Pituitary tumor and myalgia

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Generalized myalgia with painful, tender muscles as a major presenting complaint usually reflects an acute infectious process, most often viral in etiology and requires no extensive diagnostic studies. Symptoms usually abate rapidly and prompt recovery is the rule. Polymyositis, another cause of muscle pain, usually is readily diagnosed because of the symptoms, elevated acute phase reactants in the blood, and abnormal muscle biopsy.

Within a period of a few months we examined two patients with muscle pain and aching, fatigue and weakness who were found to have pituitary tumors with multiple endocrine deficiencies. Our purpose in reporting these cases is to point out that endocrine dysfunction can be the cause of profound muscle symptoms and also to suggest that pituitary lesions should be considered when anyone has muscle complaints secondary to endocrine dysfunction.

Case reports

Case 1. A 46-year-old man became ill about June 1, 1972. He began to notice pain in his calves when walking. Shortly thereafter he experienced aching discomfort in his back and shoulder muscles. He also noted weakness of his shoulders and thighs. He became anorectic and the weakness progressed. He also had occasional, intermittent dull aching pain on the left side of his head. Initial studies

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revealed a mild decrease in hemoglobin value and an enlarged sella on roentgenographic examination. Visual fields were normal. He was referred to the Cleveland Clinic for further evaluation. He had had a successful mammary artery implant for coronary artery disease in February 1968. Prior to the current illness he had walked 2 miles daily without experiencing chest pain.

When seen at the Cleveland Clinic in July 1972, approximately 6 weeks after the onset of his illness, he had a weight loss of 8.2 kg. His main complaint was pain in the shoulders and legs which increased with movement. Examination showed weakness of the triceps, biceps, deltoid, and quadriceps muscle groups. Atrophy was evident in the shoulder girdle muscles. The neurologic examination was otherwise normal. The visual fields were again normal. Results of the following laboratory tests were normal: sedimentation rate, urinalysis, creatine phosphokinase (CPK), lactic dehydrogenase (LDH), serum glutamic oxaloacetic transaminase (SGOT), aldolase, sodium, chloride, potassium, immunoglobulins, serum protein electrophoresis, antinuclear factor, and LE test. The PBI was 5.2 μg/dl, T_3 red cell uptake (tesitope) 29.7%, and effective thyroxine ratio 0.92. All these thyroid values were in the lower range of normal. The hemoglobin was 12.3 g/dl, hematocrit 36.5%, and white blood cell (WBC) count 3,200/cu mm with a normal differential count. An electromyogram was within normal limits as was a muscle biopsy of the left vastus lateralis. Roentgenograms of the entire gastrointestinal tract, an intravenous urogram, and chest films were normal. Roentgenograms of the skull showed enlargement of the sella turcica with erosion of the floor and dorsum sella.

Having excluded an active inflammatory process of the muscles, extensive evaluation of pituitary function revealed evidence of ACTH, luteinizing hormone (LH), and thyroid-stimulating hormone (TSH) deficiencies. A low normal level of follicle-stimulating hormone (FSH) was present. Plasma cortisol was 3.6 μg/dl at 4:00 p.m. and 8:00 a.m. (normal, 6–26 μg/dl). Urinary 17-ketosteroids were 4.5 mg/24 hr (normal, 6–21 mg/24 hr), 17-hydroxycorticoids were 1.8 μg/24 hr (normal, 3–12 μg/24 hr). There was no significant increase during 2 days' use of metapyrone. With ACTH stimulation, the 17-ketosteroids rose to 23.5 μg/24 hr and 17-hydroxycorticoids rose to 37.4 μg/24 hr. The plasma cortisol rose to 55.2 μg/dl after ACTH was given intravenously. Serum FSH was 27.4 μg/dl (normal, 9–40 μg/dl). Serum LH was 1.3 μg/dl (normal, 1.8–13.0). Serum TSH was less than 2 microunits/ml (normal, 0–15). Testosterone was 131 ng% (normal, 200 to 1000).

A pneumoencephalogram revealed a pituitary tumor with 4 to 5 mm of suprasellar bulge. He was treated with cobalt-60 and replacement therapy consisted of cortisone acetate, testosterone, and thyroid. He had prompt and complete relief of all myalgic symptoms.

Case 2. A 55-year-old woman had undergone right radical mastectomy in 1968 for carcinoma of the breast. She was in good health otherwise until June 1972 when she began to notice soreness and aching in the muscles of her neck, shoulders, and arms. She could remember no antecedent illness. A physician found her to be mildly anemic and she was treated with vitamin B_{12} and iron with no abatement of symptoms. A hematologist examined her in October 1972 and found that she had hypothyroidism. She was given thyroid replacement. When examined on December 15, she had tachycardia, pedal edema, and bilateral basilar rales. Thyroid therapy was stopped and she was treated with digitalis and diuretics. She had lost 9.1 kg between June and December and continued to complain of sore, tender, aching muscles, the most severe symptoms being in the proximal muscle groups. She also complained of blurred vision at that time and reported that she had had a mild right-sided headache for the previous 2 months.

Because of the visual symptoms, skull films were done which showed an enlarged sella turcica; visual field examination revealed bitemporal field loss, more on the right. One week later, the field defects had progressed. She was referred to the Cleveland Clinic for

definitive study and treatment. When examined on January 6, 1973, she denied having polyuria and salt craving, but did notice some increased thirst. She complained of fatigue and muscle aching. She stated that her last menstrual period had been in 1971. On examination her blood pressure was 120/60 mm Hg, and pulse rate was 78. Results of physical examination were normal except for the right visual field defect, the absence of the right breast, and tenderness of the proximal muscles. There was no atrophy, but the strength of the proximal muscles of the shoulder and pelvic girdle was slightly diminished.

Laboratory studies disclosed the following values: hemoglobin, 11.5 g/dl; hematocrit, 33.2%; and WBC 4, 100/cu mm. Differential count, 27% polymorphonuclear cells, 25% eosinophils, 39% lymphocytes, and 9% monocytes. Plasma cortisol at 8:15 a.m. was 1.8 μg/dl (normal, 6–26 μg/dl); the PBI, 4.6 μg/dl; T_3 red cell uptake, 24.6% (normal, 25%–35%); and the effective thyroxine ratio 0.85 (normal, 0.86–1.13). The serum potassium was 4.3 mEq/liter; sodium, 143 mEq/liter; and the chloride, 104 mEq/liter. A glucose tolerance test was normal. The 24-hour urine for 17-ketosteroids revealed 3.0 mg/24 hr, the 17-hydroxycorticoids being 0.9 mg/24 hr; both values quite low. The 24-hr urine for gonadotrophin assay showed less than 13 mouse units, also low. Serum LH was less than 1 μg/dl and the serum FSH was 23.7 μg/dl. Roentgenograms of the skull showed erosion of the floor and dorsum of the sella turcica. Chest films and a brain scan were normal. Visual fields confirmed superior and lateral field loss on the right and superior field loss on the left.

Carotid angiography and a pneumoencephalogram confirmed the presence of an intrasellar mass with suprasellar extension. Craniotomy with removal of a cystic chromophobe adenoma was performed on January 12, 1973. The patient was discharged on a regimen of sodium levothyroxine (Synthroid), 0.15 mg a day; cortisone acetate, 25 mg in the morning and 12.5 mg in the evening; and diphenylhydantoin (Dilantin) 100 mg three times daily. When seen 3 months later she was completely free of pain, had no headache, and generally felt well. Visual fields were completely within normal limits. She was seen again 1 year after the operation and was completely asymptomatic. She was taking the sodium levothyroxine and cortisone acetate as prescribed.

Discussion

In recent years there has been increasing interest in endocrine causes of myopathy with thyroid dysfunction being implicated most often.[1-8] Proximal muscle weakness is a common finding in thyrotoxicosis, and it has been stated that proximal myopathy is present and can be demonstrated in all patients with thyrotoxicosis.[6] Muscle weakness is also a common complaint in persons with hypothyroidism.[1-5] Pain in the form of generalized aching and also occurring as cramps with muscle contraction is said to be less well appreciated as a symptom of hypothyroidism.[4] However, aching pains in muscles are not infrequent and muscle action may be painful. Collins et al,[8] in a review of 75 cases of hypothyroidism, mentioned that 72% of patients had neuromuscular symptoms. He specifically listed pain in extremities as occurring in 29% and muscle cramps or stiffness in 20% of 75 patients. Nevertheless, we agree with Golding[4] that muscular pain is not very often thought of as a presenting symptom of hypothyroidism.

Adrenal insufficiency is usually accompanied by fatigue, muscle weakness, and muscle wasting. Pain, however, is not a part of Addison's disease or secondary adrenal insufficiency except for cramping in the muscles. The cramping of muscles in patients with adrenal insufficiency is believed to be due to abnormalities in electrolytes.[9]

Other endocrinopathies are associated with myopathy. Acromegaly is commonly

associated with weakness and a myopathy has been demonstrated.[10] Myalgia or pain, however, was not mentioned as a symptom in the 11 patients studied. Myopathy also occurs commonly in Cushing's disease, but pain is not a feature.[11] Diabetes is also known to be accompanied by a myopathy as well as recognized neuropathy.[12]

The myopathy and myalgia in our two patients was most likely due to hypothyroidism rather than to any of the other endocrine deficiencies present. In these two instances the thyroid deficiency was due to a pituitary tumor with low levels of TSH. Dubansky et al[13] reviewed 20 cases of hypothyroidism with muscular symptoms and six of these patients had secondary hypothyroidism. Five of these six with hypothyroidism secondary to pituitary lesions had muscular pain as a prominent symptom. In a recent study by Faglia et al,[14] it was suggested that the incidence of impaired endocrinological test results is greater in patients with pituitary tumors with suprasellar spread than in intrasellar tumors. This is thought to be due to hypothalamic involvement.

Summary

Within a few months two patients were examined who had pituitary tumors with secondary endocrine deficiencies. The main complaints of both patients were muscle pain, soreness, and tenderness. There was no evidence of a primary muscle disorder, and the patients' symptoms responded to endocrine replacement therapy. Endocrine dysfunction, particularly hypothyroidism, should be considered in anyone who has muscle symptoms. If evidence of endocrine abnormalities is found, we suggest a roentgenogram of the skull and other studies to determine whether a pituitary lesion is present.

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