

CLINICAL RESEARCH

Correction of experimentally produced vesicoureteric reflux in the piglet by intravesical injection of Teflon

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Abstract

Vesicoureteric reflux was produced in eight piglets by opening their bladders and slitting the anterior intravesical wall of the ureter. Cystography confirmed the presence of bilateral reflux in six piglets and unilateral reflux in two. Six to eight weeks later the bladder was again opened and Teflon paste injected in the space behind the intravesical ureter, thereby creating a support for the submucosal ureter. Cystography four to six weeks after injection of Teflon paste showed absence of reflux in all animals. Intravenous pyelography showed obstruction at the vesicoureteric junction in only one of the 14 treated ureters and this was later confirmed at necropsy. Animals were followed up from one to six months and then were killed. Gross examination of the vesicoureteric region showed a well circumscribed sub-ureteric Teflon mass of firm consistency, retaining its shape and position at the site of the injection. Histological examination showed encapsulation of the implant by a thin layer of fibrous tissue and a foreign body granulomatous reaction with histiocytes and giant cells within the implant.

Hence it is technically feasible to correct experimentally produced vesicoureteric reflux in the piglet by intravesical injection of Teflon paste—a relatively inert material. It may now be possible to treat vesicoureteric reflux in man by endoscopic injection of Teflon behind the intravesical ureter.

Introduction

Primary vesicoureteric reflux is regarded as a congenital condition resulting from a short intramural ureteral tunnel and an

absence of adequate detrusor support behind the intravesical ureter.¹⁻³ Usually discovered during radiological investigation for urinary tract infection, it has been reported in 30-50% of children who present with urinary tract infection.⁴ It occurs predominantly in girls and has a high familial incidence.⁵

Treatment of reflux is either medical or surgical. Medical management is based on the observation that vesicoureteric reflux tends naturally to improve with time. About 80% of children with vesicoureteric reflux have low grade reflux and non-dilated ureters and the reflux ceases with time.^{2,6} On the other hand, about 20% children with reflux have gross reflux with dilated ureters and reflux does not cease. These patients usually require surgery for the correction of vesicoureteric reflux. Several antireflux operations have been devised, all of which entail opening the bladder and performing a variety of procedures on the ureter.⁷⁻⁹ The principle behind these is to lengthen the intravesical ureter against a solid detrusor support to allow its compression against the detrusor. A novel approach would be the creation of a solid support behind the refluxing intravesical ureter which would allow compression of the intravesical ureter against it similar to an effective valve. Polytef paste (Ethicon), a suspension of polytef particles in glycerine and polysorbate, has been used for several years for injection into the vocal cords to enlarge the displaced or deformed cord^{10,11} or for injection into the wall of the urethra to treat urinary incontinence in women.¹²⁻¹⁴ The polytef particles stimulate an ingrowth of fibroblasts at the site of the injection which help hold the particles within the tissues.¹⁵ The present experimental study was undertaken to determine whether simple injection of Teflon paste behind the refluxing intravesical ureter would correct vesicoureteric reflux.

Materials and methods

The pig is the only suitable animal with a multipapillary kidney similar to that in man, and vesicoureteric reflux has been successfully produced experimentally in this animal.^{16,17}

Vesicoureteric reflux was induced in eight female piglets between 2 and 4 weeks of age. The animals were anaesthetised with a mixture of oxygen, nitrous oxide, and halothane given through an endotracheal tube. The bladder was exposed extraperitoneally through a low midline abdominal incision, being opened in the midline, and the ureteric orifices identified. In the piglet the ureteric orifices are situated low

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down on the trigone adjacent to the bladder neck. The submucosal segment of ureter is very long, which probably accounts for the complete absence of spontaneous reflux in the piglet. The ureteric orifices were catheterised with 3.5F feeding tubes and reflux was induced by slitting the anterior lip (roof) of both intramural ureters. The ureteric catheters were removed and the bladder closed with 3/0 chromic catgut.

Six weeks after induction of reflux cystography was carried out on each animal under light general anaesthesia to confirm the presence of vesicoureteric reflux. The bladder was catheterised with a No 8 Foley's urethral catheter. Urografin was allowed to run into the bladder through an intravenous infusion set and after the bladder had filled to its capacity an x ray film was taken, radiography being repeated after suprapubic pressure had been applied to produce micturition.

Six to eight weeks after the production of reflux the bladder was opened through the previous incision. A 21 gauge butterfly needle was inserted 2-3 mm below the widely patulous ureteric orifice. The needle was advanced 0.5 cm into the space behind the intravesical ureter, and 0.5 to 1.0 ml of Teflon paste was injected with a 1 ml syringe with a Storz metallic sheet and piston. Four to six weeks after the injection of Teflon cystography was performed to determine the presence or absence of reflux. An intravenous pyelogram with Hypaque 45%, 3 ml/kg body weight, was obtained in each animal to determine any obstruction at the vesicoureteric junction.

Animals were followed up from one to six months and then killed. Detailed gross and histopathological examinations of the vesicoureteric area were carried out in each animal.

Results

Cystography confirmed the presence of bilateral reflux in six piglets and unilateral reflux in two (fig 1(a)). Cystography four to six weeks after the injection of Teflon paste behind the intravesical ureter showed the absence of vesicoureteric reflux in all animals (fig 1(b)). Intravenous pyelography showed obstruction at the vesicoureteric junction in only one of the 14 treated ureters, later confirmed at necropsy (fig 1(c)). Gross examination of the vesicoureteric region showed a well circumscribed subureteric Teflon mass of firm consistency, retaining its shape and position at the site of the injection. Histological examination showed that this implant was encapsulated by a thin layer of fibrous tissue and that the overall reaction to it was a benign foreign body granuloma containing histiocytes, fibroblasts, fibrocytes, and giant cells within the implant (fig 2).

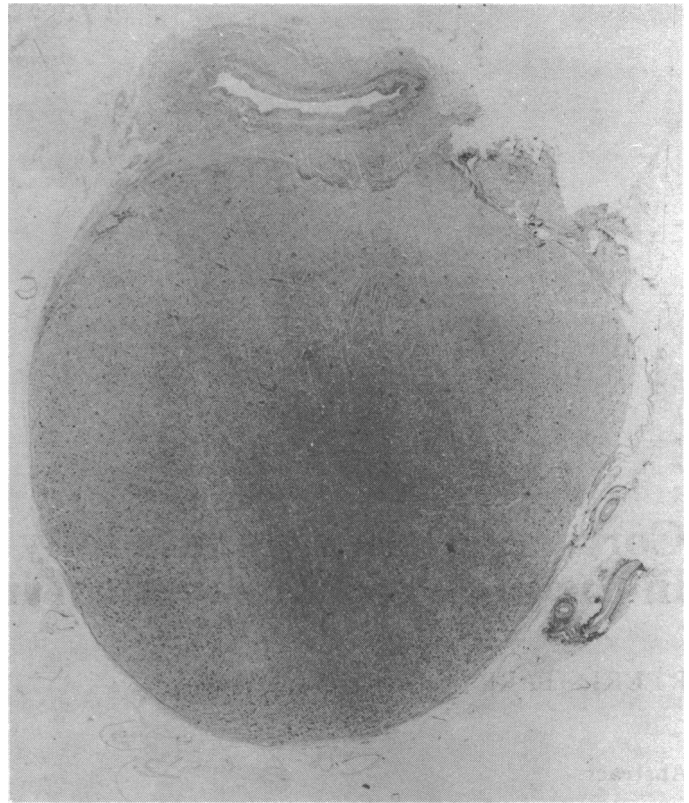


FIG 2—Photomicrograph showing Teflon implant at juxtaposition to ureter encapsulated by a thin layer of fibrous tissue and compressing ureteral lumen.

Discussion

This study shows that it is technically feasible to correct successfully experimentally produced reflux in the piglet by intravesical injection of Teflon paste—a relatively inert material. The main mechanism for an incompetent ureterovesical junc-

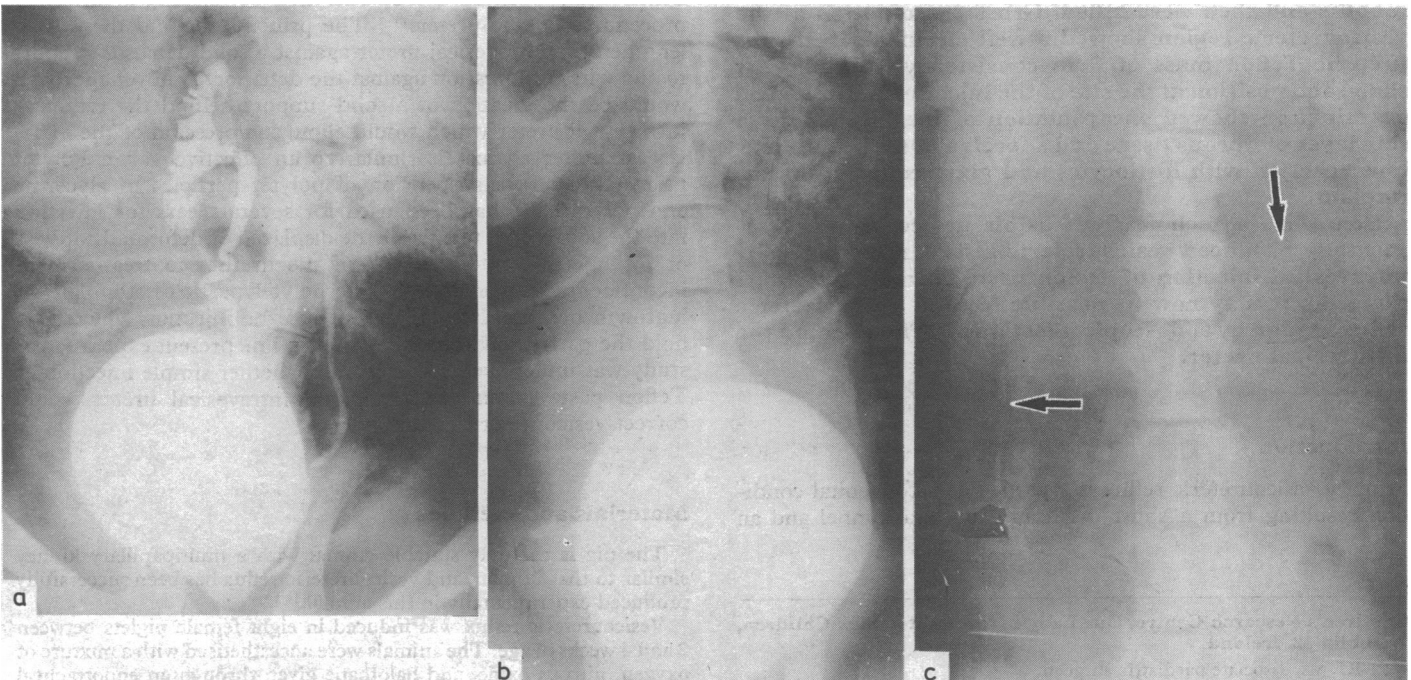


FIG 1—(a) Cystogram six weeks after reflux had been induced in a pig showing bilateral vesicoureteric reflux. (b) Cystogram in the same animal four weeks after injection of Teflon paste behind the intravesical ureter showing absence of vesicoureteric reflux. (c) Intravenous pyelogram in the same animal six weeks after intravesical injection of Teflon paste showing no evidence of obstruction at the ureterovesical junction. Arrows point towards the normal calibre.

tion is believed to be the presence of a short intramural tunnel and the absence of adequate detrusor support for the intravesical ureter. In the normal urinary tract as the ureter approaches the bladder it loses its circular fibres and within the bladder wall it is surrounded solely by longitudinal muscle fibres. These latter continue downwards beyond the ureteric orifice into the trigone, fanning out and mingling with similar fibres from the opposite side and being firmly attached to the mucosa of the trigone. Thus the ureter has only one firm attachment to the bladder—that is, at its orifice by its longitudinal muscle fibres running into the trigone. Congenital deficiency or absence of the longitudinal muscle of the submucosal ureter, as seen in primary reflux, results in upward or lateral displacement of the ureteric orifice, thereby reducing the length and obliquity of the intramural ureter. In addition to producing a solid support behind the intravesical ureter, the Teflon implant also provides a firm anchorage to the intravesical ureter, thereby preventing it from sliding upwards during micturition and thus preventing reflux. From these data we believe that it may be possible to treat vesicoureteric reflux in man by endoscopic injection of Teflon paste.

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Treatment of vesicoureteric reflux by endoscopic injection of Teflon

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Abstract

Thirteen girls with grade III-V vesicoureteric reflux were treated by endoscopic injection of Teflon paste behind the intravesical ureter. Fourteen of the 18 treated ureters showed complete absence of reflux after one injection of Teflon. Three ureters required a second injection of Teflon for successful treatment of the reflux. One ureter with grade IV reflux was converted to grade II reflux.

Properly carried out, this procedure corrects reflux. It takes less than 15 minutes, may be done as a day procedure, and avoids open surgery. There have been no complications.

Introduction

Vesicoureteric reflux has been a controversial subject since 1952, when Hutch highlighted its association with renal damage.¹ Its role in the development and progression of chronic pyelonephritis is now widely recognised. The indications for antireflux surgery have been widely debated. There is general

agreement that patients with the more severe grades of reflux (grades IV and V of the international classification²) and those who develop "breakthrough" bacteriuria while having antimicrobial chemotherapy should have antireflux surgery.

Several antireflux operations have been described. All entail opening the bladder and performing a wide variety of procedures on the ureter. The two most popular operations are the Politano-Leadbetter technique³ of transvesical reimplantation of the ureters and Cohen's transtrigonal advancement.⁴ The principle behind antireflux operations is to lengthen the intravesical ureter against a solid detrusor support to allow its compression against the detrusor. Most patients who have these procedures spend a week or more in hospital. The antireflux operations are effective but not free from complications even in the best hands. Surgery in children with high grade reflux with dilated ureters carries a higher rate of failure and morbidity than in children with low grade reflux and non-dilated ureters.⁵

We have shown in the preceding paper that it is technically feasible to correct successfully experimentally produced vesicoureteric reflux in the piglet by intravesical injection of Teflon paste—a relatively inert material.⁶ This paper describes our experience of treating vesicoureteric reflux in 13 children by endoscopic injection of Teflon.

Patients and methods

Thirteen girls, 12 with primary vesicoureteric reflux and one with secondary reflux due to neuropathic bladder, were included in the study. Their ages ranged from 6 months to 12 years (mean 6.8 years). Five patients had bilateral and eight unilateral reflux; of these, nine

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