Post-traumatic Anterior Pituitary Insufficiency Developed in a Patient with Partial Lipodystrophy

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Synopsis

A case of partial lipodystrophy developing anterior pituitary insufficiency, chronic glomerulonephritis and pulmonary fibrosis was reported. The patient died of respiratory failure secondary to pituitary crisis during the hospital course.

From the clinical course in recent several years and the postmortem examination the head injury following car accident in the past history was considered to be the most plausible cause of hypopituitarism. The etiology of pulmonary fibrosis remained unresolved.

Partial lipodystrophy is an uncommon disease developing with slowly progressive symmetrical loss of subcutaneous fatty tissue which initially involves the face and later progresses down to the trunk to the area above the pelvic region. In contrast to the clinical features of total lipodystrophy, the association of other disorders with partial lipodystrophy appears to be rare or fortuitous. However, if other diseases are present, there is a high incidence of some form of renal disease (Senior and Gellis 1964; Jeune et al., 1965; Lajouanine et al., 1968; Eisinger et al., 1972) which accounts for 25-50% of associated disorders. Other associations include abnormalities of glucose and lipid metabolism (Piscatelli et al., 1970; West et al., 1974), abnormality of growth hormone secretion, (Tzagournis et al., 1973) thyroid disorder (Murray, 1952) and pancreatitis with recurrent eosinophilia, (Boucher et al., 1973; Smith et al., 1975) or hepatomegaly (Senior et al., 1964).

Recently, the authors attended a male patient with partial lipodystrophy associated with hypopituitarism, chronic glomerulonephritis and pulmonary fibrosis. The patient died of respiratory failure secondary to pituitary crisis which was precipitated by a Metopirone test during the hospital course. The autopsy revealed a marked atrophy of the pituitary gland, probably due to the post-traumatic necrosis of the gland after the patient sustained a head injury in a car accident.

This paper deals with the clinical and postmortem findings of this particular patient.

Case Report

A forty-eight-year-old male patient was referred to our clinic with a suspected diagnosis of facio-scalpulo-humeral type of progressive muscular dystrophy in January 21, 1974. His complaints at the first visit were general malaise and dyspnea on exertion. Family history was non-contributory.

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Before the age of 21, the patient was rather obese and his face was round as shown in a photograph (Fig. 1). At the age of 22 he suffered from syphilis but recovered from it without residual symptoms with antiluetic therapy for six months. Since his marriage at age 27, his face became thin and orbital shrinking became prominent. Around age 37, the patient became much thinner, but the adiposity in the lower extremities was rather excessive and he often complained of a sore thigh.

The patient was otherwise well and had children at age 37 and 39. In November 13, 1969, at age 43 he sustained head and whole-body contusions in a car accident. At that time he lost consciousness for several hours, but neither bleeding from the ear nor neurological signs and symptoms suggestive of cranial nerve injuries were noticed. Since that time he often complained of nausea and vomiting with general malaise. At age 43, the patient was suspected to have pulmonary tuberculosis and treated with antituberculous drugs for 2 years. However, his complaints never improved. At age 46, he was admitted to another hospital where he was found to have an abnormal shadow in the chest film, proteinuria with microscopic hematuria, eosinophilia ranging from 12 to 20 percent, and hypotension.

No definite diagnosis was made at this time.

Shortly after discharge the patient was readmitted to the same hospital because of a high fever of 40°C. Laboratory examination revealed an elevated transaminase in addition to the findings found during the foregoing hospital course. Biopsies of the liver, kidney and lung were carried out to explore the complicated findings. However, lung biopsy failed to demonstrate any histological changes corresponding to pulmonary tuberculosis or Löeffler's syndrome. Liver biopsy showed no significant change and renal biopsy demonstrated mild proliferative glomerulonephritis without immunofluorescence staining for IgG and fibrinogen.

On physical examination at the admission to our clinic the patient was poorly

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Fig. 1. A portrait of the patient taken at 21 years.

Fig. 2. A photograph of the patient taken at admission, showing marked orbital shrinking and hollow cheeks. Bandage on the left upper arm is for a wound by muscular biopsy.
nourished, and showed a cadaverous countenance because of a pale face with orbital shrinking and hollow cheeks (Fig. 2). Muscular atrophy was not seen. There was no pigmentation in the skin or mucous membrane of the oral cavity. The hair was scanty. The intelligence was normal but response to the medical interview was slightly sluggish. The palpebral conjunctivae were anemic, and jaundice was not seen in the bulbar conjunctivae. The Argyll-Robertson's sign was negative. Neither cervical lymph nodes nor goiter were palpable. BP was 82/52 mmHg in the recumbent position and 54/38 mmHg in the upright. The respiratory sound was coarse in the apical region. No organomegaly was felt in the abdomen. The testes were not atrophic. Neurological examinations disclosed no abnormality. Laboratory data: Urinalyses showed a pH of 6.0, a negative to 1+ reaction for protein, with 5 to 15 red cells, 5 to 20 while cells, and negative to 20 squamous cells/h.p.f. in the sediments, and no glycosuria. Urine volumes were 700 ml to 1400 ml, Hct., 34%; RBC count, 3,280,000/mm³; Hgb., 10.3 g/100 ml; WBC count, 4,100/mm³ with 43% neutrophils, 4% banded neutrophils, 40% lymphocytes, 4% monocytes, and 13% eosinophils; platelet count, 164,000/mm³ and reticulocyte count, 1%.

Fibrinogen was 345 mg/100 ml. The erythrocyte sedimentation rate was 85 mm/hr, 104 mm/2 hr, C-reactive protein was 2+, and treponema pallidum hemagglutination test was 1+. Rheumatoid factor (RF) and ASLO were negative. Serum levels of C₃ and C₄ were 88–102 mg/100 ml and 42–47 mg/100 ml respectively. Total serum protein was 7.6 g/100 ml (albumin 53.1%; α₁-globulin 4.1%; α₂-globulin 10.2%; β-globulin 6.1%; γ-globulin 26.5%; A/G ratio, 1.23; Immunoglobulin A (IgA), 102 mg/100 ml; IgG, 2240 mg/100 ml; and IgM, 288 mg/100 ml).

Serum enzyme levels were within normal limits, except for LDH which showed a supernormal level of 489 units.

Conventional tests for liver function also gave normal data. U-amylase was 183 Somogyi units. Serum cholesterol was 190 mg/100 ml, and triglyceride 81 mg/100 ml. Serum sodium, 141 mEq/l; potassium, 4.9 mEq/l; chloride, 104 mEq/l; calcium, 4.4 mEq/l; inorganic phosphorus, 3.1 mg/100 ml; and iron, 72 µg/100 ml. BUN was 16 mg/100 ml, uric acid 5.3 mg/100 ml, and creatinine 0.6 mg/100 ml. Urinary excretions of sodium, potassium, chloride and creatinine were 104, 15.6, 85.8 mEq/24 hr and 0.74 mg/24 hr, respectively.

Roentgenogram of the chest disclosed cloudy shadow with callosity of pleura on the bilateral apical area of the lung (Fig. 3). On X-ray of the skull the sella turcica was normal in shape and size. ECG findings were within normal limits.

Microscopical examination of repeated smears and cultures of sputa revealed no tubercle bacilli.

Fig. 3. Chest X-ray film taken at admission, revealing pulmonary fibrosis on the bilateral apical area.
Renal function tests showed a concentration, 566 mOsm/kg/H2O (maximal value); PSP, 22.5% in 15 min and 45% in 120 min; renal blood flow, 447 ml/min; renal plasma flow, 306 ml/min; glomerular filtration rate, 85 ml/min; and filtration fraction, 0.278. An intravenous pyelography revealed bilaterally small kidneys (r: 10.2×5.7 cm, l: 9.5×5.8 cm), and renogram showed slightly delayed excretion pattern, bilaterally. A lumbar puncture gave no abnormal findings. EMG finding was normal.

Endocrinological data were as follows: Urinary 17 KS and 17 OHCS were 0.9-1.8 and 0.8-1.6 mg/24 hr, BMR -14.9%; 125I-T3-resin-sponge-uptake 27.2%; thyroxine iodine, 6.3 (3.0-6.6) μg/100 ml; total thyroxine 13.8 (7-14) μg/100 ml; basal level of serum TSH and its response to synthetic thyrotropin-releasing hormone (500 μg intravenous injection) were normal. Fasting blood sugar level was 65mg/100 ml, and blood sugar levels on the 50g-oral glucose tolerance test were 84, 84, 100, 80 and 75 mg/100 ml at the time of 30, 60, 90, 120 and 180 min after load, respectively and immunoreactive insulin (IRI) values revealed a weak response. Intravenous injection of 0.1 unit of regular insulin/kg body weight induced severe hypoglycemic symptoms and signs without plasma ACTH elevation which was determined with radioimmunoassay.

Diurnal profile of the plasma cortisol levels were 2.0 μg/100 ml (1 a.m.), 0.8 (8 a.m.), 0.6 (0 p.m.) and 0.3 (5 p.m.), and no plasma cortisol elevation was noted after 0.25 mg of synthetic ACTH-Z (1 mg/day) for successive 2 days, but urinary 17 OHCS was elevated to 5.2 mg/24 hr on the 3rd day. Plasma ACTH level at 8 a.m. was undetectable and no response to lysine-8-vasopressin was observed. After Metopirone (3.0 g orally), plasma ACTH levels at 8 A.M. increased to the levels of 15.0 pg/ml on the 2nd day and 18.9 pg/ml on the 3rd day. Human growth hormone (hGH) was undetectable and no rise was noted to an infusion of 0.5 g/kg body weight of L-arginine. Serum luteinizing hormone (LH) and follicle stimulating hormone (FSH) levels were 13.0 mIU/ml and 4.5 mIU/ml, and showed normal responses to intramuscular injection of the synthetic luteinizing hormone-releasing hormone (LH-RH 100 μg).

Ocular fundi showed Scheie HOH1 with no narrowing of visual field and the atrophic chorio retinae luetica was suspected. In the electroencephalogram, θ wave was recorded on the bilateral frontal region, but abnormal findings were noticed on brain scanning, echo and cerebral angiography. In the spirography, vital capacity was 1512 ml (42.5%) and forced expiratory volume (FEV1 sec.) was 76.2%. A Mantoux test gave 2+ in 48 hours. Biopsy specimen of the deltoid muscle showed no significant change. Renal biopsy specimen revealed a mild proliferative glomerulonephritis and no specific pathological finding was found in the liver biopsy specimen.

Hospital course:

During the initial stage of admission the patient complained of nausea and general malaise but had no difficulty in the routine physical activity. After a Metopirone test on the 91st hospital day, the patient developed general weakness with severe anorexia and fell into hypoglycemic coma with occurrence of respiratory failure 3 days later. Blood sugar level was 10 mg/100 ml and blood pressure became unmeasurable. Immediately, an iv infusion of glucose solution with a large dose of hydrocortisone and artificial respiration after emergency tracheotomy were initiated. By this treatment the patient recovered sufficiently enough to respond to a call by his wife. However, his general state was again deteriorated after pneumonia and postrenal azotemia secondary to shock developed. The patient died 2 days after this episode.
Post-mortem findings (Fig. 4, 5):

At autopsy the most remarkable changes were observed in the pituitary and adrenals. The pituitary gland decreased to one third of normal in size, and microscopically extensive infradiaphragmatic scarring with focal calcification was present. No pathological findings were found in the other regions of the brain, including the hypothalamus. The posterior lobe revealed partial softening. The adrenal glands were also markedly decreased in size and “paper thin”, weighing 1.5 g each. The atrophy of the gland was especially pronounced in the cortex; lipid depletion was extreme and slight irregularly distributed small round cell infiltration was seen in the reticular zone. No further significant changes were recognized in the other endocrine organs, nor in the sexual glands.

Another remarkable change was interstitial pulmonary fibrosis developing principally in the subpleural areas, especially of the bilateral apexes. There was no evidence of pulmonary tuberculosis, though localized pleural adhesion was seen at the apexes. Except for slight small round cell infiltration occasionally mingled with eosinophiles, there were no active changes suggestive of the etiologic factor.

In the kidneys, a few glomeruli showing complete fibrosis were present microscopically. A recent shallow gastric ulcer at the antrum, measuring 1.3 × 0.9 cm in size, with hemorrhage down to the oral half of the jejunum, was considered one of the results of pituitary crisis. No pathological change was found in the liver.

Discussion

The present case was diagnosed as late-onset form of partial lipodystrophy, based on the characteristic cadaverous appearance which developed after adult age. Neuromyopathic disorders were ruled out by the lack of serum enzyme abnormalities, EMG and muscle biopsy findings. In the specimen taken from the buccal area at autopsy showed a remarkable decrease of the adipose tissue. Therefore, there was little doubt about the fact that fat loss in the present case corresponded to the syndrome of partial lipodystrophy.

Another interesting facet of the clinical features in the present case is the association with several diseases such as hypopituitarism, pulmonary fibrosis and nephropathy. Moreover, it remains difficult to explain which process was more responsible
for the cause of eosinophilia, gamma globulinemia and high erythrocyte sedimentation rate. As a possible cause of hypopituitarism in this case, the head injury due to the car accident was thought to be the most plausible one. In fact, the autopsy findings demonstrated that the pituitary gland was extremely atrophic in both anterior and posterior lobes, which was thought to be the result of tissue destruction with hemorrhage due to hypophysioportal circulation disturbance following the car accident. No pathological lesions similar to those in the pituitary gland were found in the other regions of the brain, including the hypothalamus.

It has been generally believed that hypopituitarism after head injury is a rare disease (Altman and Pruzaski, 1961). However, a few reports (Ceballos 1966; Kornblum and Fisher, 1969) have pointed out that pituitary lesions after head injury are far more common than generally recognized. Moreover, some authors (Asano and Kubo, 1974; Morimoto et al., 1974) have given warning that a recent increase in traffic accidents could increase the incidence of post-traumatic hypopituitarism. Shock of circulatory failure accompanied by head injury has been considered to be the pathogenesis of anterior pituitary lesion. Kornblum and Fisher (1969) described that there was no correlation of the occurrence of pituitary necrosis after head injury with the severity of the trauma and the type and location of the injuries, and that ischemic necrosis occurred consistently in instances of shock accompanied by severe swelling of the brain and pituitary.

It is evident that partial lipodystrophy is etiologically independent of the occurrence of hypopituitarism, because the patient had 2 children at the age of 37 and 39, during which period the signs of partial lipodystrophy were progressing. Although a renal disease, proceeding rapidly to the terminal renal failure or hypocomplementemic glomerulonephritis (Ljunghall et al., 1974), and eosinophilic gastroenteritis or recurrent pancreatitis associated with partial lipodystrophy have been reported (Smith et al., 1975), the authors think that eosinophilia in this case was a consequent phenomenon of the secondary adrenal insufficiency, because autopsy revealed no histological findings characteristic of eosinophilic syndrome. Glomerulonephritis associated with partial lipodystrophy has been described to show variable histology and to develop hypocomplementemia (Ljunghall et al., 1974). In our case, there was no data suggesting the role of complement system clinically and no immuno-histological evidence for deposition of immunoglobulin in the renal tissue. So the pathogenesis of the renal disease could not be elucidated in connection with the fatty tissue disorder.

The etiology of pulmonary fibrosis in our case also remained unresolved. Neither the pathohistological findings characteristic of tuberculosis nor those of collagen diseases were found.

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References