An observant patient opens new doors for cancer screening

David Drash never thought much of the vertical white lines on his fingernails until he noticed his brother, sister and father had them too. All four family members have BAP1 tumor predisposition syndrome (TPDS), a condition caused by a germline, or inherited, mutation in the *BAP1* gene that makes them more susceptible to developing certain cancers. Wondering if there was a connection between their nail anomalies and genetics, David asked members of a BAP1 TPDS support group on Facebook to send photos of their nails. "A lot of them had the lines on their nails as well, so I brought it up at my visit to the NIH," he said.

David Drash and his wife, Dani Zhang, at Fort DeSoto Park in Pinellas County, Florida, in 2024. Photo credit: David Drash

David is enrolled in a natural history study run by Raffit Hassan, M.D., Chief of the Thoracic and GI Malignancies Branch. "Our goal is to follow these families with BAP1 TPDS long-term and look at their children or siblings to get a better sense of what their prognosis is, how we can detect cancers earlier and does that make a difference in terms of overall survival," Dr. Hassan explained.

BAP1 is a tumor suppressor gene, meaning its job is to stop tumors from forming. A mutation in this gene decreases the body's ability to suppress certain types of cancer, including mesothelioma, kidney cancer and uveal melanoma, a small tumor in the iris, which David had as a teenager.

When David was in high school, his ophthalmologist removed his eye and declared him cancer-free, but wondered why this healthy, young man had developed such a rare cancer. He suspected the cause might be BAP1 TPDS, but there was not yet a test available to confirm the diagnosis.

After his surgery, David saw his oncologists regularly for scans. However, as time went on, he visited the doctor less and less. “I was in college,” he explained. “I was just enjoying every day in the moment, and I wasn't thinking long-term.”

Almost 10 years after his initial cancer diagnosis, David had an unrelated health scare that prompted him to return to the oncologist and take the newly available *BAP1* gene test. He received a diagnosis of BAP1 TPDS in 2022. From that point on, he has been proactive about his health, encouraging his family members to also undergo genetic testing and seeking out clinical trials. This led him to Dr. Hassan’s study at the NIH.

Alexandra Lebensohn, M.S., CGC, a genetic counselor at CCR, meets with patients enrolled in the study to help them understand the results of their genetic test and how BAP1 TPDS might affect their health. She sees David regularly as part of the study and was the first person to hear about the lines on his nails.

“Immediately, I started to go back and ask all the other patients I had recently seen,” Alexandra said. “It was incredible hearing from almost all our patients, ‘Yeah, I actually do have this.’” Alexandra, Dr. Hassan, Azam Ghafoor, M.D., also from CCR, and Edward W. Cowen, M.D., M.H.Sc., a collaborator from the National Institute of Arthritis and Musculoskeletal and Skin Diseases, met shortly after to discuss a plan to investigate these nail findings.

The researchers examined the nails of 47 participants with BAP1 TPDS and found that 87% of them had some kind of nail abnormality. Eighty-three percent of the participants specifically had onychopapilloma, a benign tumor of the nail. They published these findings in *JAMA Dermatology* in May 2024.

An example of onychopapilloma from a patient enrolled in Dr. Hassan’s study. Photo credit: Lebensohn et al.

Alexandra and Dr. Hassan were thrilled by these results. Onychopapilloma is rare in the general population and looks distinctly different from other nail tumors, making it easy to spot for dermatologists and general practitioners. If a physician were to notice this nail feature during a routine exam, they could recommend a genetic evaluation to further investigate personal and family history, potentially leading to genetic testing. A positive genetic test result would then lead to proactive screening for BAP1 TPDS-related cancers.

“It's very exciting to find a benign feature that can be an early indicator for this predisposition

syndrome years before the average age at which cancers arise for someone with BAP1 TPDS," Alexandra said. "This information could make a huge difference for otherwise asymptomatic individuals. Within families with BAP1 TPDS, this physical feature may help identify carriers prior to genetic testing."

Dr. Hassan primarily works with patients who have mesothelioma, one of the cancers associated with BAP1 TPDS. He is optimistic that screening for these nail markings could improve survival rates for his patients. "If we can detect genetic predispositions early, we can detect these cancers early, and possibly at a curable stage," Dr. Hassan said. Moving forward, Dr. Hassan is continuing to run this study and collaborating with David S. Schrump, M.D., M.B.A., FACS, Chief of the Thoracic Surgery Branch, who also studies BAP1 TPDS and shares many of the same patients.

Alexandra is also grateful for the light this research shines on the vital role of genetic counselors. "It's an important part of the evaluation, not just to have a genetic test result in front of you, but to have somebody go through and explain the background and results in simple terms so that you can understand what it means," she explained.

Today, David lives a normal life, only with a few more doctors' appointments than the average person. He works as a civil engineer in Florida, loves to spend time outdoors and on the water, and is still actively participating in Dr. Hassan's study. Knowing his diagnosis of BAP1 TPDS can be stressful, but he is grateful for the tests and screenings he receives. "You have to be aware of all this stuff and manage it. But the good thing is that you might be a little more clued into your health and how to take care of yourself," he said.

David also offers advice for others who are diagnosed with similar conditions: "Try to enjoy the present without letting the uncertainty of the future weigh you down too much."

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