Clues to gigantism provided by family in Borneo Mountains

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Dr. Bin Teh and Family.

An indigenous family living in a mountainous area of Malaysian Borneo helped Van Andel Research Institute (VARI) researchers to discover information about genetic mutations associated with acromegaly, a form of gigantism that often results in enlarged hands, feet, and facial features.

The information could lead to better screening for the disease, which most often results from a benign pituitary gland tumor that can be deadly if left untreated, but which is difficult to detect until later stages when features become pronounced.

Researchers located a 31-member aboriginal family that included individuals with acromegaly living in a mountainous region of Borneo,

Malaysia when the effects of the family patriarch's growing pituitary tumor necessitated medical treatment. A medical team including VARI Distinguished Scientific Investigator Bin Tean Teh, M.D., Ph.D., and staff from the Department of Medicine at the University of Malaya Medical Centre and the Department of Medicine at the Queen Elizabeth Hospital in Malaysia subsequently traveled to the family's village several times to collect blood samples for testing.

"Researchers had recently found a mutation in the AIP gene associated with acromegaly," said Dr. Teh, "but we found that several family members who didn't have visible symptoms of acromegaly had this mutation as well. This increases the importance of screening for families with cases of acromegaly since anyone could be a carrier. On one side of the family, at least two generations carried the gene before someone showed any symptoms."

The later stages of acromegaly often produce enlarged hands and feet, protruding brows and lower jaws, thick voice and slowed speech from swelling of vocal cords, and other symptoms. When diagnosed, the tumor and entire pituitary gland are usually removed, followed by hormone therapy for the rest of the patient's life. However, because the progression of the disease is so gradual, it is difficult to detect. If left unchecked, patients can die from complications such as heart or kidney failure. Well-known acromegalics include wrestler-actor André the Giant and motivational speaker Tony Robbins.

VARI Research Scientist and lead author of the study Sok Kean Khoo, Ph.D., led researchers in scanning DNA in the family's blood to find other factors that might explain why only some family members with the genetic mutation had visible symptoms of the disease. They found regions on a few chromosomes that might lead to further insight; these findings were published this week in the journal *Endocrine-Related Cancer*.

The prevalence of acromegaly is approximately 4,676 cases per million population, and the incidence is approximately 117 new cases per million per year. However, Dr. Khoo said that the recent findings may mean that the prevalence is higher since carriers of the genetic mutation who do not have symptoms are not included.

"The sooner we know how and why people are affected differently by this disease, the sooner we can help families who have it," said Dr. Teh. "One of the women in this family was only 19 and probably thought that since her grandfather had lived so long with the disease, she would too. She chose not to go to the hospital for treatment and, sadly, died two years after our last visit."

Source: Van Andel Research Institute