A Review of Failures of Endoscopic Treatment of Vesicoureteral Reflux With Dextranomer Microspheres

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Purpose: We evaluated the appearance of the mound of failed endoscopic dextranomer microsphere injections at the time of reinjection or open ureteral reimplantation.

Materials and Methods: We performed a multi-institutional study of 80 patients (97 ureters) who were diagnosed with vesicoureteral reflux and had failed endoscopic treatment with dextranomer microspheres. Observations of injected mound characteristics were made during the time of reinjection or at open ureteral reimplantation. Correlations were made with the pre-injection grade of reflux, volume of initial injection, number of punctures used for the initial injection and presence of symptoms of dysfunctional voiding.

Results: Examination of the failed injection sites before subsequent injections or open surgery revealed mound abnormalities in all but 13 of the 97 ureters. Of the cases 49% demonstrated a shifted mound, 22% an absent mound and 10% a loss of volume in the mound. Of the 13 patients with normal appearing mounds 7 had improved reflux grade, 3 had worsened grade and 3 had no change. Patients with dysfunctional voiding symptoms had a second injection failure rate of 44%, compared to a 13% rate in those without symptoms of voiding dysfunction.

Conclusions: Most failures of endoscopic correction are associated with mound shifting. The presence of a perfect mound does not predict success. Dysfunctional voiding predicts a lower success rate after a second injection.

Key Words: dextranomer-hyaluronic acid copolymer, vesico-ureteral reflux, ureter, treatment outcome

Vesicoureteral reflux is estimated to affect 1% of children, and in association with urinary tract infection can lead to pyelonephritis, renal scarring and chronic renal insufficiency.[1] Endoscopic treatment of VUR was first popularized by O'Donnell and Puri in 1984 using polytetrafluoroethylene paste.[2] A variety of endogenous and exogenous substances have since been investigated. However, currently Dx/HA copolymer is the only approved substance in the United States for subureteral injection treatment of VUR in children. Safety and efficacy studies have largely focused on grade of reflux as an end point. Potential mechanisms of failure have not been well defined.

The commonly stated goal of injection therapy to resolve VUR is the creation of a mound under the ureteral orifice. There has been only 1 known prior study regarding Dx/HA failures that examined mound appearances and found a correlation with voiding dysfunction.[3] The purpose of our study was to evaluate the appearance of the mound of failed injections at the time of reinjection or open ureteral reimplantation. We retrospectively examined the endoscopic appearance of the ureteral mounds following failed Dx/HA injections at the time of subsequent treatment. The appearance of the mound as well as the volume injected, presence or absence of dysfunctional voiding by history alone in patients older than 3 years, grade of reflux and number of punctures were considered.

MATERIALS AND METHODS

We performed a multi-institutional study of 80 patients (17 boys, 63 girls) 3 months to 24 years old (mean 4.7 ± 3.7) who were diagnosed with vesicoureteral reflux and had failed endoscopic treatment with Dx/HA between 2001 and 2005. This outcome represents an 18% failure rate from a total patient population of 453. The number of cases contributed by each institution was varied. However, in comparing failure rates of each institution there were no significant differences. Of the 80 study subjects 27 (34%) were classified as dysfunctional voiders by medical history, and 13 (16%) presented with duplex system(s) in the right (5), left (6) or both kidneys (2). Two female subjects had a solitary kidney.

Of the 80 subjects 57 (71%) received initial bilateral Dx/HA injections, 17 (21%) received an injection in the left side only and 6 (8%) received an injection in the right side only. Patients were injected with 0.3 to 2.0 cc Dx/HA (mean 0.86). Each ureter required 1 to 3 needle punctures. Procedures were documented with videography or photography.

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Renal ultrasound and contrast or radionuclide voiding cystourethrogram were performed at 3 months postoperatively. Of the 137 observed initial injection sites 97 (71%) were classified as treatment failures (reflux grade I or higher) on reexamination (17 patients failed both sides, 37 on the left side only and 26 on the right side only). The other 40 injection sites (29%) represented bilateral injections in which 1 side was successful.

All 97 failed injection sites were assessed at the time of followup treatment, of which 28 (29%) were visualized during open surgical procedures and 69 (71%) endoscopically immediately before a subsequent injection. The appearance of the injected mound was classified as shifted (figs. 1 and 2), volume loss, extrusion, absent, combination shift and volume loss (fig. 3) or indeterminate, defined as a normally positioned mound that maintained its volume (fig. 4).

We used the independent samples t test to compare initial VUR grade and injection volume between groups positive and negative for duplex systems and voiding dysfunction. The paired t test was used to compare pre-injection and post-injection VUR grades, and VUR grade and injection volume between paired successful and failed sites for 35 bilaterally treated subjects. The chi-square test was used to assess relationships between the occurrence of mound abnormalities and voiding dysfunction, and injection success and injection quality in bilaterally treated patients with 1 successful and 1 failed site. An alpha probability of 0.05 was used as the threshold for statistical significance in 2-tailed comparisons. Means are presented ± standard deviations throughout. All statistics were performed with Stata® version 9.

RESULTS

Of the 97 treatment failures 3 ureters (3%) were of initial VUR grade I, 27 (28%) grade II, 47 (48%) grade III, 16 (16%) grade IV and 4 (4%) grade V (mean grade 2.91 ± 0.85). The VUR grade after injection was unchanged at 42 injection sites (43%), was decreased (but remained grade I or greater) at 38 (39%) and was greater at 17 (18%). Overall, the post-injection VUR grade was significantly lower than the initial grade (2.62 ± 0.68 vs 2.91 ± 0.85, respectively; paired $t = 3.01$, $p = 0.03$). Mean Dx/HA injection volume for the 97 failed sites was 0.89 ± 0.39 cc, and injection qualities were classified as excellent (63%), adequate (23%) and poor (14%). Examination of the failed injection sites before subsequent injection or surgery showed mound abnormalities in all but 13 of the 97 ureters, with 41 affected ureters (49%) exhibiting a shifted mound, 18 (21%) an absent mound and 9 (11%) a loss of volume in the mound (table 1). We did not find a correlation between the number of punctures at initial injection and the mound appearance on inspection or success/failure rate. There were no clear differences in the occurrence of abnormalities among the 5 VUR grades (table 1).

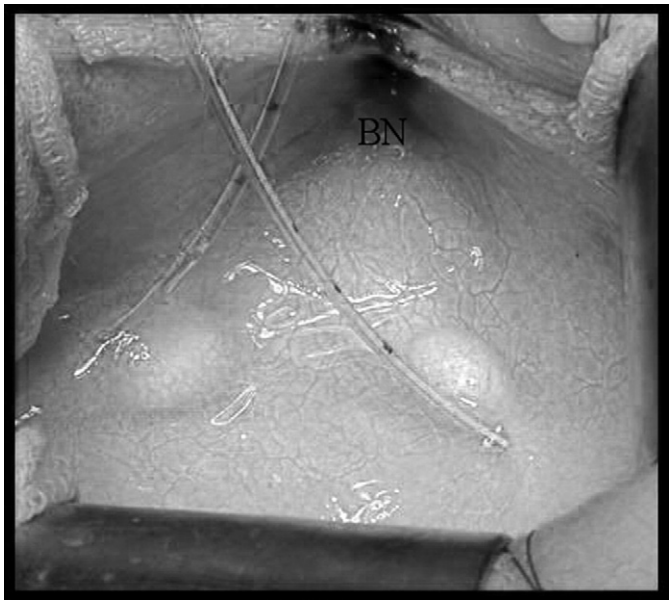

FIG. 2. Intraoperative view of shifted mounds away from orifices (catheters in ureters). *BN*, bladder neck.

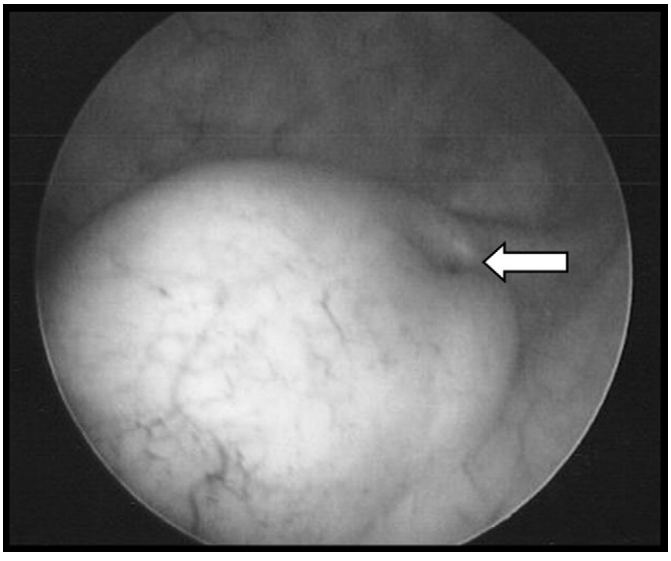

FIG. 1. Mound shifted medially and caudally, away from left ureteral orifice (arrow) toward bladder neck.

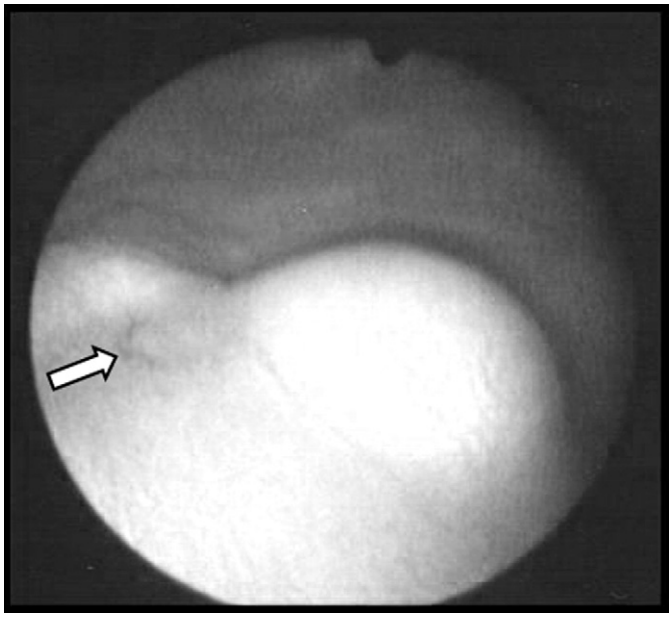

FIG. 3. Multidirectional mound shift away from right ureteral orifice (arrow).