New Generation of Urologists – Combining MIS with Oncology Principles

3 A testis-sparing approach for a tumor in a pediatric patient

6 The importance of tailoring care for vesicoureteral reflux

7 A new model of discovery for breakthrough research
Delivering the Model of Care and Discovery

Welcome to the second issue of *UH Innovations in Urology*. Here we will introduce you to our advancements in urological cancer care, our growing pediatric specialty care, and our high-throughput research production system. These are several prime examples of the University Hospitals Urology Institute's commitment to improving care and discovery for urological diseases.

In our cover story, we highlight the new expertise and expanded services of our Urologic Oncology Center. Our fellowship-trained urologic oncology surgeons provide expert treatment as well as advancements in the field, particularly with prostate cancer.

In the early 1990s, the field of urology welcomed the addition of prostate specific antigen (PSA) as a biomarker for prostate cancer. Based on the recent results of two large randomized, controlled trials conducted over the past 10 years, we now know that early aggressive treatment of this slow-growing cancer may not always be in the best interest of the patient. It may do more harm than good by disrupting a patient’s quality of life by resulting in urinary incontinence and erectile dysfunction. Through our research at the UH Urology Institute, we are committed to developing more specific prostate cancer assays and providing evidence-based lesser invasive treatment for patients who require more than active surveillance.

You’ll also read in this issue about vital work being carried out by our Pediatric Urology Center. The Center is represented by esteemed, fellowship-trained surgeons who maintain the highest quality of care of their young patients. Through new recruitment, we are in the midst of establishing an active research component in pediatric urology.

Lastly, you’ll learn about our highly successful research production system that sets us apart as a leading center for translational research in urology. We are proud of our ability to bring together great minds to provide solutions that can benefit our patients in the near future.

Please do not hesitate to contact me with your comments, questions and suggestions.

Warm Regards,

Firouz Daneshgari, MD
Director, UH Urology Institute
University Hospitals
Lester Persky Professor and Chair
Department of Urology
Case Western Reserve University School of Medicine
Surgery for a Testis Tumor in a Pediatric Patient

A nonmalignant teratoma is ideally suited to a testis-sparing approach

A 16-month-old boy presented to Jonathan Ross, MD, Director, Pediatric Urology, University Hospitals Urology Institute, and Division Chief, UH Rainbow Babies & Children's Hospital, with a slowly growing right testicular mass that had been discovered by his concerned parents. Dr. Ross was able to reassure them, based on the pre-operative studies, that the tumor was most likely benign and treatment would not require removal of the entire testis.

EVALUATION AND TREATMENT

On exam, Dr. Ross, who also is Professor of Surgery at Case Western Reserve University School of Medicine, observed that the right testis was enlarged and very firm. Blood tests determined that the alpha-fetoprotein (AFP) level was 3 ng/dl and within the normal range, defined as less than 15 ng/dl. An ultrasound revealed a large, cystic mass nearly replacing the right testis (Figure 1).

During an inguinal exploration, Dr. Ross made an excisional biopsy of the mass by enucleation (Figure 2). The frozen section indicated a teratoma. The testis was closed and replaced in the scrotum. The final pathology confirmed a mature teratoma, a benign tumor in prepubertal patients. It is expected that the patient’s testicle will grow well and the family was reassured about the lack of any cancer risk for their son.

BACKGROUND

The incidence of pediatric testicular tumors is very low – 0.5 to 2.0 per 100,000 individuals. Testicular tumors occurring in prepubertal children are most commonly found during the first three years of life and are usually described as pure yolk sac or teratoma in histology. Unlike with adults, in which a vast majority of tumors are malignant, only a quarter of prepubertal testis tumors are estimated to be malignant. More specifically, yolk sac tumors, which may be indicated by elevated AFP, are typically malignant and not candidates for testis-sparing treatment. Teratomas in the pediatric population are rarely malignant and ideally suited to the testis-sparing approach.

NOTES

Except in the minority of cases when the pre-operative or frozen-section evaluation suggests a malignancy, the operation should begin with an excisional biopsy of the testis tumor through an inguinal approach with salvage of the testis. Follow-up studies, though limited in number, suggest that testicles “spared” in this fashion grow normally with no tumor recurrence.

Further Reading


Referring Your Patients

For referrals to the Pediatric Urology Center at University Hospitals Urology Institute, please call 1-866-UH-4-CARE, or to contact Jonathan Ross, MD, directly, call 216-844-8440.
Adding to Our Research and Clinical Expertise

The Urologic Oncology Center boasts the next generation of pioneers in combining MIS and oncology

The Urologic Oncology Center at University Hospitals Urology Institute has been expanding its service and adding new expertise to advance the field of urologic oncology. At its core, the Center hosts fellowship-trained expert surgeons who are dedicated to delivering cutting-edge treatment of kidney, bladder, prostate and related cancers. These physicians ensure comprehensive care to their patients, not just surgical expertise, and are working hard to expand services and improve clinical outcomes and options.

RESEARCH FRONTIERS

Two noteworthy clinical research endeavors at the Urologic Oncology Center address current gaps in prostate cancer treatment. The first study involves focal ablation therapy in men who qualify for active surveillance (AS) for prostate cancer but who have low comorbidities and a substantial life expectancy, and who are not satisfied with passively waiting. Few options are currently available for these patients other than traditional prostate therapy, which entails radical surgery or ablation of a large proportion of the prostate.

Image-guided focal ablation therapy would be an important addition to the prostate cancer armamentarium, because it would allow urologists to target earlier stage cancer, when only a small area of the prostate gland is involved. For focal ablation to work, the cancer would need to be visualized, and the ablation technique employed would need to allow a small area to be precisely destroyed. Ablation techniques currently used in standard treatment for prostate cancer – cryoablation, high-frequency ultrasound and radiation – produce a much broader zone of destruction and would not be ideal for focal ablation. For patients, focal therapy would potentially offer significant reduction in side effects, such as urinary incontinence and erectile dysfunction.

Robert Abouassaly, MD, MSc, Urologic Oncology Center, UH Urology Institute, and Assistant Professor, Case Western Reserve University School of Medicine, is collaborating with Dean Nakamoto, MD, Division Chief, Abdominal Imaging, and Assistant Professor, Department of Radiology, Case Western Reserve University School of Medicine; Jeff Duerk, PhD, Robert Abouassaly, MD, MSc, Urologic Oncology Center, UH Urology Institute, and Assistant Professor, Case Western Reserve University School of Medicine.

Another research program at the Urologic Oncology Center focuses on patients who have failed radiation therapy for prostate cancer. For these individuals, traditional open surgery is made difficult by the effects of radiation, extensive fibrosis and scarring. The alternative under investigation by Rabii Madi, MD, Urologic Oncology Center, and Director, Robotic Surgery, UH Urology Institute, and Co-Director, Robotic Surgery, University Hospitals, and Associate Professor, Case Western Reserve University School of Medicine, involves prostate salvage, or reoperative robotic prostatectomy. According to Dr. Madi, there is a strong interest in using robotics because “it offers accurate dissection and more meticulous handling of tissues.”

Prostate cancer target for laser ablation as visualized by MRI

Allen H. and Constance T. Ford Professor and Chair, Department of Biomedical Engineering, Professor of Radiology, and Director of the Case Center for Imaging Research; and Vikas Gulani, MD, PhD, UH Diagnostic Radiology and Assistant Professor in the Department of Radiology, to develop focal ablation for prostate cancer by combining intraoperative, live MRI that allows visualization of a small area of cancer and highly precise laser ablation (see Figure). “There are only a handful of other centers around the world that have looked at using the newest technology in MRI to visualize the prostate cancer and then try to kill those cancer foci, without injuring other structures in the area,” explains Dr. Abouassaly.

Prostate cancer target for laser ablation as visualized by MRI
EXPERTISE AND EXPANSION

Before joining the UH Urology Institute in spring 2009, Dr. Madi pioneered using robotics to perform simultaneous removal of two different cancerous organs (kidney and prostate) in two different cases. The robot-assisted radical nephrectomy/partial nephrectomy concurrent with radical prostatectomy was achieved through single ports for each aspect (with one additional port required in one case). Because both kidney and prostate were removed through the same incision/port, fewer incisions overall were needed, which translated into both patients requiring three or fewer days to discharge. These results were published in 2010 in the Journal of Endourology.

Dr. Madi’s goal is to develop the use of robotics surgery in all urologic oncologic procedures. By using robotics, a urologic surgeon is able to combine the minimally invasive advantages, like those seen with laparoscopic surgery, with the freedom and precision obtained using open surgery techniques.

As other evidence of innovative medical expertise, Dr. Abouassaly is utilizing his experience in evaluating patient population data to help determine which treatment practices in urological cancers provide the best patient outcomes. He is currently applying his background in clinical epidemiology to analyze outcomes data from the Surveillance, Epidemiology and End Results (SEER) program and data from Medicare to discover best practices for urologic oncologic procedures. Through these databases, Dr. Abouassaly hopes to evaluate markers of surgical quality relative to patient data on a population level to improve quality of care relevant to clinical practice.

Dr. Abouassaly recently published similar work based on Canadian cancer registry data to demonstrate undertreatment in upper tract urothelial carcinoma and the effect of laparoscopy on nephron-sparing surgery for the treatment of kidney cancer. (Abouassaly R, et al. Urology, published online June 18, 2010; Abouassaly R, et al. J Urol. 2010;183:467-72. Epub 2009 Dec 14.) By evaluating outcomes data at the population level, one can determine whether guideline recommendations are being followed or determine what guidelines can be established for future clinical practice, even for rare conditions.
High Fever and Infected Urine in Young Pediatric Patients

Tailoring care to avoid undertreatment and overtreatment is a key in treating vesicoureteral reflux (VUR)

Pediatric patients presenting with high-grade fever and infected urine may be at risk for renal damage. Approximately one-third to one-half of children under the age of 2 years who have urinary tract infection (UTI) also have vesicoureteral reflux (VUR).

Although by itself VUR has not been shown to cause morbidity, it is correlated with the ascension of a UTI from the lower urinary tract to the upper urinary tract. A UTI confined to the lower urinary tract may be associated with cystitis and discomfort, but it is not believed to be linked to long-term morbidity. A UTI that reaches the upper urinary tract may cause renal scarring and damage resulting in reduced kidney function and hypertension. The concurrence of a high-grade fever and UTI, with no other explanation for the fever, generally indicates renal involvement and prompts a quick response to reduce further kidney damage.

TREATMENT OPTIONS

In pediatric patients with acute febrile UTI, appropriate antibiotics need to begin immediately and may need to be followed by prophylactic antibiotics. Secondarily, an assessment of potential reflux or urinary tract abnormalities that may be underlying the UTI should be conducted using imaging studies with ultrasonography, voiding cystourethrogram (VCUG) and Tc-99m dimercaptosuccinic acid (DMSA) renal scan. The step-wise method for employing the different imaging studies varies. In some cases a bottom-up approach is used, which involves using ultrasound and VCUG studies to evaluate presence and degree of VUR, followed by a DMSA renal scan to analyze kidney function if VUR is found. Once VUR has been diagnosed, continuous low-dose antibiotic suppression is the mainstay of therapy.

"At present, the evaluation of children for UTI and underlying abnormalities is highly individualized," explains Lynn Woo, MD, Pediatric Urologist, University Hospitals Urology Institute and UH Rainbow Babies & Children's Hospital, and Assistant Professor of Surgery, Case Western Reserve University School of Medicine.

"Although empirical treatment for UTI may begin in the primary care setting based on dipstick urinalysis for proteinuria and bacteriuria, we are able to partner with primary care physicians to evaluate acute treatment based on urine culture and sensitivities and efficiently assess underlying conditions." Partnering between primary care physicians and urologists at UH Urology Institute is important because children with VUR require monitoring for febrile UTIs for several years while many of them are growing out of the condition.

DEFINING FOR SUCCESS

Several recent clinical studies have focused on how to determine which children benefit from treatment of their reflux and which children would do well without any further interventions. This is important in order to avoid over- or undertreatment. Updated guidelines published by the American Urological Association provide guidance on the use of available interventions based on disease and patient characteristics. These guidelines also help to define treatment methodologies and concepts that have shown demonstrated success. Common issues addressed include screening of siblings for VUR and rationale for step-up or step-down approaches to evaluate and treat patients.

Lynn Woo, MD,
Pediatric Urologist,
University Hospitals Urology Institute and UH Rainbow Babies & Children's Hospital

Voiding cystourethrogram (VCUG) demonstrating grade 5 vesicoureteral reflux on the right and grade 4 on the left

Grading of vesicoureteral reflux according to the international classification system as defined by the International Reflux Committee (Image adapted from International Reflux Committee: Medical vs. surgical treatment of primary vesicoureteral reflux. Pediatrics. 1981;67:392.)
The University Hospitals Urology Institute has a vision – to develop a “new model of discovery” in which clinical questions and the innovative ideas of clinicians are connected to the expertise of full-time researchers. The overarching goal is to move this connection into a productive collaboration and ultimate generation of research projects, pilot studies and innovative tools that result in answers and solutions to the original clinical problems. This model is based on the vision and track record of Firouz Daneshgari, MD, a successful surgeon-scientist and Executive Director of the Institute.

For clinicians, the pressing demands of daily practice, including the immediate needs of patients, take precedence. Ideas and questions that would undoubtedly be the topics of informative study often remain as such, and may never lead to research that is funded and provides applicable results.

To help bridge this divide between visionary thought and tangible investigation, in January 2010 the University Hospitals Urology Institute established a system for grant development that has become a model of success in moving concepts to executed research. The grants program enables the problems observed in the clinic to be discussed with translational scientists to build collaborations. “We have set up a real structure to make sure that these ideas get translated onto paper and actually are submitted,” says Kerry O. Grimberg, PhD, Director of Publications, Center for Research & Innovation, Urology Institute, University Hospitals Case Medical Center.

Successful Submission
Recently, the University Hospitals Urology Institute was awarded a planning grant to establish the Case Interdisciplinary Research Center for Urological Complications of Obesity and Diabetes. The principal investigator, Firouz Daneshgari, MD, Executive Director, UH Urology Institute, University Hospitals, and Lester Persky Professor and Chair, Department of Urology, Case Western Reserve University School of Medicine, and other members of the Institute will team with researchers from the Case Western Reserve University Center for Proteomics and Bioinformatics and the Center for Diabetes Research, and from the departments of Pathology and of Biochemistry. Specifically, this translational research grant will likely provide the necessary foundational knowledge needed to support future clinical studies at the Institute in patients with type 2 diabetes mellitus, and ultimately to improve the clinical outcomes for patients with urological complications of obesity and diabetes.

The Institute established a system for sustainable breakthrough discoveries in urology

From Idea to Paper and Bench to Bedside
Establishing a system for sustainable breakthrough discoveries in urology

Kerry O. Grimberg, PhD, Director of Publications, Center for Research & Innovation, Urology Institute, University Hospitals Case Medical Center
Introducing UH Seidman Cancer Center

On Nov. 29, University Hospitals announced that the new, $260 million, freestanding Cancer Hospital that is due to open in spring 2011 will be named the UH Jane and Lee Seidman Cancer Center in recognition of their unprecedented $42 million donation to University Hospitals. The UH Ireland Cancer Center is now the UH Seidman Cancer Center and is one of only 12 cancer hospitals in the nation and the most comprehensive, state-of-the-art cancer facility in Northeast Ohio.

UH Seidman Cancer Center builds on the legacy established by the late R. Livingston Ireland Jr., a UH Case Medical Center board member who lobbied vigorously for significant state funding to further UH's cancer program in the early 1980s. In recognition of Mr. Ireland's successful efforts the cancer center was named in his honor. A lasting tribute will be displayed prominently in the UH Seidman Cancer Center.

The 120-bed facility will have an emphasis on translational research and cutting-edge diagnostic technology and treatments, and also will include the health system’s integrated network of nine outpatient cancer programs. It will house on-site imaging services (including intraoperative MRI), a PET/MRI machine (one of only four in the world and the only one in a cancer hospital), operating rooms designed specifically for oncology surgery, advanced radiation treatment services, outpatient services, and the Goodman Discovery Center, dedicated to managing biospecimens for clinical trials.

At the new UH Seidman Cancer Center, all the multidisciplinary teams of specialists that make up the Center will be physically brought together. As one of the teams at the UH Seidman Cancer Center, the urologic oncology team will benefit from the close interaction with other specialists and from the dedicated research and clinical facilities. To learn more about the UH Seidman Cancer Center, visit UHSeidman.org.

Your Feedback Is Important

As a medical professional, your input is invaluable in helping us shape future issues of UH Innovations in Urology. We want to know what’s important to you. Do you want to read about cutting-edge research, learn about the latest technology, or hear firsthand case studies of how others in your specialty are improving and saving lives? Tell us what you want to read about and your name will be entered to win one of two Apple iPads! Simply visit UHhospitals.org/innovations.