New disease-to-drug genetic matching puts snowboarder back on slopes

June 5 2013

(Medical Xpress)—A recent article in the *New England Journal of Medicine* describes genetic testing of a rare blood cancer called atypical chronic neutrophilic leukemia (CNL) that revealed a new mutation present in most patients with the disease. The mutation also serves as an Achilles heel, allowing doctors at the University of Colorado Cancer Center to prescribe a never-before-used, targeted treatment. The first patient treated describes his best snowboarding season ever.

"I'm a crazy sports fan," says the patient. "I go 30 days a season. I may be the oldest guy snowboarding on the mountain, but I'm not the slowest!"

When he lost a few pounds from what eventually proved to be undiagnosed cancer, the patient was initially pleased. "I was lighter and could snowboard better – ride better, jump better," he says. Then he took a blood test and his white blood cell count was far in excess of the normal range. His doctor couldn't find a cause and so they watched and waited. A couple months later, another blood test showed his white count was even higher.

"That's when I decided to go to the University of Colorado Hospital," he says. There he met Daniel A. Pollyea, MD, MS, CU Cancer Center investigator, assistant professor and clinical director of Leukemia Services at the University of Colorado School of Medicine, and co-author of what would become the recent study in NEJM.

"Pollyea said my illness didn't fit into any major categories," the patient says. "I could see in his face that he'd run into something abnormal, something new. He was aggressive but didn't force his own opinion. I saw him reach out to every source he could find – every other specialist he could get in contact with."

"He'd been sent from doctor to doctor being told incorrect information," Pollyea says. "By the time we saw him, his blood counts were going in a bad direction due to the progression of his leukemia."

Pollyea had worked on blood cancers since his fellowship training at Stanford University, and through his work there developed a relationship with researchers at the University of Oregon, which had an ongoing project in blood cancers that defied common classifications. Pollyea and his team took a sample from his patient and sent it to Oregon for testing, with the hopes that if they could identify a gene mutation causing this cancer, there might be a chance they could target the mutation with an existing drug.

Sure enough, sequencing showed a mutation in a gene that makes a protein called colony-stimulating factor 3 (CSF3R). Cells with this mutation have uncontrolled growth in the bone marrow, resulting in a leukemia.

Further studies revealed a drug, ruxolitinib, could effectively target cells with this mutation. Approved to treat another condition, myelofibrosis, just months before, the drug hadn't previously been considered as a treatment for this type of leukemia. But with dwindling options, Pollyea and colleagues decided ruxolitinib was worth a try.

"There were no good alternatives other than to use the ruxolitinib," Pollyea says. "Our patient became the first person with this condition who received this treatment. His white blood count came down, his other

blood counts normalized, and his symptoms virtually disappeared."

"I had my best snowboarding season ever," says the patient. "Good, late season snow here in Colorado. Actually, I'd lived elsewhere and when I first got the disease I wondered if maybe something about moving to Colorado made it happen – you know, the altitude, the lack of oxygen. But now after working with Dr. Pollyea, I realize that I didn't get sick because I live here, I got cured because I live here. Would I have had this kind of treatment anywhere else? I'm not so sure."

Both patient and doctor are clear that "cure" is an imprecise word to use in this case, but so far improvement seems durable. This experience will now serve as the basis of a planned multi-center clinical trial to use novel targeted therapies to treat similar patients with this rare, activating mutation.

"Since this patient, we've evaluated a handful of others with similar diseases, and we're continuing to work with genetic sequencing to see if the activating mutation matches up with this or other drugs," Pollyea says. "In the case of this disease, we can now diagnose with a reliable test and even better – based on the results of this study – it's a disease we can treat."

More information: www.nejm.org/doi/full/10.1056/NEJMoa1214514

Provided by University of Colorado Denver