

BRAIN MATTERS NEWSLETTER

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A Search for Medical Help and Hope

It's hard to imagine Deg Gharti Chhetri's anguish in the fall of 2018. Deg had journeyed around the world—Singapore, Thailand, India and the United States—with his young son, Basab Gharti Chhetri, from their home in Kathmandu, Nepal, in search of medical help for his child, who had been suffering for three years from Cushing's disease—caused by a benign tumor in his pituitary gland.

"No young child should go through this," says Deg of the many tests and treatments Basab received.

An ultimate stroke of luck came when Deg sent an email late last year to Pacific Neuroscience Institute (PNI) located at Providence Saint John's Health Center. He was intrigued by information on the website detailing PNI's expertise in the treatment of all kinds of brain and pituitary tumors, including those that cause Cushing's disease.

Deg didn't know it then, but he had finally hit upon the right combination of skill, experience and compassion that would restore his son to health.

Basab is just the kind of patient that surgeons at PNI welcome. In addition to performing a broad range of procedures on common malignant and benign brain tumors and pituitary tumors, neurosurgeon Daniel F. Kelly, MD, director of PNI, and director of the Brain Tumor Center, and Pituitary Disorders Centers, and his colleagues are comfortable with unusual and complex cases or ones that have befuddled other neurosurgeons and neurologists. In contrast to medical centers that might see a few cases each year of pituitary tumors, including those with Cushing's disease, the PNI team treats approximately 100 cases per year.

Removing the tumor through the nostrils

Cushing's disease occurs when the paired adrenal glands (which sit atop the kidneys) produce too much of the stress hormone cortisol that is involved in maintaining blood pressure and blood sugar and turning food into energy. Although the adrenal glands are producing too much cortisol, the

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origin of the disease, as in Basab's case, is a benign tumor (adenoma) of the pituitary gland, which is the master gland of the body, orchestrating all hormonal functions, situated directly below the brain in the base of the skull. The small tumor produces too much adrenocorticotrophic hormone (ACTH), which causes the adrenal glands to make too much cortisol.

Cushing's disease can be difficult to diagnose in children and adults. Basab's was diagnosed after his uncle, who is a surgeon, noticed the child's puffy face and short stature (both telltale symptoms) in 2016 and urged the family to take him to an endocrinologist. But the family's odyssey was just beginning. They visited doctors in Nepal and India before they chose a surgeon in Singapore to remove the pituitary tumor. However, the seven-hour surgery failed. "They got a lot of the tumor out, but you have to get it all out to get people into remission," Dr. Kelly explains.

Still searching, Deg and his family traveled to Pittsburgh in May 2017 for a surgical procedure to remove Basab's tumor with Gamma Knife radiosurgery. The Gamma Knife radiation also failed. One year later, an MRI scan showed the tumor was still present. Medication to lower cortisol levels also failed to help the child and his symptoms of weight gain and arrested growth persisted. That's when Deg found Dr. Kelly.

Dr. Kelly and Chester F. Griffiths, MD, director of the Eye, Ear & Skull Base Center at PNI and an ENT and facial plastic surgeon, performed a three-hour procedure to remove the tumor, inserting instruments through the nose and sphenoid sinus of the skull base up to the pituitary gland in an approach called endonasal endoscopic surgery.

Getting well and growing up

Within hours of surgery, Basab's cortisol and ACTH levels dropped

into the low (non-measurable) range, indicating that the tumor was completely removed. Since then, his levels have stayed low and he is on cortisol replacement with a medication called hydrocortisone, prescribed by Dr. Norman Lavin, a pediatric endocrinologist at Providence Tarzana Medical Center who collaborates with Dr. Kelly and Dr. Griffiths.

Basab's case is a good example of why it's important for patients with challenging conditions to seek care at an experienced center or a "center of excellence," says Dr. Kelly, who has one of the world's largest endonasal pituitary surgery experiences with more than 2,000 surgeries performed and more than 60 peer-reviewed publications relating to endonasal surgery for pituitary tumors.



Pregnancy Could Be Linked to Onset of Cushing's Symptoms

More than 25 percent of women with Cushing's disease experienced their first symptoms within one year of giving birth, a small study by the Pacific Neuroscience Institute found.

The findings suggest a possible causal relationship between the biological stress of pregnancy and Cushing's disease (CD), with more than a two-fold risk of women developing the disease within one year of pregnancy. The study, "Pregnancy-associated Cushing's disease? An exploratory retrospective study," found

eighty percent of Cushing's disease cases are women, and most are of reproductive age.

Levels of the body's main stress hormone, cortisol, normally increase during pregnancy. In the last weeks before birth, cortisol levels are two to three times higher than normal, similar to Cushing's disease. Because cortisol levels gradually increase during pregnancy, a diagnosis of Cushing's disease within the gestation period is problematic.

Circumstantial "evidence suggests a higher incidence of CD immediately following pregnancy, in the peripartum period [in the weeks and months after childbirth]," the study's authors wrote.

64 women with biochemically-diagnosed Cushing's disease and treated at Providence Saint John's Health Center in Santa Monica, CA, from July 2007 to December 2017 were studied.

Patients were divided into three groups:

- Women with pregnancy associated CD
- Women of reproductive age
- Women not of reproductive age at the time of CD onset

All patients underwent surgery to remove pituitary adenoma resulting in sustained remission rates for groups 1, 2 and 3 at 91%, 80% and 83%.

Full results of this study can be found in the [article](#) published in the journal, *Pituitary*, the official publication of the Pituitary Society and the Growth Hormone Research Society.

For more information, contact Pacific Pituitary Disorders Center by calling 310-582-7450.



Is It Safe For Patients With Brain Tumors To Fly?

Doctors address concerns about air travel safety for patients with brain tumors in this study.

The global reach of medicine is becoming increasingly easier to achieve. Thanks to the ever-increasing availability of medical information available online as well as the capabilities for long distance tele-health consultations, patients have expanded options to undergo multidisciplinary treatment for their conditions with experts worldwide.

Traveling for neurosurgical care

The field of neurosurgery and brain tumor management is no exception. Patients often will seek second or third opinions at a high-volume brain tumor center of excellence and receive definitive treatment at these facilities effectively giving increased access to those living in cities without experienced teams treating such conditions.

This is most relevant to patients in rural areas and those living in countries with limited resources. Hence, traveling for medical treatment (medical tourism) has demonstrated value for the patient opting to receive the best possible care for their condition, while showing financial savings when patients have fewer complications, shorter hospital stays and earlier return to work. This model has been adopted by large health systems and insurers with positive results for complex procedures like heart and transplant surgery.

Is it safe for brain tumor patients to travel by air?

A major question regarding the safety of airflight had, until recently, not been answered, despite the increasing volume of patients with large brain tumors traveling long distances for surgery. In particular, the air pressure changes that occur on high altitude jet airplane flights (which can be equivalent to immediately ascending to an altitude of 8,000-10,000 feet) has been a concern for increasing brain swelling (edema) which could cause major symptoms during flight.

We recently studied this at the Pacific Neuroscience Institute, which is a destination for many patients from national and international locales. In a study recently published in the *Journal of Neuro-Oncology*, "Safety of commercial airflight in patients with brain tumors: a case series," (Phillips et. al. 2018), we reported the safety data for these patients.

Overall, airflight was found to be safe for patients with brain tumors.

There was no correlation with brain tumor size or pre-operative symptoms. Of the 41 patients, ten (24.4%)

reported new or worsened symptoms during airflight, although most of these symptoms were minor and resolved after landing. Only one patient developed a major symptom (seizure), which was also transient. If patients had no symptoms prior to their flight, none of the patients developed new symptoms during or afterwards.

Safety first

This publication is the largest study to date assessing the safety of airflight for patients with brain tumors. It is however important to note that this was a relatively small study in terms of sample size and although air flight overall was shown to be safe, one patient with a relatively large benign brain tumor did have an inflight seizure.

The patient went on to have a successful surgery and is doing well now with no issues related to his seizure or surgery. This patient's experience highlights that careful consideration by both doctor and patient are essential prior to allowing a patient to fly for their care at another center.

Specifically, for larger tumors, consideration should be given to



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preflight and inflight administration of steroids to reduce brain edema and anticonvulsants to reduce seizure risk. In some patients with very large brain tumors already causing cranial pressure, air flight may be considered unsafe and not recommended.

We hope that results from our study will be the impetus for larger studies to be performed to validate this data. Certainly, this study has implications for patient mobility with the goals of improving equal access to quality brain tumor treatment at established centers of excellence.

An everyday question is answered

Since its publication, the article has not only influenced the scientific community, but has also elicited a positive response from the patient community, as many have appreciated a research study that so directly impacts their lives.

Nevertheless, if patients have brain tumors and seek to travel by plane, they should have discussions with

their neurosurgeon or neuro-oncologist to ensure individual safety. This data. Certainly, this study has implications for patient mobility with the goals of improving equal access to quality brain tumor treatment at established centers of excellence.



Professional Spotlight

Katherine Araque, MD

Director of Endocrinology,
Pituitary Disorders Center

Dr. Katherine Araque is a board-certified endocrinologist at Pacific Pituitary Disorders Center. As director of endocrinology at Pacific Neuroscience Institute,

she oversees clinical trials and the clinical care of patients with endocrine conditions.

Dr. Araque provides special expertise in clinical and research projects in the diagnosis and treatment of pituitary hormone deficiency in adults, Cushing's disease, prolactinomas, acromegaly, sellar masses and other pituitary tumors. Dr. Araque is also a member of the pituitary and endocrinology society.

Uniquely experienced in diagnosing and treating patients with pituitary and neuroendocrine conditions, Dr. Araque completed her internal medicine training at Yale New Haven Health Bridgeport Hospital in Connecticut and through a fellowship in adult endocrinology at The National Institutes of Health in Maryland.

Dr. Araque recently published a paper on [thyroid hormone harmonization](#).

For more information or an appointment, call 310-582-7663.

ENDOGENOUS CUSHING SYNDROME

AFFECTS ONLY **1 IN 500,000** ADULTS PER YEAR.

Grace Study for Endogenous Cushing Syndrome: Enrolling Now

The purpose of the Grace Study is to evaluate the effectiveness (benefits) and safety (side effects) of an investigational study medicine, relacorilant, in treating participants with endogenous Cushing syndrome, also known as hypercortisolism.

For more information email Neuro.Trials@pacificneuro.org or call Neurosciences Clinical Trial Team at 310-829-8265

Upcoming Events

Sunday, March 1, 2020

[Sean Hunter Research in Action Bowl](#)

Thursday, March 12, 2020

[Providence sponsored OWL International Women's Day Celebration 2020](#)

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