Kidneys sometimes removed unnecessarily due to misdiagnosis of genetic disorder

January 10 2013

Thousands of individuals have had kidneys removed unnecessarily because doctors misdiagnosed their disease.

A new, international study published in *The* Lancet indicates that approximately one of every five individuals with kidney tumors common in patients with tuberous sclerosis complex (TSC), a genetic disorder, has had a kidney removed. Moreover, 40 percent had some kind of surgical procedure performed.

Proper diagnosis could have led to treatment that would have made surgery or kidney removal unnecessary, according to John Bissler, MD, a nephrologist at Cincinnati Children's Hospital Medical Center and lead author of the study.

"I can't tell you how many times I've heard from patients who say their doctors told them a kidney looks bad, is full of tumors, isn't working and has to come out," says Dr. Bissler, who co-directs the Tuberous Sclerosis Clinic at Cincinnati Children's. "But you can do studies on these patients and find out that they have normal kidney function. The kidney looks bad, but it works. Doctors are unfamiliar with tuberous sclerosis, so when they see tumors, they think it's renal cell carcinoma, perform surgeries trying to help, but before long the kidney is gone. This approach is unnecessary. Fortunately, many people come to us from around the world for a second opinion."

In TSC, it is common for tumors to grow on vital organs. As many as 80

percent of TSC patients have these tumors, called angiomyolipomas, or AMLs. The new Cincinnati Children's study shows that everolimus, marketed by Novartis under the tradename Afinitor®, successfully shrinks AMLs in patients with TS. (Watch the story of a TS patient whose life was changed by taking the drug.)

The Food and Drug Administration in April approved everolimus to treat noncancerous kidney tumors (renal angiomyolipomas) not requiring immediate surgery in patients with TSC, based on the research led by the Cincinnati Children's team. TSC affects approximately 40,000 children and adults in the United States, with 70 to 80 percent developing kidney problems. TSC can cause multiple tumors in both kidneys that compress normal tissue as they grow, leading to kidney failure and bleeding due to uncontrolled blood vessel growth. One of five who bleeds winds up in the emergency department in shock.

The Cincinnati Children's study involved 118 TSC patients at 24 treatment centers in 11 countries. Everolimus substantially reduced angiomyolipoma tumor size in 42 percent of those treated after just a few months of treatment. Tumor reduction lasted, on average, more than five months.

For years, the primary treatment for angiomyolipomas was arterial embolization, which uses a catheter to block the artery and stop blood flow to the tumor. Embolization, however, can also damage healthy tissue.

Studies in the 1990s traced the cause of TSC to defects in two genes, TSC1 and TSC2. When these genes malfunction, the cell has higher activity of mTOR, a protein known to trigger uncontrolled tumor cell and blood vessel growth. Everolimus, a medication already approved as an antirejection agent in organ transplant, emerged as a prime candidate to treat TSC.

Some TSC patients at Cincinnati Children's have been on the drug for several years, and tumor reduction has not subsided. Novartis is sponsoring a four-year follow-up study to track longer-term effects.

Cincinnati Children's has what is believed to be the largest TSC clinic in the world, treating more than 839 children and adults. Cincinnati Children's also is a major TSC research center. David Neal Franz, MD, a neurologist who cares for TS patients, was senior author of a 2010 study published in The New England Journal of Medicine demonstrating the ability of everolimus to shrink SEGAs, a kind of brain tumor common in patients with TSC.

Provided by Cincinnati Children's Hospital Medical Center