Clinical Chemistry 62:2
413–419 (2016)

the Clinical Chemist

What Is Your Guess?

What's Wrong with the Transferrin?

Nilika Wijeratne,[1,2,3*] Ronald Tudball,[1] Kay Weng Choy,[1] Michael Fietz,[4] and James C.G. Doery[1,2]

Case Description

A 2-year-old boy presented with developmental delay and rapidly progressing spasticity of lower limbs. A serum transferrin isoform test was requested as a work-up for congenital disorders of glycosylation (CDG). Figure 1 shows his serum transferrin isoelectric focusing pattern.

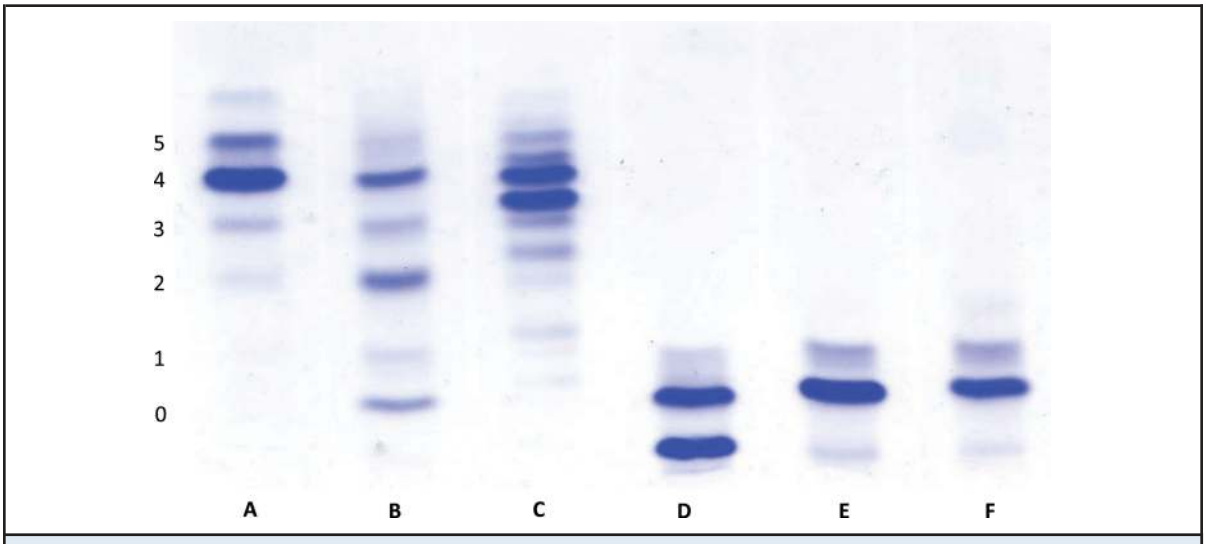

Fig. 1. Lanes A–C, isoelectric focusing without neuraminidase; lanes D–F, isoelectric focusing after in vitro treatment of serum with neuraminidase.

Lane A, normal serum; lane B, CDG type 1 patient; lane C, this patient; lane D, this patient; lane E, normal serum; lane F, CDG type 1 patient. The numbers 0–5 indicate the number of sialic acid residues.

Questions

1. What is the possible cause for the serum transferrin isoform pattern?
2. What is the reason for using neuraminidase in this test?

The answers are on the next page.

[1] Department of Pathology, Monash Health, Clayton, VIC, Australia; [2] Department of Medicine, Monash University, Clayton, VIC, Australia; [3] Dorevitch Pathology, Heidelberg, VIC, Australia; [4] Department of Biochemical Genetics, National Referral Laboratory, SA Pathology, Adelaide, SA, Australia.

* Address correspondence to this author at: Dorevitch Pathology, 18, Banksia Road, Heidelberg, VIC 3084, Australia. E-mail nilika.wijeratne@monash.edu.

Received March 23, 2015; accepted May 29, 2015.

DOI: 10.1373/clinchem.2015.241083

Answers

Diagnosis of CDG is challenging in the presence of transferrin variants *(1–3)*. The neuraminidase removes charged sialic acid residues from the transferrin, revealing any changes in the isoelectric point of the transferrin molecule *(2–3)*. If the abnormal pattern is due to defective *N*-glycosylation, neuraminidase will reduce the profile to a predominantly single band at the position of asialotransferrin (Fig. 1, lane F). This patient has duplication of all bands preneuraminidase (Fig 1, lane C) and duplication of the asialated band postneuraminidase (Fig 1, lane D). This indicates that the altered isoelectric point is due to a change in the transferrin protein (i.e., transferrin variant) and not defective glycosylation.

Author Contributions: *All authors confirmed they have contributed to the intellectual content of this paper and have met the following 3 requirements: (a) significant contributions to the conception and design, acquisition of data, or analysis and interpretation of data; (b) drafting or revising the article for intellectual content; and (c) final approval of the published article.*

Authors' Disclosures or Potential Conflicts of Interest: *No authors declared any potential conflicts of interest.*

References

1. Zühlsdorf A, Park JH, Wada Y, Rust S, Reunert J, DuChesne I, et al. Transferrin variants: pitfalls in the diagnostics of congenital disorders of glycosylation. Clin Biochem 2015;48:11–3.
2. Park JH, Zühlsdorf A, Wada Y, Roll C, Rust S, Du Chesne I, et al. The novel transferrin E592A variant impairs the diagnostics of congenital disorders of glycosylation. Clin Chim Acta 2014;436:135–9.
3. Guillard M, Wada Y, Hansikova H, Yuasa I, Vesela K, Ondruskova N, et al. Transferrin mutations at the glycosylation site complicate diagnosis of congenital disorders of glycosylation type I. J Inherit Metab Dis 2011;34:901–6.