Case Report

Spontaneous regression of one nonfunctioning pituitary macroadenoma associated with abnormal liver enzyme tests

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Abstract

Background: *Nowadays, drug and observation are advised to patients with lymphocytic hypophysitis and in some cases with nonfunctioning pituitary macoadenoma, instead of surgery.*

Case presentation: *In this article, we report a woman with nonfunctional pituitary macroadenoma and panhypopitutarism and negative criteria for lymphocytic hypophysitis associated with increased liver enzymes. After three months adenoma rapidly regressed and liver function tests were normal without any treatment.*

Conclusion: *Seemingly, viral infection as one of the factors may be considered in cases with spontaneous regressed pituitary nonfunctional adenoma.*

Key words: *Pituitary Macroadenoma, Regression, Liver enzyme test.*

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The prevalence of pituitary adenomas in general population was reported around 10% (1).The estimated prevalence of pituitary macroadenomas(*>1cm*) is considerably lower approximately 0.2% (2). Clinically, about 80% of all pituitary macroadenomas are nonfunctioning macroadenomas (3-6) which will relatively grow in 50% cases (3, 7, 8). The treatment of choice in patients with a nonfunctioning pituitary macroadenoma is transsphenoidal surgery. The aim of treatment in these patients is to control tumor and also to improve and protect its visual function. However in many patients, pituitary dysfunction recovery cannot happen, thus, the transsphenoidal surgery is considered for restoration of visual function, rather than pituitary function (9). On the other hand, spontaneous regression of tumor size was reported in 11% of patients with non-functioning pituitary macroadenoma (9). Ischemia of tumor and pituitary apoplexy are some causes of decrease in tumor size. In addition, lymphocytic hypophysitis should be considered in the differential diagnosis (10). Thus, for some patients, observation is better although attention to symptoms and signs that predicts the increase or decrease of tumor volume is very important. In this paper, we report a 46-year-old woman with pituitary macroadenoma, hypopituitarism, abnormal liver enzymes and negative thyroid antibody that after three months, pituitary adenoma spontaneously regressed and liver enzymes and pituitary hormones returned to normal.

Case Presentation

A 46-year-old woman with a history of weakness, malaise, inactivity, excess need to sleep and a 2 kg weight loss in about 2 months was referred to endocrine center of Imam Khomeini hospital in sari, mazandaran.

Mense retardation and amenorrhea have occurred about 2 months before her referral. She denied illnesses and taking any drug previously. She did not have personal or family history of autoimmune disorders such as: diabetes, thyroid disease and sexual dysfunctions or past history of surgery. Her last pregnancy was about 8 years ago without any problem. On physical examination, her blood pressure was 100/65 mmHg, pulse rate 80/min and regular, body weight was 69 kg. In hormone analysis, total thyroxin (T_4) and Free thyroxin (FT_4) were low [T_4=3.9 (5-12 µg/dl), 0.5(0.93-1.7ng/dl)]. Tri-iodothyronine (T_3) was normal T_3=0.8 ng/ml, [with normal range in 0.5-1.9 µg/dl] and Thyroid-Stimulating Hormone (TSH) inappropriately was low (TSH=0.3) (table 1). Serum Alanine Transaminase and Aspartate Transaminase (AST) slightly increased but in repeated testing after that, LFT was normalized (table 2). HBs Ag and HCV Ab were negative.

In this case, prolactin was mildly higher than normal (35ng/l, NL range: 0.5-30). LH and FSH were normal as well but these tests were low and inappropriate for low serum estradiol and amenorrhea (table 1). Serum cortisol was 50nmol/l (NL range: 150-720) and because of its decrease, adrenocorticotropic hormone was requested which was inappropriately low suggestive of pituitary-adrenal axis hypofunction (table 1). Then, cosyntropin test (with 1000 µg cosyntropin) was done.

Increase in serum cortisol after 24 hours (to 46.4, µg/dl) was indicative of central hypoadrenalism. These laboratory findings and biochemical tests consistent with decreased free T_4, cortisol, estradiol associated with low TSH, ACTH and FSH were suggestive of central hypopituitarism. Therefore, brain Magnetic Resonance Imaging (MRI) was requested. Evaluation of brain hypophysis demonstrated a symmetrically enlarged pituitary gland (18*15*15 mm) and upward bulging of diaphragma sella with minimal mass effect on optic chiasm, which recommended macroadenoma. No thickening or disruption of stalk was seen.

Table 1. Serial pituitary hormones

Date (time)	Normal range	In the first visit	3month later	15months later	32months later
Total T_4	5-12 µg/dl	3.9	6.2	6.6	7.7
FT_4	0.93-1.7 µg/dl	0.5	1.2		1
TSH	0.4-6.20 IU/l	0.3	1.4	2.1	2.6
Cortisol	150-729 nmol/l	50	360	510	326
ACTH	up to 63 pg/ml	12		28	53.4
LH	0.5-15 IU/l	5	7	10.3	15.2
FSH	0.5-15 IU/l	8	14	8.7	19.5
Prolactin	0.5-30ng/l	35	17	17.6	20
Estradiol	12.5-166 Pg/ml		22	55	13

Table 2. Serial liver function tests

Liver function testa	Normal range	In the first visit	3month later	15months later	32months later
AST(SGOT)	5-40 Iu/l	82	35	14	15
ALT(SGPT)	5-40 Iu/l	67	33	10	7

ALP	65-340Iu/l	150	187	187	148

In this period, the patient did not return for any follow up. She returned after 3 months. At this time, weakness, inactivity and amenorrhea were spontaneously resolved and the patient felt well.

A repeated three month MRI, showed partial empty sella, and homogeneous density of pituitary gland, both before and after contrast administration. After 32 months follow up, the volume of pituitary gland decreased and empty sella was seen but she remained well clinically without any treatment after 32 months.

Discussion

In this study, we found that a patient had one clinically nonfunctioning pituitary macroadenoma which spontaneously regressed in very short time. She suffered from hypopituitarism without visual defect. Liver function tests were abnormal at first time but after three months, in addition to MRI and pituitary hormone assay; these tests became normal as well.

About 80% of all pituitary macroadenomas clinically are nonfunctioning macroadenomas (3-6). Estimated prevalence of pituitary tumors presenting with disturbances of hormonal secretion or mass effect is 200/1 000 000 and its incidence is 2/100 000 per year (11–13).

The natural course of these tumors is not well known, because the majority of the patients with nonfunctioning pituitary macroadenoma are operated. Spontaneous regression of tumor size was reported in 11% of these patients (9).

Some studies were done for finding the factors that could predict tumor growth or regression. Igarashi classified MRI findings into cystic and solid type and reported that cystic type frequently will shrink or even disappear spontaneously but solid type will often grow (14). In our patient, tumor type was solid but regressed in short time. Decker and Sanno in two separate articles proposed a conservative approach in selected patients with NFMA without visual field defects (15, 16). Our patient did not have any visual defect but in MRI there was a minimal mass effect on optic chiasm. Lymphocytic Hypophysitis (LYH) should be considered in the differential diagnosis of pituitary macroadenoma (10) LYH is thought to represent an autoimmune disease of the pituitary gland, which can impair pituitary hormonal secretion. The disease occurs during or shortly after parturition, but it was also reported after menopause and 15% in male as well (16). Lymphocytic Hypophysitis was first reported in 1962 by Goudie and Pinkerson.They reported a woman who suffered from post partum hypothyroidism, amenorrhea, and died because of adrenal crisis (17).

In several studies, transient regression of the sellar mass and partial improvement of the hypopituitarism was induced by treatment with corticosteroids and they suggested that the diagnosis of lymphocytic hypophysitis can be assessed clinically; conservative management with corticosteroids should be considered prior to surgical intervention (18-20). In this patient, we performed biopsy on the pituitary but pituitary MRI was not suggestive for lymphocytic hypophysitis mass and also thyroid antibody was negative.

Our case had prodromal symptoms, increased AST, ALT and negative virology screening such as HBsAg and HCV-Ab. After spontaneous resolving of patient's lesion in MRI, the liver enzymes became were normal too. Thus, a possible viral etiology as a potential disease mechanism may be suggested in this patient. This case remained well without any treatment, even in the presence of a radiological normality and in the absence of autoimmune phenomenon in past history. However, past reports and recurrence can never be excluded.

Careful follow-up of these patients is needed (21,22). Conclusion: In this paper, we introduced a patient with nonfunctional macroadenoma and panhypopitutarism and negative criteria for lymphocytic hypophysitis associated with increased liver enzymes that rapidly regressed without treatment. Thus, it seemed that lymphocytic hypophysitis as

other factors of viral infection may be considered in cases with spontaneous regressed pituitary adenoma.

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