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Case of Syndromic Tufting Enteropathy Harbors *SPINT2* Mutation seen in Congenital Sodium Diarrhea

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In 2007, we described a syndrome of intractable diarrhea of infancy, owing to tufting enteropathy, with findings of choanal atresia/stenosis, mild shortness of stature, mild facial dysmorphism, chronic corneal inflammation, episodic cytopenia and abnormal hair texture. Bird *et al*. (2007). These findings were seen in variable combination in three siblings.

The proband originally described, now a ten-year old boy with continued chronic diarrhea and dependence on total parenteral nutrition, receives only small trophic feeds of rice cereal. His current height is 136.6 cm (5–10%) and weight is 36.4 kg (30–50%). He was initially diagnosed with cholestatic liver disease with subsequent resolution of the cholestasis but persistence of hepatic transaminase elevation. He has a scarred, opaque right cornea and a dry left eye that is treated with topical lubricants. His hair remains coarse.

Some of the congenital anomalies described in this family, specifically choanal atresia and corneal erosions, have also been reported in congenital sodium diarrhea (CSD). Müller *et al*. (2000) Mutations in *SPINT2* (Kunitz-type serine- protease inhibitor) have recently been shown to be associated with a syndromic form of CSD. Heinz-Erian *et al*. (2009). Given the clinical similarities of the proband and those patients with syndromic CSD, DNA from the proband was sequenced to assess for mutations in *SPINT2*. The proband was found to be homozygous for the c.488A>G (p.Y163C) mutation in *SPINT2*, the most frequent mutation in syndromic CSD patients. Mutations in EpCAM (epithelial cell adhesion molecule), seen in tufting enteropathy (TE), were also screened in this family, but not found to be present. Sivagnanam *et al*. (2008), Heinz-Erian *et al*. (2009). The proband has yet to undergo trial of enteral sodium preparation, which has been shown to be therapeutic in some patients with CSD.

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This finding raises questions as to the specificity of epithelial tufts in congenital diarrheal disorders as well as potential pathophysiologic relationships between the various congenital diarrhea disorders. Now that genes for three congenital diarrheal disorders, TE, Sivagnanam *et al*. (2008), microvillus inclusion disease, Müller *et al*. (2008), and CSD, Müller *et al*. (2000), have recently been identified, practitioners evaluating these children should consider genetic testing to help define diagnosis, prognosis and potential therapies.

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References

Bird LM, Sivagnanam M, Taylor S, & Newbury RO (2007) A new syndrome of tufting enteropathy and choanal atresia, with ophthalmologic, hematologic and hair abnormalities. Clinical Dysmorphology, 16, 211. [PubMed: 17786112]

Heinz-Erian P, Müller T, Krabichler B, Schranz M, Becker C, Rüschendorf F, et al. (2009) Mutations in SPINT2 Cause a Syndromic Form of Congenital Sodium Diarrhea. The American Journal of Human Genetics, 84, 188–196. [PubMed: 19185281]

Müller T, Hess MW, Schiefermeier N, Pfaller K, Ebner HL, Heinz-Erian P, et al. (2008) MYO5B mutations cause microvillus inclusion disease and disrupt epithelial cell polarity. Nature Genetics, 40, 1163–1165. [PubMed: 18724368]

Müller T, Wijmenga C, Phillips AD, Janecke A, Houwen RH, Fischer H, et al. (2000) Congenital sodium diarrhea is an autosomal recessive disorder of sodium/proton exchange but unrelated to known candidate genes. Gastroenterology, 119, 1506–1513. [PubMed: 11113072]

Sivagnanam M, Mueller JL, Lee H, Chen Z, Nelson SF, Turner D, et al. (2008) Identification of EpCAM as the gene for congenital tufting enteropathy. Gastroenterology, 135, 429–437. [PubMed: 18572020]