

**JAMIE VAN GOMPEL:** So pituitary tumors have a wide range of pathologies, of course. And the most common are tumors that don't secrete anything, and those have a couple of different subtypes. And then there's tumors that are active-- well, chemically active. And amongst those are growth hormone-secreting tumors and prolactin-secreting tumors. But one of the more common ones that we see and actually one of the more difficult tumors to treat are ACTH-secreting tumors.

**IRINA BANCOS:** The manifestations of an ACTH-secreting tumor can lead from any manifestations of mild hypercortisolism all the way to severe overt Cushing's syndrome. And classically, overt Cushing's syndrome presents with fatter distribution, with development of supraclavicular pads, development of dorsocervical pad, moon facies, erythema of the face, thinning of the skin, signs of easy bruising. Also metabolic abnormalities, such as hypertension, diabetes mellitus, osteoporosis, and fractures.

Pituitary Cushing's disease is usually affecting young women in their 30s or 40s. And possibly because of this, it is frequently mixed up with other problems, most commonly polycystic ovarian syndrome. That is important whereas any woman with possible manifestations of Cushing's syndrome and previous diagnosis of PCOS really look at the situation and at least consider Cushing's.

It's important to note, though, that some patients with biochemically proven Cushing's syndrome may not have severe manifestations of Cushing's, while others who do have some manifestations of possible Cushing's syndrome actually end up not having Cushing's syndrome. So it's important to take a careful history and perform a physical exam, do a complete biochemical workup before proceeding to any more invasive testing.

**JAMIE VAN GOMPEL:** There's so many tests that can be done, and there's so-- there's these narrow margins that are outstanding that-- it's always good, I think, to get a second opinion if it's a question in the patient's mind either for reassurance for you so that they don't have it-- that they don't have that question in mind going forth. But honestly for their general health and well-being long-term that someone identifies a tumor that is there, that it's taken care of.

So I think an early referral for this is a very good idea. I think once they have an identified tumor, I think it's critical to, again, to see somebody who's done a lot of pituitary surgery for this particular problem. And I think it's beyond just doing a lot of pituitary surgery-- it's for Cushing-- that's a very specialized subset, and there's only-- there's not a lot of people across the country that have a particular expertise in it.

ACTH-secreting tumors don't all cause Cushing's disease, which is an important distinction, because Cushing's disease is a syndrome complex. But it's also important in tumors that stain for ACTH that are not clinically symptomatic to understand that those tumors are more aggressive than your run-of-the-mill nonfunctioning tumors and need to be watched closer. And especially certain subtypes, especially a subtype called Crooke's cell adenoma.

So collecting those at a center that's seen a lot of those I think is very critical. People with obvious Cushing's disease may be easy to diagnose, but then meeting with somebody that's very good at understanding Cushing's disease and understand where these tumors can lie, it's very interesting that not every tumor that causes Cushing's disease is inside of the pituitary gland.

We know about the 5% to 10% of patients that have tumors that could be in the lung or elsewhere in the body, but even within the head, some of the tumors aren't even actually in the pituitary gland. Sometimes they're actually just next to it in the cavernous sinus. You can go and look in the pituitary gland and never find the tumor.

**IRINA BANCOS:** So I believe that any patient with an incidentally-discovered pituitary tumor or with suspected or confirmed Cushing's syndrome will benefit from being [INAUDIBLE] at Mayo Clinic just because of our multidisciplinary approach and high expertise in pituitary tumors and other endocrine disorders.

We can provide full care for people with Cushing's of any kind, anywhere from making diagnosis, a testing which - such as in theory the petrosal sinus sampling, which is very much dependent on expertise of interventional radiology, all the way to a curative surgery in perioperative management, which is quite challenging in this situation as well.

**JAMIE VAN GOMPEL:** When it gets down to it, the patient's primary surgery if they're to have a pituitary surgery is by far the most critical time in becoming cured, because there's no scar there, there's fresh plains, and it should be done by someone that's done a lot of Cushing's cases, because that's our best chance to cure the patient.

There's a lot of nuance into it. It's not like normal pituitary surgery, it's a lot more delicate, it's a lot more microsurgery, and it's very important that it's done correctly and well, both for preserving the patient's pituitary function, but also in getting them a cure long-term.

**IRINA BANCOS:** We have an ongoing adrenal research program which includes Cushing's syndrome. This is mainly based on development of new biomarkers, but also a few therapeutic trials in patients with persistent Cushing's syndrome despite surgery.

**JAMIE VAN GOMPEL:** There are new medications available for it. In fact, one of our endocrinologists has opened a trial recently with that. I think this field is very ripe for research treatments, and those are definitely coming out in papers and ideas, and some of those trials are available here. Or alternatively, there's a support society for Cushing's disease that oftentimes keeps up-to-date on the most recent studies out there, and to travel and find out about those studies.