Welcome to the 5th edition of the Society for Fetal Urology Year in Review. In the year 2009, we had two excellent meetings with an attendance of well over 125 members in each meeting. The spring meeting was held in Chicago and was chaired by Dr. John Gatti. This meeting focused on the “Nuts and Bolts” of evidence based research. Guest lecturers were Dr. William DeFoor Jr., assistant professor in pediatric urology from Cincinnati Children’s Hospital and Dr. Pablo Aguayo, surgical scholar fellow from The Children’s Mercy Hospital in Kansas City. Dr. John Park gave us a complete review of urologic embryology. The fall meeting was held in Washington, D.C. and was chaired by Dr. Seth A. Alpert. The meeting focused on Neonatal Surgery: Anesthetic and Physiologic Considerations. The guest speakers were Dr. Don K. Nakayama, professor and chair of the department of surgery in Mercer University School of Medicine, Georgia and Dr. Peter D. Winch, assistant professor in pediatric anesthesiology from Nationwide Children’s Hospital in Ohio. Dr. Thomas Kolon gave us an update on disorders of sex development. Both meetings included our traditional case presentations with outstanding participation from our members.

Our prenatal hydronephrosis registry continues to recruit patients in its fourth year of existence with over 130 patients enrolled. Currently, 9 academic centers have received IRB approval and are actively recruiting patients. Information regarding the database and how to participate can be found on our website: www.main.uab.edu/fetalurology or by contacting Dr Anthony Herndon at anthony.herndon@ccc.uab.edu.

We are proud to announce the completion of our consensus statement on prenatal hydronephrosis. The collaborative effort from our members is in line with the objectives of the SFU. The SFU has been committed towards the ongoing education of afflicted families and practitioners that are dedicated to the treatment of medical conditions related to fetal urology. The intent of the consensus is to present our current position on prenatal hydronephrosis. The consensus statement will be published in the new fetal urology section in the Journal of Pediatric Urology.

The year 2010 should be exciting for our society with the spring meeting being held during the first World Congress of Pediatric Urology in collaboration with all the pediatric urology societies from around the world. (www.worldcongresspediatricurology.org) Our fall meeting will be held in San Francisco and chaired by Dr. Carlos Estrada. With continued support from our membership, we continue to grow as a society and move stronger towards the new decade.

Marcos R. Perez-Brayfield M.D., F.A.A.P., President

The Society for Fetal Urology continues to grow in numbers and stature. Leadership has taken an active role in defining the subspecialty of fetal urology through establishing goals for patient management of prenatally detected abnormalities as well as research objectives. In this particular issue, you will notice a section on evidence based research headed by John Gatti. Robert DeFoor provides an excellent overview of the beginnings of evidence based research and how it should be used in our daily practice. Pablo Aguayo then discusses how randomized control trials can be done even in single institutions, as they developed an excellent model at Children’s Mercy Hospital in Kansas City. The case reports are interesting, informative, and to the point.

Dialogues in Pediatric Urology continues to enjoy an excellent affiliation with the Society for Fetal Urology and we appreciate the opportunity to work with this organization.
Special Edition: Society for Fetal Urology - Year in Review
Index of Papers in this Issue

42nd Biannual Spring Meeting, April, 2009, Chicago

Nuts and Bolts of Evidence Based Research ....Page 3
John Gatti, MD, Associate Professor of Surgery and Urology,
Director of Minimally Invasive Urology
Children’s Mercy Hospital, Kansas City, Missouri

Evidence Based Research 101 .......................Page 3
W. Robert DeFoor, Jr., MD, MPH, Associate Professor, Director of
Clinical Research, Division of Pediatric Urology, Cincinnati
Children’s Hospital, Cincinnati, Ohio

A Practical Approach to Prospective
Randomized Trials ................................Page 4
Pablo Aguayo, MD, Shawn D. St. Peter, MD, Center for Prospective
Clinical Trials, Department of Pediatric Surgery, Children’s Mercy
Hospital, Kansas City, Missouri

Fungus Balls in a Pre-term Infant with Posterior
Urethral Valves ........................................Page 5
Stephen M. Graham, MD, John M. Gatti, MD, Romano T. DeMarco,
MD, J. Patrick Murphy, MD, Department of Surgery, Section of
Pediatric Urology, Children’s Mercy Hospital and Clinics, Kansas
City, MO, Department of Urology, University of Kansas Medical
Center, Kansas City, Kansas

Perineal Cystic Mass with Normal Amniotic
Fluid Index and Normal Kidneys on Prenatal
Evaluation – An Unusual Presentation of Anterior
Urethral Valves .......................................Page 6
Devendra Joshi, MBBS, MS, Rafael Gosalbez, MD, FAAP, Division
of Pediatric Urology, Miami Children’s Hospital, Department of
Urology, University of Miami/Jackson Memorial Hospital,
Miami, Florida

A Rare Bladder Exstrophy Variant ..............Page 7
Heidi A. Penn, MD, Romano T. DeMarco, MD, John M. Gatti, MD,
J. Patrick Murphy, MD, The Department of Surgery, Children’s
Mercy Hospital and the Department of Urology, University of
Kansas, Kansas City, Kansas

42nd Biannual Fall Meeting, October, 2009
Washington, DC

Two Unique Cases of Urethroanal Malformations:
Urethral Duplications, Fistula, or Anorectal
Malformation? ......................................Page 8
Aaron P. Bayne, MD, David A. Burkland, Lars J. Cisek, MD, PhD,
and Edmond T. Gonzales, Jr., MD, Scott Department of Urology,
Baylor College of Medicine, Texas Children’s Hospital, Houston, Texas

Antenatal Diagnosis of Megacystis Microcolon Intestinal
Hypoperistalsis Syndrome: Case Report and
Implications for Urologic Management ..........Page 9
Paul R. Bowlin, MD, Duncan T. Wilcox, MD, and Jeffrey B.
Campbell, MD, Department of Pediatric Urology, The Children’s
Hospital, Aurora, Colorado

Renal Agenesis: Genetics and Model Development ....................Page 10
Jason Clarke, Patrick Brophy, MD, University of Iowa, Department
of Pediatrics, Division of Nephrology, Iowa City, Iowa

Prenatal Diagnosis of 46,XY Ambiguous Genitalia with
Postnatal Diagnosis of Epispadias ..................Page 11
Nicholas G. Cost, MD,1 Bruce J. Schlomer, MD,1 Theodore Barber,
MD,1 Diane Twickler, MD,2 Kevin Magee, MD,1 Linda A. Baker,
MD,1 1 Department of Urology, Division of Pediatric Urology, 2
Department of Radiology,1 Department of Obstetrics and Gynecology,
Division of Maternal and Fetal Medicine, University of Texas,
Southwestern Medical Center and Children’s Medical Center of
Dallas, Dallas, Texas

Male Pseudoexstrophy Associated with Cryptorchidism
and Abnormal Karyotype .........................Page 12
Scott P. Cuda, MD, Andrew Kirsch MD, Department of Pediatric
Urology, Children’s Healthcare of Atlanta, Emory University School
of Medicine, Atlanta Georgia

Antenatal Renal Vein Thrombosis: Presentation and
Management ...........................................Page 13
Pablo Gomez, Susan Connolly, Richard S. Lee, Department of
Urology and Radiology, Children’s Hospital Boston, Harvard
Medical School, Boston, Massachusetts

Bladder Neck Abnormality in a Patient with an
Imperforate Anus ..................................Page 14
Jonathan F. Kalisvaart MD1, George R. Raschbaum MD2, J. Damien
Grattan-Smith MD3, Edwin A. Smith MD1, 1Departments of Pediatric
Urology, 2Pediatric Surgery and 3Radiology, Children’s Healthcare of
Atlanta and Emory University, Atlanta, Georgia

Spinal Anomalies in Hypospadias Patients ....Page 15
Michiko Nakamura, Eiji Hisamatsu, Yuichi Hasegawa, Mikiko
Miyasaka1, and Katsuhiko Ueoka, Department of Pediatric Urology
and Radiology1, National Center for Child Health and Development,
Tokyo, Japan
Outcomes based research has become increasingly important in objectively evaluating the efficacy and safety of modern medicine. A basic understanding of the components of study design is critical to forwarding the discipline of fetal/neonatal urology.

At the 42nd Biannual SFU meeting in April, 2009, in Chicago, Dr. William DeFoor, Director of Clinical Research for Pediatric Urology at Cincinnati Children’s Hospital addresses the issue of why clinical outcomes research is so important, focusing on key concepts such as study design, level of evidence and journal impact factor. Dr. Pablo Aguayo, Clinical Research Fellow with the Center for Prospective Clinical Trials in the Department of Pediatric Surgery at the Children’s Mercy Hospital in Kansas City, Missouri, then discusses the creation of a center for prospective clinical trials focusing on the practical application of these concepts. He emphasizes the logistics, pitfalls, and productivity of creating such a center, including practical advice for study development.

The specialty of pediatric urology was developed from pioneering surgeons in the last century who used creativity and surgical innovation to take the management of children with urologic disorders to a higher level. These physicians made careful clinical observations on a case-by-case basis to document their experiences. Anecdotal outcomes and case studies were the basis for subsequent advances in the early era. Finally, a better understanding of the pathophysiology of the disease conditions coupled with improved magnification, finer suture materials, and remarkable technical advances in endoscopic equipment further refined our ability to maximize patient outcomes. Recognition for these efforts was formalized in 2006 when the Certificate of Added Qualification was approved for the subspecialty of pediatric urology.

In light of these extraordinary advances, it has become incumbent on clinicians to be able to critically evaluate the evolution in medical and surgical management. Pressure from governmental agencies and third party payers as well as increasing sophistication from parents have brought the need for “evidence-based medicine” to the forefront. The transition from “in my experience” to a more rigorous scientific basis should be fueled by the desire to provide the best possible care for our patients. Moreover, we as clinicians should be able to appropriately interpret the available literature for our patients regarding the safety and efficacy of the treatments that we provide.

The importance of educating the next generation of pediatric urologists in the process of critical appraisal of clinical evidence cannot be understated. The concepts that urologists should become familiar with include the various types of epidemiological study designs, including clinical trials and observational studies, with knowledge of their specific advantages, limitations, and sources of potential bias. A working knowledge of the levels of evidence system is necessary to be able to evaluate the strength of a manuscript. Approaching a published paper in a logical, organized fashion with an understanding of the statistical methods and a critical eye towards the conclusions is a skill set that will be useful throughout one’s career. The primary questions one should routinely ask on reviewing a paper include the following: what are the study results, are the study results valid, and how do these results apply to my patient population?

It is beyond the space limitations of this abstract to delve deeply in the details of all these important topics. Some pediatric urology fellowship programs have begun to tailor the required basic science laboratory year to make time available for further advanced work in this area, including the pursuit of a Master’s in Public Health with an emphasis on Clinical Effectiveness. Although not every training program can allocate time for fellows and residents to undertake formal class work training in statistics and epidemiology, there are many published and online resources that have been made available for urologists. A series of well-written articles by Dr. Philipp Dahm and colleagues published in the *Journal of Urology* called the *User’s Guide to Urological Literature* is a good overview of the core concepts of evidence-based medicine (EBM). In the September 2007 issue, an article in the series entitled “Evidence Based Clinical Practice: A Primer for Urologists” gives step-by-step guidelines for practicing EBM and offers a wealth of resources for obtaining further information. A new program by the American Urological Association Office of Education has been initiated to provide urologists with critical appraisal skills and allows for continuing medical education credit. More information can be obtained at the following link: [http://www.auanet.org/eforms/ebru/CMEstatement.cfm](http://www.auanet.org/eforms/ebru/CMEstatement.cfm).

In conclusion, the therapeutic benefits of the procedures and treatments that we render often seem intuitively obvious. However, in a changing landscape of healthcare in the United States, clinical practice pathways and guidelines based on solid outcomes evidence will most likely become mandatory from governmental and third party payers. The ability to design and conduct good clinical research as well as interpret and critique the available literature are skill sets that our graduating fellows will need throughout their career. Evidence-based medicine has become mainstream and is no longer a quaint sideline to our practice. It is paramount that those in our specialty understand and subscribe to its principles.
While the term “evidence based” was first coined in a manuscript by David Eddy in JAMA in 1990, the cycle of observation, hypothesis and experimentation was in fact first published in the western literature almost a thousand years prior. Currently we define evidence based medicine (EBM) as the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients. EBM is a new paradigm based primarily on the practice of the scientific method. It is a paradigm that focuses on de-emphasizing clinical intuition, personal experience and pathophysiologic rationale as sufficient grounds for clinical decision making. More importantly, it is a concept that moves away from the traditional practice of medicine which has historically been based on knowledge handed down from mentor to apprentice. In essence, the development of EBM as an entity is a simple consequence of the use of the scientific method in pursuit of proven truths.

While the concept of EBM is certainly nothing new, acceptance as standard practice in the area of pediatric surgery has been challenging. This can best be appreciated by keeping in mind that the current leaders in the field of pediatric surgery are only the second or at the most third generation of trained pediatric surgeons. Therefore, it is not difficult to see how practice patterns based on the philosophies of only a few surgeons have been transmitted to the entire practicing population. In fact, the practice of pediatric surgery has generally gone on without any extensive critical analysis. Since the establishment of the first pediatric surgery training program in 1930, the literature has been dominated by retrospective case control studies and case series with very few publications entailing comparative analysis, and even in these, the majority are retrospective in nature.

Acknowledging the lack of and the need for studies providing level 1 evidence and after completing a prospective randomized trial (PRT) comparing open versus laparoscopic pyloromyotomy for pyloric stenosis, the Center for Prospective Clinical Trials was created at the Children’s Mercy Hospital. The idea of PRTs conjure up images of large, multi-institutional studies with 3,500 patients in each arm, a team of statisticians, titles with play on word acronyms like the CEASAR trial, ACAS or ACUTE, and a co-author list that reads like a who’s who of medicine. However, our experience has taught us that a practicing group can conduct important trials that impact daily practice.

Prior to embarking on any study there are a few general considerations that allow us to identify situations in which a trial can be utilized. The first is equipoise. Equipoise simply assumes that two treatments are considered to be equal and thus a head-to-head comparison may be warranted to identify which one is superior. Second is patient volume. Certainly, adequate patient volume is required. While this is simple for common conditions, in the field of pediatric surgery there are a large number of individually rare conditions that preclude acquiring a large number of patients. For these situations, focusing on attaining a smaller sample size to detect larger differences through either pilot studies or lower powered studies remains a reasonable option. Third are population characteristics. The most important consideration is the homogeneity of the disease. A treatment modality performed on patients for a multitude of indications does not usually lend itself to PRTs. Fourth, relevance on practice patterns needs to be considered. For instance, a very complex treatment protocol may provide superior outcomes, however, its complexity would limit its use in general practice thus greatly diminishing its value. Additionally, when determining relevance, it is important to ask several questions: 1) Does a problem really exist? 2) Is it applicable to a typical practice? 3) What is the event rate? 4) What is the burden? Retrospective review of the institution’s experience often helps answer these questions precisely.

Over the past six years we have learned several important and noteworthy lessons. The need to abandon the “art” of medicine for the sake of data is paramount. Individual egos and dogmatic beliefs are the greatest source of contention towards a study and should be identified and addressed at the beginning of a trial. Next, a strong relationship with the hospitals’ Institutional Review Board (IRB) is not only encouraged but mandatory. Active and continual engagement with the IRB assures administrative success and keeps small problems from becoming large ones. At the clinical level, it is important to keep in mind that complex treatment algorithms should be avoided whenever possible. Introducing complex protocols is unlikely to be successful as a result of non-compliance by either caretakers or patients. With this in mind, we use computer generated order sets with preset dosages, timing, parameter checks, etc. Finally, if one or more people fail to take full ownership of a study, failure is almost universal. Almost daily maintenance includes following each patient’s consent, assuring the randomization sequence is intact, identifying and correcting protocol violations, providing feedback for providers demonstrating a lack of understanding of the protocol, and maintaining constant communication with the IRB and the research staff.

As of 2009, five PRTs have been completed through the Center for Prospective Clinical Trials at the Children’s Mercy Hospital. A sixth study is awaiting maturation of the data and six other studies are currently in the recruitment phase.

In summary, embarking on prospective, randomized clinical trials takes a tremendous amount of effort. It is, however, extremely rewarding. We have shown at our institution that success is not necessarily dependent on research grants or large, complex studies, but rather on a motivated team of individuals who are involved in a busy clinical practice and who are interested in advancing the care of patients through the use of the scientific method.

References
Fungus Balls in a Pre-term Infant with Posterior Urethral Valves

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Introduction

The identification of patients with posterior urethral valves is crucial to minimize irreversible damage to the upper tracts. When other life-threatening issues such as respiratory or cardiac distress are present, though, prophylactic antibiotics should be started until definitive treatment can be performed. Prolonged use of excessive antibiotics, however, can increase the risk of developing bacterial resistance or other infections, namely candiduria. We present the case of a male neonate with posterior urethral valves who developed bilateral renal fungal balls.

Case Report

A newborn male was delivered via emergent cesarean section at 32 weeks secondary to severe oligohydramnios. A prior 20-week fetal ultrasound was normal. The infant’s perinatal presentation included respiratory distress, a distended abdomen, and decreased urinary output. After being placed on a respiratory oscillator, the urology service was consulted for further evaluation of the distended bladder and low urine output. Bladder decompression was performed by placing a 5-French feeding tube, and cephalexin was recommended for urinary prophylaxis. Prophylactic Cefepime®, a 4th generation cephalosporin, was started.

After 25 days, urine culture obtained for fever demonstrated Candida utilis. Renal sonography was obtained for further evaluation and revealed bilateral renal pelvic masses consistent with fungal balls (Figure 1). Intravenous fluconazole was used initially, but this was changed to systemic amphotericin B when the patient continued to have persistent fungal urinary cultures. After several weeks of therapy and with the patient more medically stable, diagnostic voiding cystourethrogram was performed which demonstrated posterior urethral valves (Figure 2).

The patient underwent endoscopic valve ablation with circumcision at 37 days of age. Despite systemic IV antifungal therapy, however, the fungal infection persisted and bilateral percutaneous nephrostomy tubes were placed. Amphotericin B was infused directly through the nephrostomy tubes to focially treat the renal fungal balls. After one to two weeks, the urine cleared of infection and both nephrostomy tubes were removed prior to hospital discharge. The patient’s renal function on discharge was stable, with a creatinine of 0.5 mg/dL, and his final urine culture was negative.

Discussion

Management of patients with posterior urethral valves is well established. Proper management includes stabilization of any life-threatening complications, temporary bladder decompression, prophylactic antibiotics, diagnostic imaging studies, and relief of obstruction with valve ablation or vesicostomy as soon as medically feasible. For those patients with other life-threatening issues, generally accepted prophylactic antibiotics regimens include cephalexin or amoxicillin. Prolonged use of antibiotics, however, especially broad-spectrum antibiotics, can increase the risk of developing bacterial resistance or systemic candidal infections. In this case, the patient was placed on a 4th generation cephalosporin which, combined with other risk factors for candidiasis including prematurity and the presence of central lines, predisposed him to developing bilateral renal fungal balls.

Generally accepted first-line therapy for neonatal renal candidiasis involves systemic anti-fungal therapy such as intravenous fluconazole or amphotericin B. If that fails or if the patient becomes obstructed by fungal balls, one may place percutaneous nephrostomy tubes, with or without instillation of anti-fungal therapy. On occasion, endoscopic treatment is required. Our patient had failed initial systemic therapy, and bilateral nephrostomy tubes were placed—daily irrigation of amphotericin B was then added to supplement the intravenous therapy.

In summary, patients with posterior urethral valves are often managed by perinatologists, neonatologists or pediatricians for other co-morbidities. These physicians need to be informed of the appropriate antibiotics used for urinary tract infection prophylaxis so that bacterial resistance and iatrogenic infections can be avoided. In addition, therapy for neonatal fungus balls should begin with intravenous anti-fungal systemic therapy and advance to more invasive treatment as indicated.

References


Figure 1

![Figure 1](image1)

Figure 2

![Figure 2](image2)
Perineal Cystic Mass with Normal Amniotic Fluid Index and Normal Kidneys on Prenatal Evaluation – An Unusual Presentation of Anterior Urethral Valves

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Introduction
Anterior urethral valve (AU) as a cause of urethral obstruction is 8–10 times less common than posterior urethral valves and has variable presentation. We present an interesting case of anterior urethral valves that was diagnosed antenatally with normal kidney function and no oligohydramnios.

Case report
A 29 year old G1P0 mother was evaluated at 39 weeks of gestation. The previous prenatal evaluation had revealed a single fetus with normal amniotic fluid index and perineal cystic mass measuring 8.6 x 3.6 x 4cm. A baby boy was delivered via Caesarean section and he had an uneventful perinatal period. His postnatal evaluation revealed a dysmorphic phallic structure, approximately 14 cm long and 14.5cm in circumference at base. There was tight phimosis and glans corpora cavernosa bilaterally were not palpable. This swelling involved the entire scrotum and part of perineum and mild urinary dribbling on pressure was noted suggesting a distended urethra with distal obstruction. He had a left inguinal testis with a right inguinal hernia and non-palpable right testis. Ultrasound and MRI scans showed bilateral normal kidneys with a very thick-walled bladder and a large megalourethra. The glans penis and corporal bodies could not be satisfactorily evaluated clinically nor on MRI. An initial presumptive diagnosis of scaphoid megalourethra vs. anterior urethral diverticulum with distal obstruction was made. The patient was operated on Day 7 of life. On opening the urethra ventrally, there was a membranous anterior urethral valve, just proximal to fossa navicularis and a large diverticulum of the penile urethra that had dissected proximally along Buck’s fascia to the level of the urogenital diaphragm and involved the entire scrotum. The proximal urethra, glans and bilateral corporal bodies appeared normal. Excision of anterior urethral valve with partial excision of the urethral diverticulum along with a penile urethrostomy and circumcision were performed. VCUG in the immediate post-operative period showed bilateral G3-4 VUR. The patient did well with the urethrostomy. A complete penile reconstruction with scrotoplasty was performed at 7 months of age. His left testis descended spontaneously on follow-up and the patient underwent right orchiopexy at 11 months of age. Patient had an excellent post-operative result and at approximately 1 year of age, VCUG showed left Grade 2 and right grade 1 VUR. He is doing extremely well on antibiotic prophylaxis.

Discussion
AU valves are rare and often associated with urethral diverticulum. They are commonly described in bulbar urethra (40%), penoscrotal junction (30%) and penile urethra (30%). Presentation is variable, depending upon age and degree of obstruction. Various hypothesis have been proposed to explain their origin, including intra-uterine obstruction (preputial adhesions, congenital stricture etc), incomplete hypospadias, faulty union of the penile and glanular urethra, abortive urethral duplication, and congenital cystic dilation of periurethral glands. They have been classified into four types (Type 1 to Type 4) ranging from mild urethral distension to severe changes in upper tract. Treatment is individualized as follows:
1. Valve fulguration or single-stage urethroplasty if urethra is adequate with good corpus spongiosal support,
2. Staged urethroplasty for massive urethral diverticulum,
3. Vesicostomy for high-grade bilateral reflux or persistent azotemia.

References

Fig. 1: Urethral diverticulum opened ventrally to show anterior urethral valve just proximal to fossa navicularis
A Rare Bladder Exstrophy Variant
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Introduction
Variants involving the epispadias-exstrophy complex are extremely rare. Because of the scarcity of cases, variants can be confusing and difficult to classify.

Case Report
A newborn term male presented with what initially was thought to be classic bladder exstrophy. On physical examination the child had an extrophic bladder plate and associated epispadias. At the time of repair on his first day of life he was found to have a normal ventral urethra in addition to a split glans dorsally and a dorsal urethral plate extending proximally to the extrophied bladder. The polypoid bladder mucosa communicated posteriorly through a small central opening to more normal appearing bladder tissue. Urine emanated from the posterior bladder segment. At the time of surgery, the aperture between the extrophied bladder and the posterior bladder tissue was opened widely in a Heineke-Mikulicz fashion and the two bladder segments closed in continuity. The fascia and abdominal skin were approximated without osteotomies. Eight months later the dorsal urethral plate was excised and the dorsal glans and shaft skin were approximated. The child has done well following both surgeries.

Discussion
Classic bladder exstrophy is a rare condition, occurring in approximately 1 in 40,000 live births. The incidence of exstrophy variants is much less, thought to occur ten times more infrequently. Classifications of bladder exstrophy variants have been proposed to help with identification, understanding, and treatment. Four types have been described and are the most recognized. These include pseudo-exstrophy, superior vesical fissure, duplicate, and covered exstrophy. Other less frequent bladder exstrophy variants have been reported. Urethral duplication is a rare anomaly and only a few cases associated with exstrophy have been reported. One institution’s experience included five cases, of which only one was recognized prior to primary closure, with common findings of a larger than expected penis and a more deeply situated bladder plate. All patients voided normally and were continent after excision of the dorsal urethral plate. Our case represents an unusual variant and constitutes components of duplicate exstrophy, superior vesical fissure, and urethral duplication. While accepted nomenclature for variants is helpful, it is important for the clinician to realize that the epispadias-exstrophy complex has a wide range of presenting findings and patients may not fit into a particular classification system.

References
Two Unique Cases of Urethroanal Malformations: Urethral Duplications, Fistula, or Anorectal Malformation?

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Introduction

Urethral duplication is a rare congenital anomaly with an unclear etiology. Y-type urethral duplication, urethral perineal fistula, and many cases of anorectal malformation (ARM) involve a communication between the urethra and perineum and/or anorectal complex. Evaluation and management of these anomalies varies widely and depends on the etiology and associated symptoms. Here we describe two cases of urethroanal malformations to highlight essential parts of the presentation, diagnosis, and anatomic variability of this rare anomaly.

Case Reports

The first child is an 11-day-old boy with a prenatal diagnosis of unilateral MCDK and patent urachus. He was noted to have normal urethral voiding by his parents but had one reported episode of a stream of water from his rectum. A VCUG was ordered but was not completed due to difficulty passing a catheter. He was scheduled for surgery to evaluate the urinary tract and urachus.

The second case is a 13 year old boy with a lifelong history of watery stools. He was noted on anorectal manometry to have a heavy urine stream passing from his rectum. He was referred for urologic evaluation where a VCUG showed a secondary urethral tract to the rectum with opacification of the rectum on voiding.

Both children on examination had a fistulous tract connecting their external anal sphincter complex with the proximal urethra. The younger child also had an anteriorly displaced anus and was evaluated by general surgery. Both children had a normal caliber penile urethra with a short mid-bulbar circumferential narrowing. The older boy was able to accommodate a 16F catheter easily through the narrowed segment with no dilation required. The proximal urethra had a normal caliber and the external urethral sphincter was intact. Both children had a history of urethral voiding and the older child had normal urethral continence.

On cystoscopy both children had normal appearing trigones and bladder necks with the younger child have a patent urachus. Neither child had vesicoureteric reflux on cystogram.

Discussion

These cases provide a natural history of this rare anatomic variant. The unique findings of a good caliber penile urethra with only a narrowed bulbar segment and anal involvement suggest this may instead be a variant of ARM. The younger child has this urethral fistula in association with an anorectal malformation and MCDK. If these two cases are considered a spectrum of ARM then they may reflect the natural history of these particular malformations. Viewing these malformations as variations of ARM suggests that a different surgical approach may be used than the techniques used for traditional Y-type duplication. We would recommend that children with this particular anomaly be managed more conservatively with repair focused on fistula tract excision with preservation of the dorsal urethra if feasible. This would spare the child an extensive reconstruction associated with multiple possible complications that normally accompany Y-type duplication treatment. Urethroanal malformations represent a spectrum of disease from urethral duplication to ARM and management should be tailored to the underlying etiology and quality of the dorsal urethra.

References

Antenatal Diagnosis of Megacystis Microcolon Intestinal Hypoperistalsis Syndrome: Case Report and Implications for Urologic Management

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Introduction

Megacystis microcolon intestinal hypoperistalsis syndrome (MMIHS) is a rare congenital disorder. The syndrome is often suspected during antenatal ultrasonography by the presence of a distended bladder. We describe a case report, and the diagnostic features, etiology, and issues surrounding urologic management of this condition.

Case Report

The patient was born at 34 weeks gestation via spontaneous vaginal delivery. She had earlier been found to have a distended bladder, hydroureronephrosis, and polyhydramnios on routine prenatal ultrasonography. The karyotype was 46,XX. Vesicocentesis was performed several times during the pregnancy for 60mL each time, and for 1.5L on the day of delivery to facilitate vaginal delivery. Postnatally, the patient was noted to have a distended abdomen with poorly developed musculature. Postnatally, the urinary tract was managed with clean intermittent catheterization (CIC) and UTI prophylaxis. The serum creatinine was initially 1.5 mg/dL, and progressively decreased to a nadir of 0.18 mg/dL. An upper GI series demonstrated delayed transit of minimal contrast into the duodenum, and a gastrograffin enema demonstrated microcolon, confirming the diagnosis. The patient was managed supportively with total parenteral nutrition in anticipation of multivisceral organ transplantation.

Discussion

First described by Berdon in 1976, MMIHS is a rare condition that is usually fatal. Inheritance is autosomal recessive with a female predominance. The hallmark features include a dilated, non-obstructed urinary bladder and a hypoperistaltic gastrointestinal tract with microcolon (Figure 1). Other radiologic findings include a dilated stomach and bowel, and polyhydramnios. Ultrasound is usually the preferred modality for following this condition prenatally, but fetal MRI and amniotic fluid assays have also been utilized. Various etiologies of the genitourinary manifestations of this condition have been proposed, including myogenic causes related to interstitial cells of Cajal and defects in the nicotinic acetylcholine receptor genes. Management of the genitourinary tract is usually accomplished through CIC or a vesicostomy. As with other urologic conditions, the role of a prophylactic antibiotic remains unclear. The genitourinary management is a supportive adjunct to allow time to coordinate multivisceral organ transplantation. As the treatment of the associated nonurologic components of this disease progress, there may be a role for more definitive genitourinary management.

References


Figure 1: Gastrograffin enema demonstrating microcolon.
Renal Agenesis: Genetics and Model Development

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Introduction

Renal agenesis and renal adysplasia are two of the most common urogenital birth defects. Both have been shown to lead to hypertension, proteinuria and are predictors of dialysis treatment. It is imperative that in order to fully understand the implications of these conditions that we develop an animal model that closely mimics phenotypes observed in humans.

Case Report

A case of possible familial bilateral renal agenesis (BRA) was presented to our laboratory. The proband was noted to have absent kidneys, preauricular skin tags and pulmonary hypoplasia. An earlier pregnancy was also lost due to BRA but was unavailable for analysis. Following collection of DNA and health histories, we hypothesized that this was a misdiagnosed case of branchio-oto-renal syndrome. Through mutational analysis of the pedigree we were able to determine that the affected members carried a mutation in the EYA1 gene that caused a 50% decrease in gene dosage and a variable renal phenotype. Both the proband and his father had the same EYA1 mutation and auricular phenotypes, but only the proband exhibited a renal phenotype. EYA1 is a part of the PAX/EYA/SIX genetic pathway that is critical for the development of the urogenital system. Monogenic and polygenic mutations in components of this pathway can lead to variable renal and non-renal phenotypes in a dose dependent manner.

Discussion

Renal agenesis in humans most often presents with a genetic etiology, with incomplete autosomal dominant inheritance and expressivity. While it is known that mutations in EYA1 are often associated with BOR syndrome, our current case illustrates the nature of mutations in the PAX/EYA/SIX pathway and the variable phenotypes a single mutation in a component of the pathway can cause. We hypothesize that in humans unilateral and bilateral renal agenesis, renal adysplasia and hypoplasia are all within the same developmental continuum. The PAX/EYA/SIX genetic pathway is ideal for studying the renal developmental pathway in a dose dependent manner. We have created a multigenic mouse model involving other components of this pathway that supports this hypothesis and mimics what we have observed in affected humans. These mice are compound heterozygous null for the transcription factor PAX2 and the receptor tyrosine kinase Ret. Compound heterozygous mice have an autosomal dominant renal phenotype that presents with hypoplasia, unilateral agenesis or bilateral agenesis. To further pursue this hypothesis we have been collecting DNA and data from pedigrees with bilateral renal agenesis. Consent forms to enroll in this study can be found at www.kidneygenes.com. Using SNP and linkage analysis as well as new technology to analyze copy number variants, we intend to elucidate the gene(s) associated with renal agenesis in humans.

References


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Prenatal Diagnosis of 46,XY Ambiguous Genitalia with Postnatal Diagnosis of Epispadias
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Introduction
Modern prenatal imaging techniques can detect many congenital anomalies, including ambiguous genitalia. In these cases with 46,XY fetal karyotype, the differential diagnosis is broad and there are no clear recommendations for prenatal evaluation.

Case Report
Routine prenatal ultrasound (US) at 18wks gestational age (GA) was unable to determine the fetal sex. Repeat US at 25wks showed normal amniotic fluid levels in a fetus without other anomalies except micropenis vs. enlarged clitoris, and also a possible scrotum. At 27wks, fetal karyotype by amniocentesis was 46,XY, SRY+. Prenatal MRI (Figure 1) demonstrated a markedly diminutive phallus (8mm) for GA and suggested bilateral testes. No uterus or ovaries were seen and the adrenals, bladder and kidneys were normal. At 29wks, US revealed a midline triangular phallus, a fused midline scrotum and descended testes.

At term birth, examination showed a healthy male with a normal scrotum containing descended testes. The 2cm phallus appeared ‘concealed’ with irreducible foreskin, but atypical because the dorsal shaft skin was decreased compared to the ventral shaft raising the question of epispadias. Following topical betamethasone treatment, the foreskin retracted, demonstrating isolated penopubic epispadias. After cystoscopy with cystography identified a competent bladder neck, no vesicoureteral reflux, and 50mL capacity bladder, epispadias repair was performed via full penile disassembly technique.

Discussion
In 1977 Stocker and Evens first described the sonographic diagnosis of fetal sex;1 now well-established US nomograms exist for penile size adjusted for GA.2 By US, hypospadias can be diagnosed prenatally by detecting penile curvature and the ventrally ectopic urinary jet. Coved by Meizner et al., the “tulip sign” describes the ventrally curved penis between the bifid scrotum.3 To assess ambiguous genitalia, the bladder to rectum distance can identify Müllerian structures.4 In 1995, Gearhart et al. established prenatal US criteria for classic bladder extrophy, focusing on the extrophetic bladder.5 To define isolated epispadias in utero, we suggest the following criteria: 46,XY karyotype, a normal to small capacity bladder, a short phallus for GA with triangular shape and no ventral curvature, descended testes and no Müllerian structures. As epispadias is not associated with other birth defects, termination of pregnancy is not indicated. Thus, prenatal diagnostic criteria may be helpful.

References
Male Pseudoexstrophy Associated with Cryptorchidism and Abnormal Karyotype

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Introduction

Covered or pseudoexstrophy is a rare variant of the male epispadias/exstrophy complex. Patients with pseudoexstrophy most commonly present with an abnormally low set umbilicus and an intact bladder and urinary tract. Associated genetic abnormalities have thus far not been described in the literature.

Case Report

A 2 month-old male infant presented with umbilical discharge for evaluation of a possible urachal remnant. Physical exam revealed a low set umbilicus with palpable midline herniation, mild separation of the pubic symphysis, a small phallus with a normal meatus and intact urethra, and bilateral palpable undescended testicles (Figure 1). Initial operative management consisted of cystoscopy, excision of the native umbilicus with flap umbilicoplasty and bilateral inguinal exploration and inguinal orchiopexy via a midline incision. During the procedure both testicles were noted to be small but with normal vas deferens and epididymal attachments. Microarray chromosomal analysis revealed a 10.8 megabase duplication of genetic material on the long arm of the X chromosome (Xq27.3 -28). Further workup with an MRI of the brain for developmental delay was significant for hypomyelination of the corpus callosum.

Discussion

Bladder exstrophy is a rare congenital anomaly affecting between 1:10,000 to 1:50,000 live births. The most commonly described exstrophy variants include covered exstrophy, pseudoexstrophy, superior vesical fistula and duplicate exstrophy. Variants account for approximately 3% of all bladder exstrophy cases. In the spectrum of epispadias/exstrophy, pseudoexstrophy is the mildest form and in certain cases may not require treatment. Exstrophy is thought to result from delayed regression of the cloacal membrane preventing medial migration and ingrowth of mesenchymal tissue. The literature on pseudoexstrophy is sparse consisting of individual case reports. Other reported anomalies include, imperforate anus, renal anomalies, palatal defects and omphalocele. This is first report of multiple congenital anomalies in association with an abnormal chromosome analysis in a patient with pseudoexstrophy.

References


Figure 1 - Preoperative photo showing a low set umbilicus, anteriorly displaced anus, and intact urethra and phallus.
Antenatal Renal Vein Thrombosis: Presentation and Management

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Introduction

Renal vein thrombosis (RVT) is an entity rarely diagnosed antenatally. We present two cases of in-utero detected RVT its presentation, diagnosis, management and outcome.

Case 1

A G6P1 female with a history of Factor V Leiden and enoxaparin anticoagulation underwent a 29 week ultrasound (US) which revealed mild bilateral antenatal hydronephrosis. Follow-up US at 38 weeks showed an enlarged, hyperechoic left kidney with loss of the cortico-medullary differentiation and a RVT extending into the IVC (Figure 1A). Labor was induced and postnatally the infant was well with a normal clinical exam. Day 1 US confirmed the diagnosis of RVT and the patient was treated with anticoagulation (enoxaparin). At the two-month follow-up the kidney had normal flow and appearance by Doppler US with no evidence of RVT.

Case 2

A G4P1 female was referred for a left adrenal cystic mass identified on a 36 week antenatal US. US showed hyperechoic branching vessels in the left kidney, a calcified IVC thrombus with proximal flow restoration and a left RVT (Figure 1B). MRI confirmed that the adrenal mass was consistent with an adrenal hemorrhage. The infant was born at term and was followed conservatively without anticoagulation. At 3 months US demonstrated normal renal blood flow. The IVC had persistent mural calcification but adequate flow. The left adrenal hemorrhage showed radiologic improvement.

Discussion

RVT is a rare and challenging diagnosis in the antenatal period. We present two cases of RVT with dissimilar presentations and imaging findings. The reported incidence is 2.2/100,000 births. Risk factors for RVT include dehydration, fetal distress, maternal diabetes, umbilical catheters and prothrombotic status. Antenatal US findings include an enlarged kidney, loss of cortico-medullary differentiation and branching hyperechoic vessels. Often, an IVC thrombus is seen with decreased or no flow in the affected renal vein.

Neonatal signs of RVT include gross hematuria, large palpable kidney(s) and thrombocytopenia. The diagnosis should be suspected based on US findings and if necessary further investigated with MRI or venography. In general a conservative approach with or without anticoagulation is preferred to a surgical intervention. Complications of RVT include atrophy (70%), hypertension (20%), acute and chronic renal failure (8%), hydrops, and fetal demise.

References

Bladder Neck Abnormality in a Patient with an Imperforate Anus
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Introduction
Genitourinary abnormalities are common in patients with an imperforate anus, but they generally take the form of ambiguous genitilia, vesicoureteral reflux, or renal agenesis. We present a case of a male with an imperforate anus and a bladder neck anomaly.

Presentation
This is a male who was diagnosed at birth with an imperforate anus. He was seen for definitive management at 16 months of age. Prior to surgery he had VCUG which showed right Grade 3 reflux, left Grade 5 reflux and a posteriorly oriented insertion of the urethra with a wide open bladder neck. His pelvic and intraoperative MRI confirmed this finding with a posteriorly shifted, elevated urethra (Figure 1).

He then underwent an MRI assisted ano-rectoplasty and bilateral cross-trigonal ureteral reimplantation. On cystoscopy he was noted to have an enteric fistula just proximal to the veru-montanum, a wide, incompetent appearing bladder neck and a distally displaced trigone with the ureters inferiorly positioned. The remainder of his intra-operative and post-operative course was unremarkable and he has done well since with a negative post-operative VCUG.

Discussion
Genitourinary abnormalities are a common finding in patients with an imperforate anus. Previous studies have found approximately 50% of patients with an imperforate anus having other abnormalities with up to 80% of these occurring in the genitourinary system. The most common are renal agenesis, hypospadias, reflux and neurogenic bladder. Structural abnormalities of the bladder neck have not generally been noted in cases of imperforate anus. The developmental reason for this finding in this patient is unclear. One possibility is that the imperforate anus is caused by a field defect. The concept of a field defect has been suggested to explain multiple anomalies in syndromes such as the omphalocele, exstrophy, imperforate anus, spinal defects (OEIS) complex in which a defect in the homeobox family of genes is thought to lead to the variety of abnormalities. This idea is supported by recent studies which have found several signaling molecules that appear to be associated with both hypospadias and imperforate anus, including the Eph/ephrin group. Mice that are homozygous for the mutant form of the gene show a 100% rate of high imperforate anus and urethral anomalies or cloacal abnormalities. The abnormality seen in this patient may similarly result from a common pathway or signaling molecule gone awry.

References
Spinal Anomalies in Hypospadias Patients
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Introduction
Hypospadias is said rarely to have associated anomalies except undescended testis (UDT), inguinal hernia and utricle unless it is a part of some syndrome. We describe our experience with the association of hypospadias and spinal anomalies.

Case 1
A 29 y.o. male had undergone hypospadias repair 5 times. He presented with inguinal pain. His pain was located in the left scrotum and inguinal area. There was stenosis and hair growth in the constructed urethra, an enlarged utricle, and bladder wall irregularity. Because the stenosis was thought to be the cause of his symptoms, staged hypospadias repair with buccal mucosa graft (Bracka) was undertaken in the supine position. Despite the successful repair, the pain continued and also began to have pyuria, constipation and numbness in the legs. A neurogenic abnormality was suspected and MRI was performed. A terminal filum lipoma was detected. Excision of lipoma yielded palliation of symptoms.

Case 2
A 29 y.o. male had undergone hypospadias repair 5 times. He complained of terminal dribbling. There were diverticulum, stenosis and hair growth in the constructed urethra. A Bracka repair was undertaken in the supine position. After the first stage operation, he complained of a sensation of residual urine and post-voiding pain, which eventually resolved. However, he also complained of severe perineal pain and pins-and-needles sensation in the glans soon after the second stage. He also had pyuria, constipation, and numbness in his toes. MRI revealed terminal filum lipoma (Figure 1). Excision of lipoma yielded almost complete disappearance of his symptoms.

Discussion
To our knowledge, there is no report to date of a patient with isolated hypospadias and a spinal anomaly. From October 2005 to March 2009, we treated 194 hypospadias patients. Those who had open spina bifida, imperforate anus, multiple anomalies or sex chromosome DSD were not included in this series. Of those, 60 patients underwent MRI because of abnormal cutaneous findings in lower back or suspicion of voiding and/or bowel dysfunction. Fifteen out of 60 had a spinal anomaly. This is close to the incidence of associated undescended testis (7-9%).

Conclusion
We believe screening for the spinal anomalies should be considered in the infant with hypospadias.

Reference