creases pulmonary artery pressures quickly and improves the results of the lung scan and arteriogram at 12 and 24 hours. However, thrombolytic agents produced no overall decrease in mortality compared with heparin therapy.

Thrombolytic therapy should not be used in patients with active internal bleeding or a recent stroke (within 2 months). It also should not be used in anyone who has an intracranial neoplasm or abscess. The major complication associated with thrombolytic therapy is bleeding; this can be minimized by selecting the patient carefully and avoiding invasive procedures. Vessels that cannot be directly compressed should not be invaded.

The inferior vena cava can be interrupted with a filter to prevent recurrence of a massive pulmonary embolism or chronic recurrent small emboli. Other indications for this procedure are a contraindication to anticoagulation in a patient with deep vein thrombosis or pulmonary embolism, major complications with anticoagulation, and recurrent pulmonary embolism despite adequate anticoagulation.

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MEDICAL TREATMENT OF PITUITARY TUMORS

Medical therapy produces better results than surgery in patients with prolactin-secreting adenomas, which account for about half of all pituitary adenomas. Dopamine agonists such as bromocriptine (Parlodel) and pergolide (Permax) effectively reduce prolactin secretion and reduce the size of these tumors, but these drugs are not very effective in treating acromegaly, where they lower elevated growth hormone and insulin-like growth factor-1 levels only 10% of the time. A relatively new agent, octreotide (Sandostatin), is about 90% successful in treating acromegaly, and it also may be used to treat the quite rare pituitary tumors that secrete thyroid-stimulating hormone.

HYPERPROLACTINEMIA AND PROLACTINOMAS

Prolactin is unusual in that it is controlled primarily by an inhibiting factor, dopamine. Drugs that deplete dopamine stores or that directly stimulate prolactin secretion can elevate serum prolactin levels. Some of the more commonly used drugs that can do this include metoclopramide, methyldopa, oral contraceptives, and the phenothiazines. Prolactin levels are elevated in pregnancy, chronic renal failure, and primary hypothyroidism. Trauma and tumors that affect the hypothalamus or stalk also may raise prolactin levels. For the same reason (injury or traction on the stalk), primary empty sella syndrome is sometimes associated with hyperprolactinemia.

In women, hyperprolactinemia produces galactorrhea, changes in periods, and infertility. Men may experience infertility or impotence, or they may present later in the course of the disease, when a mass effect from the growing tumor produces changes in visual fields or severe headaches. Symptoms in women tend to be proportional to circulating levels of prolactin.

Because prolactin-inhibiting factor may be obstructed by structural lesions, there may be a high prolactin level in patients who have tumors that don't actually make prolactin. These are called pseudoprolactinomas.

Diagnosis of prolactinomas

Once a high serum prolactin level is found and nontumor causes are ruled out, magnetic resonance imaging and endocrine studies should be performed as clinically indicated to rule out deficiencies of adrenocorticotropic hormone or thyroid-stimulating hormone. The prolactin level is usually proportional to the size of the tumor.

Thus, the finding of a large tumor with a prolactin level of only 60 implies the presence of a pseudoprolactinoma. In most cases, prolactin-stimulating drugs, hypothyroidism, or an empty sella result in prolactin levels between 30 and 90 ng/mL. Pregnant women can have prolactin levels between 100 and 200 ng/mL, and in kidney failure the prolactin levels

can go as high as 150 to 200 ng/mL. Levels in excess of 200 ng/mL probably indicate a tumor.

Treatment of prolactinomas

Pituitary microsurgery was available long before dopamine agonists; 15 years ago almost all patients underwent pituitary microsurgery. However, surgery can only achieve a cure rate (as demonstrated by a normal prolactin level) of approximately 50%, and 50% of these patients will experience a relapse.

Now many experts favor drug therapy over surgery. Patients who do not respond to bromocriptine or who cannot tolerate dopamine agonists can be managed with radiation therapy or surgery. Medical therapy improves or normalizes prolactin levels over 90% of the time. Dopamine agonists also shrink the tumors. Some patients who have a mild problem may need observation only. The only dopamine agonist approved for infertility secondary to hyperprolactinemia is bromocriptine.

Long-term effects

The long-term effects of medical therapy are still not known. Based on our experience and that of others, approximately half the patients treated for 3 years experience either a permanent improvement or a remission. The complication rate probably varies with the size of the tumor.

We do not really know the natural history of pituitary tumors. All large tumors must start out as small tumors, but small tumors probably become large only rarely. It takes approximately 5 to 7 years for a tumor to double in size, but we have observed some patients for up to 15 years with radiography and have not seen some small tumors get bigger.

ACROMEGALY

Acromegaly is usually due to a primary growth hormone-secreting pituitary adenoma. Tumors that secrete growth hormone-releasing hormone, such as carcinoids and islet cell tumors, are rare. There are about 3 or 4 cases of acromegaly per million per year. The patient may initially seek help for changes in bite or for carpal tunnel syndrome. Some symptoms will get better with therapy: headaches, sweating, carpal tunnel syndrome, cutis verticis gyrata, and skin tags. Other features that will not improve are acral enlargement, facial changes, separation of the teeth, change in bite, and voice changes.

Laboratory diagnosis is usually easy. A growth hormone level higher than 3 ng/mL, an elevated level of insulin-like growth factor-1, or a growth hormone level higher than 5 ng/mL 2 hours after taking 75 mg of glucose (Glucola) confirms the diagnosis.

Because most patients have had the disorder for a long time when they present (more than 10 years in many cases), the pituitary tumors are often large when the diagnosis is made. Thus, surgery often is not curative. If surgery fails, radiation therapy is often advised. Growth hormone levels may not subside to normal until several years after surgery.

The somatostatin analogue octreotide (Sandostatin) has not yet been approved to treat acromegaly. However, a multicenter trial using this drug demonstrated good results, with about 90% of patients responding well. In contrast to bromocriptine for prolactinomas, where good control of tumor size is the rule, octreotide therapy for acromegaly gives only modest tumor shrinkage. The major side effect is gallstone formation.

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