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California Center for Pituitary Disorders at UCSF

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Medical Therapy for Acromegaly

By Lewis Blevins Jr, MD

Some patients will have residual acromegaly despite undergoing a successful transphenoidal surgical procedure by experienced neurosurgeons. Fortunately, there are a number of pharmacologic agents that have demonstrated efficacy in the management of patients with residual and recurrent acromegaly and in those who are not candidates for primary surgery. Some of these drugs have changed the natural history of treated acromegaly. As a result, many of the more severely distressing end-stage manifestations of the disorder are now seen only infrequently.

Dopamine Agonist Drugs

D2 dopamine receptors are expressed on a small proportion of growth-hormone-secreting pituitary tumors and are seen most commonly in those tumors that can secrete prolactin. Dopamine agonist drugs may inhibit growth hormone secretion, and thereby lower IGF-I levels, in a small proportion of patients. Bromocriptine normalizes IGF-I

levels in about 10% of patients. Cabergoline has been shown to normalize IGF-I levels in roughly one third of patients; response rates are probably higher in patients who have prolactin co-secretion. Patients with acromegaly usually require higher doses of these agents than do patients with prolactinomas. The convenience of oral administration and lower costs of these drugs when compared to other agents to treat acromegaly make them attractive choices as first-line adjuvant treatment for residual or recurrent disease.

At the California Center for Pituitary Disorders, cabergoline is the preferred dopamine agonist drug for acromegaly. We usually initially treat with cabergoline (0.5 mg twice weekly) and escalate the dose, as needed, based on IGF-I levels obtained every 4 weeks to a maximum dose of 1.5 mg 3 times weekly. Side effects of therapy include nausea, headache, fatigue, and, rarely, psychotic features.

Somatostatin Analogs

Somatostatin receptors are expressed in one half to two thirds of growth-hormone-secreting pituitary tumors. The somatostatin analogs bind to these receptors and inhibit growth hormone secretion resulting in a lowering of IGF-I levels. At this time, there are two available somatostatin analogs: lanreotide (Somatoline[®] Depot) and octreotide/IM injection (Sandostatin[®] LAR[®]).

Normalization of IGF-I levels are achieved in roughly 50 to 65% of patients treated with these agents. Clinically important regression of pituitary tumors may be seen in up to three quarters of treated patients. In one study, tumor volume decreased by a mean of 44% and the maximum vertical diameter decreased by a mean of 24%. Surgical debulking of unresectable growth-hormone-secreting pituitary tumors appears to result in improved biochemical control by somatostatin receptor antagonists.

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Spotlight on Staff



Manish K. Aghi MD, PhD is an assistant professor of neurosurgery in the California Center for Pituitary Disorders at UCSF. He joined the faculty in January 2008 after completing neurosurgery training at the Massachusetts General Hospital in Boston. Prior to that, he earned an MD and PhD in neuroscience at the Harvard Medical School.

His clinical interests include the neurosurgical management of pituitary disorders, neurosurgical endoscopy of the anterior skull base, and neurosurgical management of glioneuronal neoplasms. He is actively involved with and has published numer-

ous articles describing clinical research of pituitary tumors and glioneuronal tumors.

He is also the principal investigator of a basic science laboratory in the UCSF Brain Tumor Research Center (BTRC) at the Helen Diller Cancer Research Center on the Mission Bay campus. His laboratory studies brain tumor angiogenesis, supported by multiple grants from the National Institutes of Health and private foundations. In his spare time, Aghi might be seen jogging through the hilly streets of San Francisco or taking his three-year-old daughter to preschool.

News & Events

- Our annual CME course “Pituitary Disorders: Advances and Management” took place October 16, 2009 at the grand Hyatt Hotel in downtown San Francisco. We are pleased to announce it was a resounding success and marked the highest attendance to date. The program is designed for endocrinologists, neurosurgeons, neurologists, primary care providers, trainees in these fields, nurse practitioners, physician’s assistants, and other allied health professionals to improve their understanding of diagnosis and management of pituitary tumors and disorders of pituitary function.

We will be posting news of future programs in this newsletter and additional information can be found at <http://www.cme.ucsf.edu>.

- A lecture on acromegaly delivered by Lewis Blevins MD has been archived on the Internet. Visit <http://acromegalylive.tv> in order to view the presentation.

- Market research data indicate that the California Center for Pituitary Disorders at UCSF has become the busiest of all pituitary centers in the United States. We now record nearly 500 new patient visits annually and accomplish over 200 pituitary surgical procedures each year. But more importantly, our great success at rendering patients disease-free and in either preserving or restoring pituitary functions has been reinforced by feedback from our patients. Patient satisfaction surveys indicate that about 95% of treated patients would highly recommend our services to other patients.

We would not have achieved this level of success without the confidence and support of you, our referring physicians, and the opportunities to partner with you in the management of your patients. We appreciate your continued support of the Center.

- UCSF Medical Center recognizes that support from family and friends is a critical element in a patient’s healing process. Recently, neurosurgeon Manish Aghi MD, PhD removed a pituitary adenoma from patient Ann Aureoles, who had an unusual inner circle of support: her service dog, Henry Miller. Aureoles was disabled and visually impaired when she underwent transsphenoidal surgery, and her canine companion had been with her for over 12 years. The faculty and staff of the Department of Neurological Surgery made every effort to ensure that Aureoles’ dog would be treated as a part of her support system. He was able to accompany her to the doors of the operating room and comforted her after the procedure in her recovery room.

To find out more about this inspiring story, view the Abc7 news coverage at: <http://abclocal.go.com/kgo/story?section=news/health&id=6765409>.

Medical Therapy for Acromegaly

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In one study, normalization of IGF-I levels was seen in 42.3% of patients prior to surgery and in 88.5% of patients after surgery. These observations suggested that surgical debulking definitely improves the outcome of patients after treatment with lanreotide. In our practice, we employ somatostatin analogs when there is a significant tumor burden and when patients choose an injectable medication that is administered infrequently. We follow the dosing protocols recommended by the manufacturers of these products. Side effects of treatment with these agents include gastrointestinal discomfort, cholelithiasis, hyperglycemia, hypoglycemia, and bradycardia. Most side effects improve with continued administration of the drug.

Growth Hormone Receptor Antagonists

Pegvisomant is a growth hormone receptor antagonist that is

often used to treat patients with acromegaly refractory to surgery and radiotherapy. IGF-I levels can be normalized in as many as 95% of patients. A recent study suggests that pegvisomant does not promote tumor growth. There are several reported cases of tumor growth likely related to the natural history of progression of these tumors and also possibly related to rebound growth after discontinuation of treatment with somatostatin analogs. We usually select pegvisomant therapy when it is the patient's preference and for patients who have not been helped by treatment with somatostatin analogs and dopamine agonist drugs. Dosing schedules follow the recommendations of the manufacturer. We favor this drug when residual or recurrent acromegaly is not accompanied by a large tumor burden.

Combined treatment for acromegaly with somatostatin analogs and pegvisomant is em-

ployed in the following settings: (1) when there has been a partial response to somatostatin analog therapy, (2) when tumor progression is seen in the setting of pegvisomant therapy alone, (3) in patients who have normalized IGF-I levels on pegvisomant therapy yet have continued headaches, as low-dose, once-daily subcutaneous octreotide often will resolve the headache syndrome, and (4) when patients who have normalized IGF-I levels on therapy with somatostatin analogs have continued symptoms that might be directly related to ongoing growth-hormone hypersecretion. Side effects of pegvisomant include local skin reactions and mild transiently elevated liver enzymes in 15% of patients.



Recent Publications from the California Center for Pituitary Disorders at UCSF

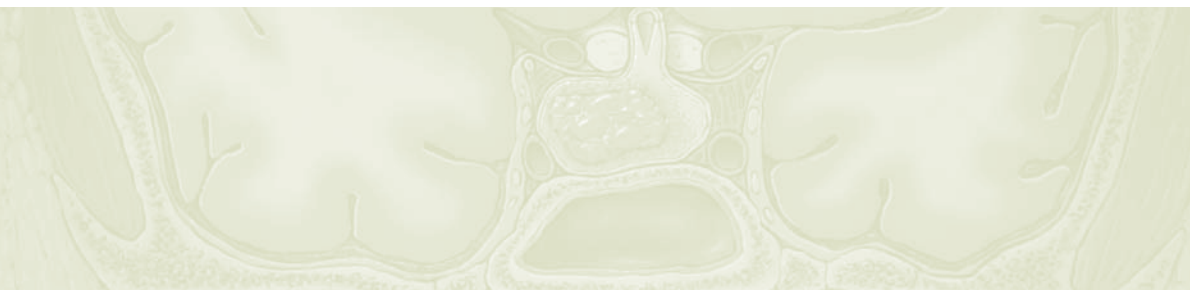
Aghi M, Kunwar S, Blevins L. Recent advances in the treatment of acromegaly. *Curr Opin Endocrinol and Diabetes Obes* 2009;16:304-307.

Summary: This article reviews the current data and recommendations pertaining to the use of stereotactic radiotherapy

and pharmacologic agents in the management of patients with acromegaly.

Blevins LS Jr, Sanai N, Kunwar S, Devin JK. An approach to the management of patients with residual Cushing's disease. *J Neurooncol* 2009;94:313-319.

Summary: This manuscript reviews our current evidence-based and practice-outcomes-driven approaches to the management of patients with residual Cushing's disease.



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Have a question about one of your patients? Write directly to Lewis Blevins Jr. MD at blevinsl@neurosurg.ucsf.edu or to Sandeep Kunwar MD at kunwars@neurosurg.ucsf.edu

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Center physicians are available for either consultation or assumption of care regarding diagnostic and management strategies for patients with pituitary tumors and other disorders of the hypothalamic-pituitary unit. We are committed to excellence in patient care and the education and involvement of referring physicians in the care of their patients referred to our center.

To schedule an appointment call 1866-559-5543 or (415) 353-2948

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