A Comprehensive Look at TSC-Associated Renal Angiomyolipomas: Diagnosis, Complications, and Treatment Options

Tuberous sclerosis complex (TSC) is a genetic (autosomal dominant) condition that manifests as hamartomas, or benign tumors, in various organs over a patient’s lifetime. These hamartomas can develop in the brain, kidneys, heart, skin, lungs, eyes, and gums, causing serious complications in multiple systems.¹ ² The disorder’s clinical manifestations vary extensively from patient to patient and over the course of a lifetime, but neurologic complications, such as epilepsy, and dermatologic conditions are the most common presenting features that lead to initial consultation.¹ ² There are approximately 50,000 people affected by TSC in United States.³

Beginning in childhood, patients with TSC are at risk for renal complications such as angiomyolipomas, cysts, or renal cell carcinoma.⁴

4 of 5 patients with TSC will develop angiomyolipomas during their lifetime, most often in the kidneys.⁵

Although the majority of adults with TSC have renal angiomyolipomas, they also can appear in children. Indeed, 16% of children aged <2 years have renal angiomyolipomas.⁶

An article that appeared in the September 24, 2016, issue of The Journal of Urology provides the most up-to-date statistics on the incidence of renal angiomyolipomas due to TSC per age group. In this study, a retrospective chart review was conducted of patients with TSC in the United States from 2004 to 2014. Criteria for study inclusion were a clinical or genetic diagnosis of TSC and at least one renal imaging study on file (N=145).⁷

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The complications of renal angiomyolipomas

Renal angiomyolipomas secondary to TSC are known to cause potentially life-threatening complications, including retroperitoneal hemorrhage, renal insufficiency, and renal failure. Additionally, renal angiomyolipoma cells have been shown to infiltrate normal renal tissue, leading to a need for dialysis or, potentially, partial or complete removal of the kidney.

The greater medical community is becoming increasingly aware of the dangers of renal angiomyolipomas in people with TSC. A 2016 study published by John Bissler, MD, chief of Pediatric Nephrology at Le Bonheur Children’s Hospital and director of its tuberous sclerosis center of excellence, demonstrated that TSC patients with renal angiomyolipomas are at a higher risk for renal morbidity relative to the general population.

In the commercial insurance sample, in both age groups (<18 years and ≥18 years), the incidence of each measured clinical outcome was higher in the renal angiomyolipoma with TSC cohort than in the control cohort, with differences reaching statistical significance for several outcomes.

Among patients aged ≥18 years, the incidence rate of negative clinical outcomes per 100 patient years was significantly higher (P<0.05) in the group with renal angiomyolipomas associated with TSC than in the control group for hematuria (20.4 vs 0.4), chronic kidney disease (CKD; 9.6 vs 0.3), and kidney failure (1.9 vs 0).

Patients with TSC not only had higher rates of negative clinical outcomes, but also developed them more quickly. Patients aged ≥18 years with TSC developed hematuria (13.6 vs 47.5 months; P<0.05), CKD (15.1 vs 26.2 months; P<0.05), and kidney failure (20.1 vs 57.3 months; P<0.05) more quickly than controls.

The importance of surveillance

Based on the unpredictability of TSC-associated renal angiomyolipomas, it is imperative that every patient suspected of having TSC have regular renal imaging. Follow-up should be scheduled based on the results of previous imaging tests and as clinically indicated.

Monitoring Recommendations of the 2012 International Tuberous Sclerosis Complex Consensus Conference on Tuberous Sclerosis Complex Surveillance and Management

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Facts about renal angiomyolipomas due to TSC

11 years
Median age at which the first renal angiomyolipoma appeared

18 years
Median age at time of surgical intervention

5.0 cm
Median renal angiomyolipoma size at surgical intervention

*Data are from 8 patients who underwent a combined 13 surgical interventions.

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In the past several years, there has been a shift in approaches to treating TSC-associated renal angiomyolipomas. For decades, surgical resection was the standard of care for these growing renal lesions. However, in some cases, surgery or invasive interventional therapies may not be the most optimal treatments for patients with tumors that are non-emergent. The 2012 International TSC Guidelines discuss medication that is available for these patients.

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References:

Flank Pain in an 18-Year-Old Male: A Case Report*

An 18-year-old with a childhood diagnosis of tuberous sclerosis complex (TSC) visited his primary care physician with mild flank pain and light discoloration on his face. The physician was not made aware of the patient’s TSC diagnosis or his previous complications, monitoring, and treatment (asymptomatic subependymal giant cell astrocytoma diagnosed at age 9 years, annual brain MRIs). The physician felt a palpable mass on the left kidney. Blood pressure was 139/86 mm Hg.

The patient was referred to a local urologist who prescribed an abdominal ultrasound and contrast-enhanced computed tomography (CT). A highly echogenic lesion in the left kidney was identified on the ultrasound but no significant intratumoral fat density was exhibited on the CT. Unaware of the TSC diagnosis, the urologist prescribed a nonsteroidal anti-inflammatory drug to control pain as needed.

The patient continued to have flank pain and a palpable mass, leading to a follow-up abdominal MRI. Results showed a large fat-poor tumor (14.6 cm in diameter) in the left kidney and multiple tumors (4 cm and smaller) in the right kidney. Meanwhile, the patient had an annual visit with his pediatric neurologist, to whom he mentioned his flank pain. The neurologist contacted the urologist and discussed the patient’s TSC diagnosis. Based on concern of potential hemorrhaging, tumor embolization was performed in the left kidney. Six months later, the patient is now seen regularly by the urologist and has a treatment plan in place to help manage growth of the remaining tumors. The neurologist has shared the patient’s childhood medical records to ensure the urologist has all relevant information regarding the TSC diagnosis and its manifestations.

Discussion:

- How would a pediatric-to-adult transition plan have helped this patient?
- How could doctors have helped the patient be more engaged in his medical care?
- Could the pediatric neurologist have intervened earlier regarding the renal complications?

*Not an actual patient; for illustrative purposes only.
Transitioning Patients From Pediatric Neurologic Care to Adult Care

Neurologists have a significant role in successfully transitioning youth with tuberous sclerosis complex (TSC) and related neurologic conditions into the adult health care system. Appropriate planning of a child’s transition may help to:

» Prevent gaps in care and avoid preventable health crises
» Avoid duplicative tests and services
» Ensure appropriate surveillance and symptom management to prevent costly medical complications

According to recommendations of the 2012 International Tuberous Sclerosis Complex Consensus Conference on Tuberous Sclerosis Complex Surveillance and Management, regular surveillance of all organs known to be affected by the condition is necessary throughout the lifetime of a patient with TSC.1 Additionally, the Neuropsychiatry Panel of the conference recommended that comprehensive formal assessments for TSC-associated neuropsychiatric disorders should be performed at key developmental time points.2 According to the authors of the guidelines, “Appropriate management is...crucial for optimal quality of life of affected individuals...especially during the critical transition from pediatric to adult health care.”3

CNF transition guidelines

This past July, the Child Neurology Foundation (CNF) released a set of guidelines on transitioning pediatric patients. These guidelines have been endorsed by the Child Neurology Society, the American Academy of Neurology, the American Epilepsy Society, and the American Academy of Pediatrics.4

The CNF’s Neurology Transition Consensus Panel worked for 2 years to develop the guidelines. The interdisciplinary team included child neurologists and neurology nurses, adult neurologists, rehabilitation specialists, and neurology patients and family members. These guidelines outline 8 common principles for promoting the successful transition from pediatric to adult health care for the neurology patient.

The 8 common principles for transition to adult care

Responsibilities of the child neurology team include the following:2

1. Discuss with the youth (before age 13 years) and caregivers the expectation of the future transition to the adult system
2. Assess the youth’s self-management skills beginning by age 12 and annually thereafter
3. At age 13 and annually thereafter, engage each youth and caregiver in phased transition planning, patient education, and transfer readiness
4. Initiate discussion by age 14 with caregivers regarding expected legal competency (ie, whether there is need for legal guardianship and powers of attorney)
5. In collaboration with other providers, school personnel, etc, ensure the transition plan meets the needs of the youth
6. Develop and verify the neurologic component of the plan and update it annually
7. Along with the youth and caregivers, identify an appropriate adult care provider before the time of transfer
8. Communicate directly with the adult provider to confirm that he or she has agreed to accept the patient and that an appointment is scheduled and kept

References:

Nursing Matters

Nurses play an essential role in educating patients and their caregivers about the manifestations of tuberous sclerosis complex (TSC) and effective screening and treatment strategies. Because TSC is a lifelong condition without a cure, ongoing coordination of specialty care, testing, and therapies is a challenging responsibility that is well suited to the holistic approach of nursing practice.

The role of nurses in caring for patients with a chronic illness such as TSC provides a clinical context for developing a caring relationship with patients while working in collaborative relationships with physicians. Successful interventions focused on chronic diseases address psychosocial and lifestyle issues, as well as physical problems.

The rise in the prevalence of chronic disease is driving changes in nursing practice in the areas of patient education (with a focus on patient centricity), shared decision-making, and self-management. Nurses, physicians, and hospital/clinic management all face challenges in implementing the changes needed to support this approach.

How nurses can help

The Chronic Care Model, developed by providers at the Group Health Cooperative and advisors to the MacColl Institute for Healthcare Innovation, provides a guide for creating effective chronic care delivery systems. It outlines several essential elements that must be addressed for optimal chronic illness care, including:

1. Delivery system design. The structure of medical practice may need updating to create teams with distinct roles for the physicians, nurses, and pharmacists. For nurses handling TSC cases, this can mean accepting more responsibility for the coordination of care among specialists, such as neurologists, dermatologists, nephrologists, urologists, pulmonologists, ophthalmologists, cardiologists, geneticists, pediatricians, internal medicine specialists, psychiatrists, and psychologists.

In fact, TSC management typically has the greatest success when a collaborative approach is taken by health care teams, with specialists connecting regularly to coordinate their patients’ care.

2. Self-management support. Patients (and their families) can act as the principal caregivers if possible. Support must be provided to assist patients with acquiring skills and confidence in self-management, and to assist with acquisition of supplies and medications necessary for the daily self-care behaviors outlined in their treatment plan. Nurses can support these patients by advising them on how to advocate for themselves with health insurance and various government agencies, such as social services.

3. Decision support. Evidence-based guidelines should be integrated into everyday practices through reminders and consultation with clinical experts.

4. Community resources and policies. Connections are needed between the provider and various community resources, like health clubs, social services, and home care agencies. Because TSC affects everyone differently, having personal and specific conversations about symptoms with patients might help them begin an effective management plan more quickly. Additionally, encouraging patients to join a support group might also help them cope with the emotional elements of the condition and its manifestations.

References:

Latest News & Events

Spotlight on recent TS Alliance events

The LIDS Step Forward to Cure Tuberous Sclerosis Complex® New Jersey walkathon was held October 16, 2016, at Oak Ridge Park in Clark, New Jersey. It was a beautiful day to #Step4TSC and everyone enjoyed having their pictures taken with Turbo & Scott, a fictional boy and his dog developed by Novartis Pharmaceuticals Corporation to help children understand tuberous sclerosis complex. The walkathon was sponsored by Novartis Pharmaceuticals Corporation. (Step Forward to Cure Tuberous Sclerosis Complex® is a registered trademark of Tuberous Sclerosis Alliance Corporation.)

Sound Bites, An Evening of Food, Wine and Music at The Metropolitan in Golden Valley, was held October 20, 2016, in Minneapolis, Minnesota. Sound Bites provided an opportunity to recognize people who have significantly impacted the fight against tuberous sclerosis complex. The program included a presentation of the Courage in Leadership Award to the Ihle family and also honored Sarah Hoey. Jim O’Heir of the television sitcom Parks & Recreation emceed this incredible event!

To launch Infantile Spasms Awareness Week (ISAW), which was December 1 to 7, 2016, the Child Neurology Foundation hosted an Infantile Spasms Advocacy Forum in August with representatives from 14 different advocacy, provider, and industry partners, including the American Academy of Neurology, the American Academy of Pediatrics, the Child Neurology Society, the Association of Child Neurology Nurses, the American College of Emergency Physicians, the American Epilepsy Society, CURE, Seizure Tracker, the Danny Did Foundation, LGSF, Global Genes, TS Alliance, Lundbeck, and Mallinckrodt. All organizations signed on as official partners for ISAW 2016, as did RARE Science and Novartis.

Spotlight on recent Child Neurology Foundation events

After the August publication in Neurology of the Child Neurology Foundation (CNF) consensus statement, The neurologist’s role in supporting transition to adult health care, which identifies 8 common principles for neurologists to adapt and employ to support the medical transition of youth with neurologic conditions to the adult health care system, CNF teamed with the Child Neurology Society, the American Academy of Neurology, the American Academy of Pediatrics, the Association of Child Neurology Nurses, and others to develop a Transition Project Advisory Committee. The committee was charged with identifying and implementing strategies for dissemination of the transition consensus statement as well as implementing and assessing projects reflecting the 8 common principles for transition identified in the statement.

The Child Neurology Foundation connects partners from all areas of the child neurology community, so those navigating the journey of disease diagnosis, management, and care have the ongoing support of those dedicated to treatments and cures.

The Tuberous Sclerosis Alliance is the only national organization dedicated to finding a cure for TSC while improving the lives of those affected. It works to improve quality of life for individuals and families affected by TSC by stimulating and sponsoring research, creating, progress, support services, and resource information; and developing and implementing public and professional education programs designed to heighten awareness of TSC.

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Silver Spring, Maryland 20910
301-258-5900
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The Child Neurology Foundation
201 Chicago Avenue, #200
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TSC Support

There are several resources available to your patients who would like more information on tuberous sclerosis complex (TSC).

**Tuberous Sclerosis Alliance**

The Tuberous Sclerosis Alliance (TS Alliance) was formed in the 1970s by 4 mothers with a desire to provide fellowship, generate awareness, pursue knowledge about TSC, and provide hope to those with the condition. These goals still drive the organization today.

The alliance has a comprehensive website with information and educational materials for patients and their families about living with the disease (www.tsalliance.org). It also organizes frequent fundraising activities for TSC patients, including the LIDS Step Forward to Cure Tuberous Sclerosis Complex movement, the TS Alliance’s largest national event, organized in more than 30 communities across the United States. This walk program offers the opportunity to make an impact on the lives of those living with TSC as well as fund research into cures for other diseases like epilepsy, autism, and cancer.

The TS Alliance’s TSC Connect is an organized partnership of people whose lives have been affected by TSC. It provides the latest medical information, education, and support to anyone seeking to understand TSC and offers them words of encouragement and empowerment.

Volunteers bring to the network a wealth of knowledge, awareness, and experience. They offer support and share their experiences with others who are facing the challenges of TSC. The program connects people by geographic area, manifestations, or age of the person with TSC and lets volunteers choose the issues they have personal experience with and are willing to discuss with others. Patients can join TSC Connect by visiting www.tsalliance.org.

**The TS Alliance Educator Mentor program**

The TS Alliance also offers support to school systems that are educating a student with TSC and need support in understanding TSC or strategies to use in the classroom. The TS Alliance Educator Mentor program includes teachers, therapists, and administrators with experience in educating children with TSC. For more information, please contact Dena Hook, vice president of outreach, at dhook@tsalliance.org or 1-800-225-6872.

**Inspire.com**

Inspire.com provides an online patient support community for 750,000 patients and 3,400 TSC board “peers.” The organization partners with respected national patient advocacy groups to provide safe online health and wellness communities in which patients, families, friends, and caregivers connect with one another for support and information.

On the website, TSC patients can join groups about health topics that are important to them, make friends who share health interests, and control what they share with extensive privacy settings.

**Tuberous-sclerosis.com and the TSC Central app**

Tuberous-sclerosis.com is a website sponsored by Novartis Pharmaceuticals Corporation that provides information and resources to patients and caregivers. Patients can download the TSC Central mobile app, an easy-to-use tool to help patients and their caregivers keep track of medical appointments, symptoms, and test results while enabling them to store useful information and questions to ask their doctor.

TSC Central is an app for patients’ mobile devices that provides on-the-go access to:

- Appointment reminders
- Test results
- Symptom trackers
- Medication trackers
- Transition tools
- Contacts
- Up-to-date information about TSC
- Helpful resources for TSC
Upcoming TSC Events

TS Alliance Spring Walks and Regional Conferences

LIDS Step Forward to Cure TSC is the TS Alliance’s largest national fundraising event, organized in more than 30 communities across the country by local volunteers and families who are affected by TSC.

This successful grassroots fundraising effort not only generates vital funds for TSC research but also raises awareness about TSC and the need for increased research funding to combat this complex disorder.

Register for a walk at www.tsalliance.org

Visit www.stepforwardtocuretsc.org to confirm the exact date of a walk near you.

Comedy for a Cure® 2017

Join the TS Alliance for the 16th Annual Comedy for a Cure on April 2, 2017, at the Globe Theater, Universal Studios, California. Comedy for a Cure is a fun-filled evening benefiting the TS Alliance that will showcase the hottest comedians in Hollywood. (Comedy for a Cure is a registered trademark of Tuberous Sclerosis Alliance Corporation.)