ERNDIM PROFICIENCY SCHEME (NORTHERN EUROPE)

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Annual Report for the Sheffield Diagnostic Proficiency Scheme for 2011

ERNDIM Proficiency Scheme Report – Samples 11.1, 11.2, 11.3, 11.4, 11.5, 11.6

Six samples were distributed in one batch to 21 participants; returns were received from all 21 participants.

Patient 11.1

7 year old girl with developmental retardation, in particular speech delay. She has epilepsy, for which she is treated with valproic acid
This was the "common" sample and will be reported at the ERNDIM workshop but is presumed to be from a patient with GAMT deficiency

Findings

2/21 laboratories identified an increased excretion of guanidinoacetate and a reduced excretion of creatine. 15/21 laboratories identified an increased excretion of valproate metabolites

Conclusions

2/21 laboratories correctly concluded that this sample was from a patient with GAMT deficiency. An additional 5 participants considered that GAMT deficiency or a defect of creatine synthesis was possible on the basis of the clinical details supplied

Further investigations

11/21 would have recommended measurement of guanidinoacetate or creatine

Comment

It is disturbing that given the clinical details only 50% of labs did or would have measured creatine/guanidinoacetate.

Patient 11.2

6 year old girl, developmental delay and dyskinesia
This sample was obtained from a child with glutaric aciduria type 1

Findings

20/21 laboratories identified and increased excretion of glutarate and 3-hydroxyglutarate

Conclusions

20/21 participants concluded that glutaric aciduria type 1 was the most likely diagnosis

Further investigations

19/21 participants would have recommended confirmation by enzyme assay with 14/21 advising that acylcarnitine analysis should be undertaken. Only one laboratory would have opted only for acycarnitines as a confirmatory test

Comment

It is reassuring that almost all participants identified an increased excretion of glutarate and 3-hydroxyglutarate, the lab which did not do so appears to have transposed samples 11.1 and 11,2.

Sample 11.3

5 year old boy pre-adoption medical

This sample was from a normal 5 year old boy

Findings

Nearly all labs reported no abnormalities for the investigations undertaken. One laboratory reported and elevated excretion of urate, one a slightly increased excretion of leucine described as a non-specific finding and one laboratory noted an increased excretion of 4-hydroxy-phenylacetate

Conclusions

20/21 laboratories reported “no metabolic disease” or similar. One laboratory offered no conclusion.

Further investigations

No laboratory advised specific additional metabolic investigations

Comment

It is encouraging that nearly all labs concluded that no metabolic disorder could be identified and refrained from advising additional needless investigations

Sample 11.4

3 year old boy with frontal bossing and odd hands

This sample was obtained from a 5 year old boy with MPS type 1

Findings

20/21 participants reported an elevated quantitative MPS result, 1/21 did not undertake MPS analysis. 18/20 reporting elevated MPS excretion also commented on an increased excretion of dermatan and/or heparan sulphate. 1/20 simply reported an abnormal pattern and 1/20 did not report a qualitative result

Conclusions

20/21 participants concluded that MPS type 1 was a possible or likely diagnosis, only one laboratory failed to raise this possibility.

Further investigations

19/20 participants who reported an elevated MPS excretion would have advised enzyme assay for further characterisation

Comment

It is reassuring that almost all labs identified an increased excretion of mucopolysaccharides and included MPS type 1 in the possible diagnoses. The laboratory who failed to perform MPS analysis explained that this was due to a temporary technical difficulty

Sample 11.5

30 year old male, keratitis

This sample was from a patient with tyrosinaemia type 2

Findings

21/21 participants identified an increased excretion of tyrosine. This was quantitated by 18 laboratories who reported a mean tyrosine excretion of 85 µmol/mmol creatinine (range 38-100). All 21 laboratories also commented on an increased excretion of 4-hyroxyphenyl – lactate, and/or -acetate, -pyruvate, 5/21 also noted excretion of N-acetyl tyrosine. Only 13/21 noted that succinyl-acetone excretion was *not* elevated.

Conclusions

21/21 participants concluded that tyrosinaemia type 2 was the most likely diagnosis

Further investigations

18/21 would have recommended measurement of plasma aminoacids and 14/21 would have advised mutation analysis or enzyme assay to confirm the diagnosis.

Comment

It is encouraging that all participants identified an increased excretion of tyrosine and correctly concluded, helped by the clinical details, that tyrosinaemia type 2 was the most likely diagnosis. It is of some concern that 8/21 did not comment on the absence of succinylacetone when reporting the findings or drawing the conclusions.

Sample 11.6

9 year old boy, small stature, macrocephaly

This sample was obtained from a patient with MPS type 4

Findings

19/21 participants reported a quantitatively increased excretion of MPS. I/21 did not undertake the assay (citing technical difficulties) and 1/21 reported normal excretion. 16/21 laboratories identified an increased excretion of keratan sulphate on qualitative MPS analysis.

Conclusions

16/21 laboratories concluded that MPS type 4 (A or B) was the most likely diagnosis, 4/21 simply concluded an MPS disorder of some type was possible or probable. 1/21, despite reporting a slightly elevated MPS excretion, concluded that he patient did not have a metabolic disorder, perhaps falsely reassured by an apparently normal 1-D electrophoresis result.

Further investigations

20/21 laboratories would have advised enzyme confirmation.

Comment

It is reassuring that 20/21 labs would considered that the patient may have an MPS disorder and would have recommended enzyme assay.

Overall comment

Sample 11.1, the common sample from a patient with GAMT deficiency was challenging for the UK group but the clinical details were suggestive and this raises the possibility that these cases could be missed

Otherwise the results were reassuring.

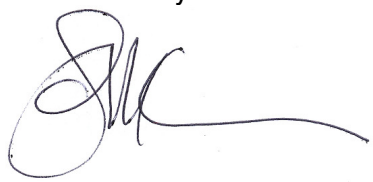
Sample receipt and results return

Circulation 11.1,11.2,11.3,11.4,11.5,11.6

Six participants received the samples on the day following dispatch; 7, 2 days later; one, 7 days later; two, 9 days later; one, 11 days later; one 14 days later; one 15 days later; and two 22 days later. We need to investigate these postal delays many in the UK

All participants except one reported the results on time, one laboratory was a few days late for one set.

Yours sincerely



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