HEALTHY CONNECTIONS HOMECARE SERVICES: 4TH QUARTER 2008

PITUITARY TUMORS IN WOMEN

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quire intervention. High levels of prolactin will cause galactorrhea, which can be the presenting symptom of this condition. Here to, menstrual irregularity is common, as are infertility and loss of libido. If the excess production of prolactin is prolonged, osteoporosis becomes an issue as well. Thus, endocrinologists will typically perform bone density testing on patients with incompletely treated prolactinomas and intervene pharmacologically if density is shown to be insufficient.

PSYCHOSOCIAL ASPECTS

Patients with pituitary tumors routinely express symptoms consistent with psychological disruption and with impaired quality of life. The most profoundly affected are those with Cushing's Disease in whom excess cortisol can produce a host of psychological symptoms ranging from moderate depression to frank mania. Psychiatric disorders *per se* are not more common in patients with pituitary tumors than in the general population. Nonetheless, there is often an overwhelming sense of malaise expressed either as a direct emotional dysphoria or is somaticized into any number of physical symptoms. These include (but are not limited to) headache, tendonitis, tingling or numbness, memory loss, and impairment of cognition. Depression, anxiety, behavioral disturbance, and personality change may reflect the adjustments that pituitary tumor patients must make to deal with the physical symptoms caused by alterations in the various hormonal axis affected by the tumor. However, it is equally possible (although at this time unprovable) that the pituitary tumor may itself not be the direct cause of the emotional or cognitive changes experienced by the patient. It is entirely possible or even likely that disruption within the hypothalamus on a molecular rather than structural level may trigger the formation of the pituitary tumor and concomitantly may directly produce the psychosocial disruption the patient feels. Connections from the hypothalamus to other limbic structures (e.g. prefrontal cortex) may cause alternations in personality and mood. Intervention for this constellation of psychological disruption is feasible but may require intervention by psychiatrists in those most profoundly affected. Generally treatment begins with optimization of hormone levels but may in addition require drug therapy including antidepressants. Psychological testing can yield a detailed profile of the specific areas of impairment and suggest compensatory strategies. In particular, pituitary tumor patients complain of depression, fatigue, and poor memory function. These are real symptoms of physical disease, but the treatment for them is complex and often requires multidisciplinary input.

RADIOLOGY

The best way of diagnosing pituitary disease radiographically is by an MRI focused on the *sella*. CT scan has insufficient resolution to show small tumors and does not confer the anatomic detail found in MRI. A standard MRI of the brain is also inadequate for showing pituitary disease, as it may result in the pituitary being shown by only 1 or 2 slices that are too thick and too widely space to show a pituitary lesion properly. Therefore, if a pituitary tumor is suspected, it is wise to order an MRI of the *sella* upfront to avoid having to send the patient back for repeat scanning.

TREATMENT

Once a diagnosis has been made or is at least entertained with a strong level of suspicion, the referral to an endocrinologist and a neurosurgeon is advisable. Even a "simple" prolactinoma may have ramifications on other pituitary – end organ axis that are not immediately obvious from the gynecologic perspective. In our practice, all patients referred for pituitary tumor are seen by both the endocrinologist and the neurosurgeon to provide opinions from a medical and surgical perspective respectively. A further word of caution is mandated here. Most endocrinologists can perform an effective workup of a pituitary tumor and make appropriate diagnosis and, where appropriate, medical treatment recommendations from that workup. However, within the neurosurgical community, a wide spectrum of expertise in pituitary disorders exists. Patients with resources tend to consult a relatively small cadre of nationally prominent subspecialists in this area while many neurosurgeons with the theoretical ability to do pituitary surgery actually see only 1 or 2 patients per year, an insufficient number to develop true facility with such procedures. Statistics have been compiled that show true expertise (as judge by success in achieving cure and in avoiding complications) comes only when a surgeon has completed 500 or more trans-sphenoidal surgeries. Thus, for optimal care, referral to a known center of excellence is advisable. The referral practice at The University of Texas MD Anderson Cancer Center is the largest within the state of Texas or any neighboring state.

Medical therapy generally consists of replacing hormones when levels are low or in suppressing them when they are high. Prolactinomas are generally treated with medical therapy as the first line approach due to the fairly good success achievable with Dopamine agonists such as bromocriptine (Parlodel®) or cabergoline (Dostinex®). These drugs will not be effective in patients with pituitary tumor types other than prolactinoma, but in the prolactinoma category they do have excellent success in lowering prolactin levels and reasonable (but lesser) success in causing tumor shrinkage. Patients with prolactinomas come to surgery for several reasons. In some, the drug(s) is ineffective or produces debilitating side effects, typically gastrointestinal in nature. In others, drug therapy has been successful but not completely so, and debulking the tumor is felt to be helpful in allowing medical therapy a better chance to work on a smaller volume of disease. Finally, a number of patients present for surgery because of what one might term "medication fatigue," namely a desire to free themselves of the necessity for taking what may amount to a lifelong medication requirement. For patients with Cushing's disease or acromegaly, the first line treatment is almost always surgical; and for patients with non-functional tumors causing hypopituitarism or large enough to endanger vision by compressing the optic chiasm, surgery is also the first line choice. Radiation therapy is used mainly as a backup for tumors that have been treated by other means and yet have recurred, or that small group of invasive, hormonally functional tumors that surgery cannot cure and which have proven refractory to medical therapy.

Trans-sphenoidal surgery is the most common method of removing a pituitary tumor today. Over 95% of pituitary tumors will prove amendable to that app[illegible] variations (endonasal versus sublabial, endoscop[illegible] etc.). The trans-sphenoidal approach is popular because it provides a relatively direct route of access that travels along the septum of the nose, through the sphenoid sinus, to the *sella* just behind it. When properly performed, this method avoids the brain altogether and is a very safe procedure. Craniotomy is only necessary for tumors that show special features such as persistent recurrence in the suprasellar space, lateral extension in the cavernous sinus or around the supraclinoid carotid artery, or for tumors too large to be dealt with by trans-sphenoidal surgery. Because the brain must be retracted somewhat to expose the *sella* during a craniotomy for pituitary tumor, the trans-sphenoidal approach tends to be safer.

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SUMMARY/IMPORTANT POINTS

- Prolactin levels allow the important distinction to be made between a true prolactin-producing adenoma and a non-functional adenoma with stalk effect with relative security in most patients.
- Patients with prolactin-secreting pituitary tumors (prolactinomas) should be treated first-line with Dopamine agonist therapy, while non-functional or other tumors should not be.
- Surgery may still be necessary for a prolactinoma and is almost always needed as first-line treatment in patients with other functional pituitary tumor types.
- Because the hormonal systems of the pituitary are complex, a wide variety of clinical syndromes can be caused by pituitary tumor. However, because the majority of pituitary tumors are either prolactinomas are nonfunctional tumors, the symptoms of those two types (menstrual disruption, infertility, galactorrhea, headache, and/or visual disturbance) should raise the issue of pituitary tumor in patients who complain of one or more elements of that constellation.
- The cognitive and psychosocial disruption exhibitive by patients with pituitary tumors is real and should be viewed as a manifestation of physical disease that can be amenable to appropriately directed therapies.

Although women with pituitary tumors may be diagnosed by their obstetrician/gynecologist, ultimate treatment of such tumors should be carried out under the joint care of an endocrinologist and neurosurgeon.

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PHYSICIAN/PATIENT RESOURCES

Many thanks to Dr McCutcheon for this newsletter article. Having recently had transphenoidal removal of a pituitary tumor, I know what an excellent resource he is to patients in the Texas Medical Center. Pituitary tumor patients' care is multi-disciplinary, as mentioned in this newsletter. The Pituitary Network Association has been a wonderful resource for me and thousands of others. This website, www.pituitary.org provides the most current medical information on pituitary disease and treatment of the whole patient.

Thanks for your continued support of Healthy Connections. Happy Holidays to all of you! Gaylynn Thomas, RN, BSN

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PITUITARY TUMORS IN WOMEN

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Pituitary tumors represent a special clinical problem in women. Although their diagnosis is relatively straight forward once the suspicion has been raised, patients with pituitary tumors can go undiagnosed for years in spite of symptoms that should have raised such suspicion and led to definitive testing. This article seeks to highlight the symptoms that such tumors produce, to describe the best way of confirming the presence of the tumor, and the most appropriate ways of treating such lesions.

DIAGNOSIS

Pituitary tumors can cause symptoms by either of two methods. In some, they compress the adjacent normal pituitary gland, and thereby impair hormone secretion and produce a lack of one or more of the hormones produced by the gland. Alternatively, the tumor can itself produce hormones in excess, leading to high levels of hormones, each of which produces a specific clinical syndrome. Others symptoms of significance include visual loss, caused by a tumor large enough to reach from the pituitary to the optic chiasm running above the *sella*. Typically a tumor must be greater than 1.5 cm in diameter to create loss of vision, and many patients with tumors larger than that have intact vision. In addition, headache is commonly experienced by patients with pituitary tumors. In some of them the tumor causes the headache by local dural compression or infiltration. In many, however, headache represents a second, unrelated issue which will not necessarily clear if the tumor is eliminated.

The most common pituitary tumor is the "clinically non-functional" adenoma, representing 40-45% of cases. Such tumors make no clinically significant hormone and are usually found incidentally, by virtue of low hormone levels they produce, or because of visual loss when a tumor is relatively large. The second most common is the prolactin-producing tumor, "prolactinoma", representing 30% of cases. These are the tumors most likely to be seen in a gynecologic practice, given their impact on reproductive function, the menstrual cycle, and libido. Prolactinomas tend to be relatively small and exert their effects by virtue of raising serum prolactin levels attendant to them. To be secure in the diagnosis of prolactinoma, a patient should have a prolactin >100 ng/ml. Because certain drugs (e.g., Risperdal® or other phenothiazines) raise prolactin levels to a similar degree, they must be excluded by history before concluding that a patient with a high prolactin level has a pituitary tumor. Patients with lower levels of prolactin that are still supra-normal (*i.e.*, >25 ng/ml) may have either a prolactinoma or a non-functional tumor exerting "stalk effect", namely a distortion of the gland from local pressure which blocks the tonic hypothalamic inhibition of prolactin secretion and thus allows prolactin levels to rise. The distinction is important because prolactin excess caused by tumor secretion is treated in the majority of patients with Dopamine agonist therapy, whereas prolactin elevation due to stalk effect suggests that such therapy will be ineffective. Distinction is not always an easy one and an endocrinologist should be involved for any patient suspected of having a pituitary tumor. They can offer help in deciding whether a tumor is non-functional (with stalk effect) versus a true prolactinoma, and can, in addition, perform hormonal screening for all areas of pituitary function. It is not sufficient to simply check prolactin and perhaps thyroid hormone levels, as is often done in women in whom a pituitary tumor is suspected. A full hormone panel should be drawn and the nuances in interpreting this make involvement of an endocrinologist very helpful.

Other tumor types include those which secrete growth hormone (causing acromegaly), those secreting ACTH (causing Cushing's Disease), and those rare tumors secreting TSH (producing a hyper-thyroid state commonly mis-diagnosed as primary hyper-thyroidism and often treated inappropriately with thyroid ablation). Three-quarters of all pituitary tumors will, however, be either non-functional or prolactin-secreting adenomas, and understanding of which is vital in any gynecologic practice.

The hormone system most vulnerable to extrinsic pressure is the pituitary-gonadal axis. Minor disturbances of the pulsatile rhythms of FSH or LH production can affect fertility and libido and can disrupt the menstrual cycle. Thus, any pituitary tumor can cause infertility, and the search for such tumors should be part of any infertility workup, particularly when low levels of FSH and/or LH can be shown. Low levels of prolactin are not considered to be significant or to re-

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A FEW WORDS FROM Healthy CONNECTIONS ...

HEALTHY CONNECTIONS realizes that these are challenging economic times in which we live. With the current state of the economy, the last few months have not only been difficult for patients, but also for physician practices. It is our sincere hope that HEALTHY CONNECTIONS continues to provide a value to you and your patients as more and more decisions are predicated on cost. HEALTHY CONNECTIONS believes that the fewer patients that require hospitalization or Emergency Room visits, the less taxing it is on the patient, physician, and on the healthcare system. Our homecare services cost far less than hospitalization and still provide excellent care & oversight for well-selected pregnant patients with pre-term labor, hyperemesis, hypertension or diabetes.

With the increasing likelihood of private insurers adopting economic credentialing for physicians, judicious use of healthcare resources is even more critical. Homecare services may help obviate the need for numerous hospitalizations for your pregnant patients. We are happy to demonstrate for your practice and staff how HEALTHY CONNECTIONS can assist you in decreasing such hospitalization/utilization costs.

HEALTHY CONNECTIONS wishes you and your staff all of the best for the upcoming holiday season! We hope that 2009 brings you and all those close to you health, prosperity and peace.
We appreciate the opportunity to continue to work with you, your staff, and your patients at improving the healthcare of pregnant women!
THANK YOU!