UK/SCANDINAVIA PROFICIENCY SCHEME

ANNUAL REPORT

Samples distributed

Six samples were distributed to 23 participants in the first cycle and 24 participants in the second.

Samples were derived from:-

03.1 - A patient who has ingested ethylene glycol

03.2 - A patient already diagnosed with succinic semiadldehyde deficiency and on treatment with vigabatrin.

03.3 - A normal child.

03.4 - A patient with Zellweger syndrome.

03.5 - A patient with pyrimidine responsive cysthionine ß-synthase deficiency.

03.6 - A patient with sialidosis

Results

The results are shown below:-

Sample 03.1

Returns were received from all of the 23 participants.

All 23 noted an increased excretion of glycolate with 14/23 also commenting on an increased excretion of lactate and 3-hydroxybutrate and 17/23 an increased excretion of oxalate. All but one of the participants indicated that the findings were consistent with ethylene glycol intoxication and a number of these commented on the present of two unidentified peaks commonly seen in association with ethylene glycol poisoning. One of the participants identified these as a dimer and trimer containing one or two molecules of ethylene glycol in association with propylene glycol. (J Pediatr 1992; 120; 421-4)

14/23 participants indicated the need for additional toxicological investigation to quantitate the concentration of ethylene glycol in plasma as a guide to treatment (i.e. the need for possible dialysis) and 6/23 laboratories suggested that plasma

calcium should be measured to help identify the hypocalcaemia known to be associated with ethylene glycol ingestion.

14/23 participants highlighted the role of ethanol infusion in the treatment of ethylene glycol poisoning and 11/23 referred to the potential use of the newer alcohol dehydrogenase inhibitor 4-methylpyrazole.

Sample 03.2

Returns were received from all 23 of the participants.

21/23 participants noted an increased excretion of 4-hydroxybutyrate and 12 of these noted excretion of the associated derivatives of 4-hydroxybutyrate. 16/23 participants noted an excretion of valproate metabolites and 17/23 an increased excretion of pyroglutamate. 5/23 also recorded an increased excretion of vigabatrin on amino acid analysis. One participant reported an increased excretion of 4-hydroxyhippurate but this seems to have been a typographical error.

22/23 participants correctly concluded that the sample came from a patient with succinic semialdehyde dehydrogenase deficiency and all of these indicated the need for enzyme confirmation. Seventeen participants would have alerted the clinicians to the potential therapeutic use of vigabatrin with a number inferring that the patient was already receiving vigabatrin as evidenced by amino acid analysis and/or pyroglutamate excretion. Five participants suggested that any siblings should be tested.

Sample 03.3

Returns were received from 22 of the 23 participants.

All 22 participants who returned reports agreed that no diagnosis was indicated from the results of analyses on this sample. 4/22 would have asked or a repeat sample and 5/22 would have advised exclusion of a peroxisomal disorder or a disorder of glycosylation prompted by the clinical description of “dysmorphia”.

Sample 03.4

Results were returned from 22 participants.

8/22 participants noted an increased excretion of dicarboxylic or long chain hydroxy dicarboxylic acids.

14/22 noted an increased excretion of 4-hydroxyphenyl-lactate.

10/22 laboratories considered that the findings/clinical details indicated a possible peroxisomal disorder with 3 laboratories specifically highlighting the possibility of Zellweger syndrome.

13/22 would have recommended VLCFA analysis among further investigations to be undertaken.

It is perhaps a little disappointing that with highly suggestive clinical features "dysmorphia and hypotonia" and some supportive biochemical findings including an increased excretion of 2-hydroxy sebecate together with evidence of liver dysfunction, that only two-thirds of participants would have raised the possibility of a peroxisomal disorder or suggested that VLCFA's should be analysed.

Sample 03.5

Results were received from 22 participants.

15/22 noted an increased excretion of homocystine. In our laboratory this was 41 µmol/mmol creatnine.

Interestingly only 9/15 considered CBS deficiency as a possibility, a number excluding this on the basis of a normal excretion of methionine. Twelve of those laboratories identifying the increased excretion of homocystine would have recommended measurement of total plasma homocysteine and 14 would have suggested quantitative plasma amino acid analysis.

It is alarming that 7 laboratories did not identify an increased excretion of homocystine in this sample. It is tempting to conclude that this could have been caused by sample deterioration. However, the sample was left a room temperature in our1 laboratory for 7 days and re-tested without loss of homocystine and the longest recorded postal delay was two days, so these results remain difficult to explain.

Sample 03.6

Results were received from 22 participants.

All 6 laboratories performing oligosaccharide analysis reported unusual findings, 3 of these raising the possibility of sialidosis. Unsurprisingly none the laboratories who did not perform oligosaccharide analysis suggested this diagnosis. Because of the suggestive clinical details, 7 participants felt that Morquio disease should be excluded.

This sample may have seemed a little "unfair" to participants not performing oligosaccharide analysis. Although interestingly with plausible clinical details only 3/16 who did not perform this analysis would have included it in the range of further investigations to be undertaken. If this had been a real referral this case may well have remained undiagnosed in a number of centres.

Conclusions

The major causes for concern were:-

- One participant felt that the increase glycolate in Sample 03.1 was attributable to hyperoxalouria type 1.

- One participant failed to identify an increased excretion of 4-hydroxybutyrate or associated lactones in sample 03.2

- Seven of 22 laboratories failed to identify an increased homocystine excretion in sample 03.5. Sample deterioration could have been contributory but did not have an effect in the sample left at room temperature for one week in our keeping.

- Thirteen of the 16 laboratories who did not perform oligosaccharide analysis in sample 03.6 did not go on to suggest this in the “further investigations to be undertaken” despite suggestive clinical details.

These were quite taxing samples for participants and on the whole the results were reassuring with the exceptions listed above.

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