic acidaemia). Since so many participants in the scheme failed to make the correct diagnosis this sample was classified as an educational sample and was not included in scoring.

Once again, we are extremely grateful to the centres that have provided informative material for circulation. If any participants can provide samples in the future it would enormously facilitate this scheme, providing, as it does, genuine clinically derived samples for assay and interpretation. 3-4ml of lithium heparin anticoagulated whole blood or 65-70 30-50μl blood spots on Whatman (Schleicher & Schuell) 903 or Perkin Elmer/Ahlstrom 226 paper would provide sufficient material for one circulation. Samples for use in the scheme should be accompanied by a short clinical history and confirmation that informed consent/local ethical approval (as required in the referring centre) for use of the sample has been obtained.

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