Re: Incidence of Deflux® Calcification Masquerading as Distal Ureteric Calculi on Ultrasound

F. Yankovic, R. Swartz, P. Cuckow, M. Hiorns, S. D. Marks, A. Cherian, I. Mushtaq, P. Duffy and N. Smeulders

Department of Paediatric Urology, Great Ormond Street Hospital NHS Foundation Trust, London, United Kingdom

J Pediatr Urol 2012; Epub ahead of print.

Objective: Dextranomer-hyaluronic acid (Deflux®), the most widely used compound in the endoscopic treatment of vesico-ureteric reflux (VUR) today, is believed to provoke only minimal inflammation. Reports of calcification of Deflux® are increasing. We ascertain the incidence of Deflux® calcification appearing as distal ureteric calculi on ultrasound. Methods: Three cases (2 external patients) of ureteroscopy for calcified submucosal Deflux® prompted a retrospective review of the notes and imaging of all children treated with Deflux® for VUR between December 2000 and January 2011 at Great Ormond Street Hospital. Results: 232 children (M:F = 5:3) received Deflux® for VUR at median age 2 years (range 2 months-12 years). Follow-up annual ultrasound, performed in all, identified calcification in 2. The interval between Deflux® injection and presentation of its calcification was 4 years. 104 of the 232 children had been followed up for 4–10 years. Considering the observed lag-period, after 4 years the incidence of calcification of Deflux® on ultrasound was 2% (2/104). Conclusions: Patients should be warned that calcification of Deflux® can occur. Misinterpretation as ureteric stones is common and may lead to unnecessary ureteroscopy. In this series, the incidence of calcification of Deflux® on ultrasound after 4 years was 2%.

Editorial Comment: Urologists need to be aware that dextranomer/hyaluronic acid in the distal ureter may mimic intramural stones on computerized tomography as well as ultrasound!

Dean G. Assimos, M.D.

Suggested Reading

Cerwinka WH, Qian J, Easley KA et al: Appearance of dextranomer/hyaluronic acid copolymer implants on computerized tomography after endoscopic treatment of vesicoureteral reflux in children. J Urol 2009; **181:** 1324.

Stenberg A, Larsson E and Lackgren G: Endoscopic treatment with dextranomer-hyaluronic acid for vesicoureteral reflux: histological findings. J Urol 2003; **169:** 1109.

Re: Chaga Mushroom-Induced Oxalate Nephropathy

Y. Kikuchi, K. Seta, Y. Ogawa, T. Takayama, M. Nagata, T. Taguchi and K. Yahata

Clin Nephrol 2012; Epub ahead of print.

Chaga mushrooms have been used in folk and botanical medicine as a remedy for cancer, gastritis, ulcers, and tuberculosis of the bones. A 72-year-old Japanese female had been diagnosed with liver cancer 1 year prior to presenting at our department. She underwent hepatectomy of the left lobe 3 months later. Chaga mushroom powder (4–5 teaspoons per day) had been ingested for the past 6 months for liver cancer. Renal function decreased and hemodialysis was initiated. Renal biopsy specimens showed diffuse tubular atrophy and interstitial fibrosis. Oxalate crystals were detected in the tubular lumina and urinary sediment and oxalate nephropathy was diagnosed. Chaga mushrooms contain extremely high oxalate concentrations. This is the first report of a case of oxalate nephropathy associated with ingestion of Chaga mushrooms.

Editorial Comment: For those who enjoy organic foods this might be one to avoid!

Dean G. Assimos, M.D.

Suggested Reading

Chai W and Liebman M: Assessment of oxalate absorption from almonds and black beans with and without the use of an extrinsic label. J Urol 2004; **172:** 953.

Gettman MT, Ogan K, Brinkley LJ et al: Effect of cranberry juice consumption on urinary stone risk factors. J Urol 2005; **174:** 590.

Re: Four of the Most Common Mutations in Primary Hyperoxaluria Type 1 Unmask the Cryptic Mitochondrial Targeting Sequence of Alanine: Glyoxylate Aminotransferase Encoded by the Polymorphic Minor Allele

S. Fargue, J. Lewin, G. Rumsby and C. J. Danpure

University College London, London, United Kingdom

*J Biol Chem 2013; **288:** 2475–2484.*

The gene encoding the liver-specific peroxisomal enzyme alanine:glyoxylate aminotransferase (AGT, EC. 2.6.1.44) exists as two common polymorphic variants termed the major and minor alleles. The Pro11Leu amino acid replacement encoded by the minor allele creates a hidden N-terminal mitochondrial targeting sequence (MTS), the unmasking of which occurs in the hereditary calcium oxalate kidney stone disease primary hyperoxaluria type 1 (PH1). This unmasking is due to the additional presence of a common disease-specific Gly170Arg mutation which is encoded by about one third of PH1 alleles. The Pro11Leu and Gly170Arg replacements interact synergistically to reroute AGT to the mitochondria where it cannot fulfill its metabolic role (I.e. glyoxylate detoxification) effectively. In the present study we have re-investigated the consequences of the interaction between Pro11Leu and Gly170Arg in stably transformed CHO cells, and have studied for the first time whether a similar synergism exists between Pro11Leu and three other mutations that segregate with the minor allele (I.e. Ile244Thr, Phe152Ile and Gly41Arg). Our investigations show that the latter three mutants are all able to unmask the cryptic Pro11Leu-generated MTS and as a result, all are mistargeted to the mitochondria. However, whereas the Gly170Arg, Ile244Thr and Phe152Ile mutants are able to form dimers and are catalytically active, the Gly41Arg mutant aggregates and is inactive. These studies open up the possibility that all PH1 mutations, which segregate with the minor allele, might also lead to the peroxisome-to-mitochondrion mistargeting of AGT, a suggestion which has important implications for the development of treatment strategies for PH1.

Editorial Comment: Type 1 primary hyperoxaluria is a rare autosomal recessive disorder that involves development of calcium oxalate kidney stones and accumulation of calcium oxalate deposits throughout the body. Patients are at high risk for end-stage kidney disease. The defective enzyme, AGT, is normally located in peroxisomes. This enzyme diverts glyoxylate, the immediate precursor of oxalate, away from oxalate synthesis. Certain mutations promote the mistargeting of AGT to the mitochondrial compartment, resulting in hyperoxaluria. The authors performed elegant experiments in which AGT variants were transfected into Chinese hamster ovary cells. They demonstrated that the interactions of Pro11Leu mutation and 3 other mutations result in AGT localizing in the peroxisomes, where it cannot effectively limit the production of oxalate. Further insight into these interactions may facilitate the generation of novel therapies for this rare but serious disease.

Dean G. Assimos, M.D.

Suggested Reading

Holmes RP and Assimos DG: Glyoxylate synthesis, and its modulation and influence on oxalate synthesis. J Urol 1998; **160:** 1617.

Levin-laina N, Dinour D, Romero L et al: Late diagnosis of primary hyperoxaluria type 2 in the adult: effect of a novel mutation in GRHPR gene on enzymatic activity and molecular modeling. J Urol 2009; **181:** 2146.