PITUITARY CASES

Case 1

A 49-year-old attorney was admitted to the hospital because of progressive weakness with recent nausea, vomiting, and confusion. Nine years previously her menses had ceased, and she began feeling tired and listless. Her doctor said she was going through the change of life and prescribed "hormone pills." She took these on a cyclic basis for a while, with temporary return of her menstrual periods, but finally discontinued the medication and had no further menses. Over the next several years she began having intermittent bifrontal headaches and felt increasingly sluggish and weak. She thought she might have high blood pressure but was told by her doctor that her blood pressure was "low." Her appetite was sometimes poor, but she had no weight loss. Another doctor whom she saw suspected endocrine disease and ordered x-rays and urine tests. Before the results of these became available, she began to feel extremely weak, experienced nausea and vomiting, and was noted by her husband to be confused and somewhat disoriented. She was taken to the hospital.

On admission she had a temperature of 102^{o}, pulse 110, blood pressure 88/60, and appeared to be in a state of semistupor. The skin was pale, smooth, and appeared thin and finely wrinkled. Axillary and pubic hair were reduced. On examination of the breasts, one or two drops of milky fluid could be expressed by gentle pressure. (The patient herself had never noted spontaneous galactorrhea.) There was questionable delayed recovery of the deep tendon reflexes. The remainder of the physical examination was essentially within normal limits.

Admission laboratory studies included: Hgb. 11.2: WBC 10,000 (N70%, L23%, E7%); blood glucose 46 mg/100 ml (normal 60-100): serum sodium 130 mEq/liter (normal 136-145); potassium 3.8 mEq/liter; BUN normal.

When the patient's hypoglycemia became known, she was given extra glucose intravenously in addition to the 5% glucose-normal saline mixture which had been begun on admission. A marked improvement in state of consciousness followed. Further improvement was noted when it was decided to add hydrocortisone to her medications. Subsequent laboratory studies which became available showed 8 a.m. cortisol 4.1 mcg/dl (NL>10); serum T_4 3.2 μg/dl (normal 5-12); TSH 1.2 μU/ml (NL 0.4-4.5); serum FSH and LH both at low end of normal range for menstruating women; plasma prolactin 275 ng/ml (NL 5-25 ng/ml); MRI scan showed an enlarged sella turcica containing an intrasellar tumor, with upward extension of the tumor mass and impingement on the optic chiasm. Visual fields indicated a mild bitemporal field defect.

The patient rapidly became afebrile and was kept on maintenance doses of cortisone and thyroxine. When the results of the prolactin test and the MRI scan became known she was begun on cabergoline in a dose of 0.5 mg twice weekly. Within 3 weeks her serum prolactin had fallen to 22 ng/ml and her visual fields had shown some improvement. An MRI done 3 months later indicated shrinkage of the tumor by about 30%. She continued to be amenorrheic.

On a follow-up visit a month after the MRI scan her serum prolactin was found to have risen to 200 ng/ml, and the patient confessed to not having taken her cabergoline for the previous two weeks. The drug was restarted, with prompt decrease of the serum prolactin to 25 ng/ml. Her physicians debated the advisability of recommending continuation of cabergoline therapy indefinitely versus transsphenoidal surgery. Because of doubts about the patient's likelihood of compliance with long-term drug therapy, surgery was recommended, and she underwent uneventful removal of the bulk of her tumor. Postoperatively her serum prolactin was 50 ng/ml and it has remained at approximately this level during follow-up visits. On a trial withdrawal of thyroxine therapy her serum T_4 fell into the hypothyroid range, so thyroxine was resumed. Adrenal steroid replacement therapy was maintained. The patient continues to feel well, and visual fields and MRI scans have revealed no further changes over a several year follow-up.

Questions:

1. Is amenorrhea abnormal in a 40-year-old woman?
   How would you organize your differential diagnosis?

2. Does the return of menses with "hormone pills" (presumably estrogens) provide valuable endocrine diagnostic information?

3. If serum prolactin had been normal instead of elevated, what single hormonal test would best help define the etiology of amenorrhea in a 40-year-old woman?

4. Is dramatic weight loss characteristic of hypopituitarism?

5. What is contributing to this patient's decreased state of consciousness?

6. Is an enlarged sella turcica essentially pathognomonic of a pituitary tumor?

7. What is the most important nonhormonal condition to be concerned about in a patient with pituitary tumor?

8. What is the single most important hormonal aspect to be concerned about in the treatment of hypopituitarism?

9. The patient's menses did not return after her serum prolactin was normalized on cabergoline. What might be the reasons? Would you expect resumption of menses in most hyperprolactinemic amenorrheic women treated with cabergoline?

10. Why was diabetes insipidus <u>not</u> observed in this patient? Is DI a rare or common complication of pituitary adenomas?

11. Would you consider replacement of estrogen or growth hormone in this patient? What are the pros and cons?

12. What is the prognosis in this patient:

    a. For continued growth of her tumor requiring further treatment of some kind? If tumor regrowth were observed, what would be the therapeutic options?

    b. For having to stay on continued endocrine replacement therapy?

    c. For length of life?

Case 2

A 40-year-old man presented himself to Medical Clinic with complaints of diffuse joint pains, mild headaches, and chronic fatigue. His decision to see a doctor was prompted in part by the remark of a friend, who had recently seen him for the first time in several years, to the effect that his face had greatly changed in appearance. The patient believed that his features had become thicker and coarser over several years and was able to produce some old photographs which confirmed this fact. On questioning by the physician, the following additional information was obtained: His feet and hands had enlarged slowly over several years so that his shoe size had gone from a 10C to a 10 1/2 EEE. He had become somewhat clumsy with his hands and had a ring enlarged. He noticed mild chronic stiffness and soreness in the back, hips, knees, and ankles. He had gradually gained 15-20 pounds in weight and felt significantly lower in general energy than before. Libido and the frequency of sexual relations had declined considerably, although he was still potent. He was considerably bothered by excess sweating. His voice had become slightly hoarse. He had begun to have moderately frequent, usually mild but occasionally severe, bifrontal headaches. His wife complained to him that he snored all night, and at times breathed irregularly while sleeping. He denied any visual symptoms.

On physical examination vital signs were normal, except for a blood pressure of 160/104. The patient was a somewhat heavily-built man who did not appear obese. Facies were characteristic of acromegaly with thick lips, nose, ears, and prominent lower jaw. The skin was thick, coarse textured, and moist, and several sebaceous cysts were palpated around the angle of the jaw and in the back of the neck. Hearing was moderately decreased bilaterally. Fundoscopic exam was normal except for minimal hypertensive changes; gross visual field testing by confrontation revealed a moderate bitemporal hemianopsia. The tongue was large. The teeth were not abnormally widely spaced. The thyroid was questionably enlarged and somewhat firm. The heart and lungs were normal. The liver was palpable two fingerbreadths below the right costal margin. Spleen and kidneys were not felt. Genitalia were normal. Hands and feet were large, with wide thick fingers. There were no obvious joint deformities.

Laboratory findings included a normal CBC and urinalysis. An initial plasma growth hormone (hGH) level was 20 ng/ml. Fasting blood sugar was 110 mg/100 ml, and a three hour oral glucose tolerance test revealed a mildly diabetic response. Simultaneously drawn growth hormone levels were all elevated, with an initial level of 25 ng/ml and suppression to 16 ng/ml at 1 hour. Serum insulin-like growth factor-I (IGF-I) was twice the upper limit of normal. Prolactin was 20 ng/ml (nl 5-20 ng/ml). Plasma testosterone was at the lower end of the normal range; 8 a.m. cortisol was 12 mcg/dl (NL>10). 24-hour RAI uptake was normal at 18%, but his thyroid was enlarged on scan. Serum T_4 and T_3 resin uptake were normal. Calcium, phosphate, cholesterol, and liver function tests were all normal. MRI scan showed a moderately enlarged sella turcica containing a tumor measuring 1.5 x 1.2 cm, with slight suprasellar extension of the tumor mass. Spine, hip, and knee x-rays revealed mild generalized osteoarthritis.

Surgical treatment was recommended to the patient. He underwent a transsphenoidal resection of all visible tumor. Early postoperatively, the patient's visual field deficit resolved and on the 3rd postoperative day his GH returned at 5.2 ng/ml. In the first few weeks after surgery the patient had some improvements in his headaches, sweating and his general energy. The patient was followed monthly and at 3 months postoperatively he had a GH level of 4.8 ng/ml that suppressed to 3.5 ng/ml after oral glucose and an IGF-I level 1.5 times the upper limit

of normal. A MRI was done and this revealed a suggestion of residual tumor in the left cavernous sinus. Although his symptoms had improved, they were not gone. On examination his blood pressure was 140/98 and although his facial features were less coarse his tongue remained enlarged and his hands and fingers remained thick and he still felt fatigued. He continued to snore and breath irregularly at night. Pros and cons of continued observation vs. additional therapy, including radiotherapy to the residual tumor and/or medical therapies, were discussed with the patient. He opted for a trial of medical therapy with a long acting somatostatin analog and Octreotide LAR at a dose of 20 mg intramuscularly per month was begun. After 3 months, the patient's GH level was 1.0 ng/ml and his IGF-I had fallen into the normal range. His signs and symptoms continued to improve and he was continued on this therapy.

Questions:

1. Is acromegaly always indicative of the presence of a pituitary tumor?

2. Which of these patient's symptoms are directly attributable to overproduction of growth hormone?

3. Aside from those symptoms attributable to growth hormone excess, are the other symptoms of acromegaly similar to those of nongrowth hormone producing pituitary tumors?

4. If you saw a patient in your office who seemed to have acromegaly, how would you approach the problem of making the diagnosis definitively by means of hormone test(s)?

5. What forms of treatment are available for acromegaly? What are the indications for surgery?

6. How important a therapeutic objective in acromegaly is the reduction of elevated growth hormone levels to normal?