Anterior Hypopituitarism after Traumatic Brain Injury: A Case Report

Travmatik Beyin Yaralanmasından Sonra Gelişen Anterior Hipopituitarizm: Olgu Sunumu

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Abstract
A 54-year-old man, banker by profession, presented with a three-year-history of generalized weakness, weight loss, fatigue, lethargy, irritability, decreased appetite, gastrointestinal symptoms, and sexual dysfunction. The symptoms had gradually and slowly worsened in the previous three years. He had suffered severe head injury due to road traffic accident 22 years ago and had been unconscious for 12 days. Clinical examination revealed a sick-looking, pale and dehydrated middle-aged man showing postural hypotension after standing for one minute. No significant abnormality was detected on systemic examination. Investigations demonstrated normochromic normocytic anaemia and severe deficiency of anterior pituitary hormones. Magnetic resonance imaging of the pituitary gland and of the rest of the brain was unremarkable. The patient was started on replacement therapy with hydrocortisone, thyroxine and testosterone, on which he showed remarkable improvement in his clinical condition. Turk Jem 2010; 14: 44-6

Key words: Fatigue, lethargy, sexual dysfunction, traumatic brain injury, anterior pituitary hormones deficiency.

Introduction
Traumatic brain injury (TBI) is a worldwide health problem, the major cause of disability and death among young adults, and may lead to neuroendocrine dysfunction. Recent data have demonstrated that TBI-mediated hypopituitarism could be more frequent (1,2) than previously expected. Moderate to severe TBI is frequently associated with dysregulation of pituitary hormones, especially in the acute phase (3). Thirty percent of the injured patients have transient pituitary insufficiency, particularly growth hormone (GH) and gonadotrophin deficiency, which normalizes one year after injury in most of the cases (4). Chronic hypopituitarism warranting hormone replacement has been found to be associated with severe brain injuries and increased disability (5). Klose et al. have recently found in a prospective study that hypopituitarism is more frequent due to severe TBI (4 out of 15) than to mild or moderate TBI (1 out of 31) (p 0.02) (6). We are reporting a case of severe anterior hypopituitarism in a middle-aged man, diagnosed 22 years after a severe TBI.
Case Report

A 54-year-old man, banker by profession, presented with a three-year history of generalized weakness, weight loss, fatigue, lethargy, irritability, decreased appetite and gastrointestinal symptoms like vomiting, mild diarrhoea and abdominal discomfort off and on. He was having great difficulty in performing his office work and used to feel extremely exhausted by mid-afternoon. The symptoms had gradually and slowly worsened in the previous three years. His weight had been usually around 90 kg, but on presentation was 78 kg. He gave a history of decreased libido and erectile dysfunction, which he always attributed to his generalized weakness. There was no history of fever, cough, headache, polydypsia, polyuria, visual symptoms or gastrointestinal bleed. He had been thoroughly investigated by a couple of physicians in the previous two years. He was always found to be anaemic with haemoglobin around 10 g/dl, which never showed improvement with haematinics. Apart from routine tests, investigations mainly done with a provisional diagnosis of some abdominal/gastrointestinal malignancy, included computerized tomographic scan of the abdomen, barium studies and endoscopic examination of the upper and lower gastrointestinal tract. All of these tests were normal. He had suffered severe head injury due to road traffic accident 22 years ago and had been unconscious for 12 days. He had been managed conservatively without any operative neurosurgical intervention and recovered at that time fully with no sequelae. There was no history of any other significant illness in the past. He was a non-smoker and never used alcohol. There was no history of diabetes and hypertension in the family. On examination, the patient was a middle-aged man of average built, lethargic and sick-looking. His weight was 78 kg and BMI 24 kg/m². His pulse rate was 84 beats per minute and blood pressure 100/60 mmHg lying and 75/45 mmHg after standing for one minute. He was pale and dehydrated but not jaundiced. There was no pigmentation of the gums, skin and skin creases. There was no koilonychia or lymphadenopathy. Examination of respiratory system, abdomen and heart did not reveal anything significant. His haemoglobin was 10.6 g/dl with a normochromic and normocytic morphology of red cells, total leucocyte count 6.2x10⁹/l and platelets 257x10⁹/l. Serum sodium was 126 mmol/l, potassium 4.1 mmol/l, urea 7.2 mmol/l, and creatinine 88 micromol/l. Serum cortisol at 9 am was 3.7 μg/dl, serum free thyroxin level was 2.7 pmol/l (reference range: 7.0 - 21.0 pmol/l), thyroid-stimulating hormone (TSH) 3.35 uIU/ml, follicle-stimulating hormone (FSH) 1.5 mIU/ml (reference range: 2.0-17.7 mIU/ml), luteinizing hormone (LH) 0.80 mIU/ml (reference range: 2-12 mIU/ml), prolactin (PRL) 3.1 ng/ml (2.5-17 ng/ml), testosterone <0.7 nmol/l (7.35-26.1 nmol/l). Serum osmolality was 289 mOsmol/kg and urine osmolality 763 mOsmol/kg. Serum IGF-1 was 82 μg/l (reference range: 87-215 μg/l). Magnetic resonance imaging of the brain and pituitary gland revealed normal pituitary fossa, pituitary gland, stalk, and rest of the brain. The patient was diagnosed to be suffering from severe anterior hypopituitarism due to severe TBI. Serum ferritin was 147 μg/l and serum PSA was 2.4 ng/ml. Bone density was measured through dual energy x-ray absorptiometry, which revealed Z-score 1.0 and 0.8 at lumbar spine and femoral neck, respectively. He was put on long-term replacement therapy with hydrocortisone 20 mg at 6 am and 10 mg at 6 pm, thyroxine 100 μg daily and testosterone deconoate injection 250 mg every 2 weeks for 3 months, and then every 3 weeks, after monitoring the serum testosterone levels. He showed a remarkable improvement in symptoms and signs. Lethargy, weakness, fatigue, irritability and sexual performance gradually improved, and after six months his blood pressure was 110/80 mmHg without any significant postural drop. He gained about 7 kg weight, and muscle mass improved. His haemoglobin was 13.6 g/dl after six months, 24-hour urinary cortisol excretion 218.54 μg/24hr (reference range: 32.0 - 243.0), and T4 was 10.34 μg/dl. After 3 months of treatment, we wanted to check the ACTH and GH reserve of the pituitary with dynamic testing, but the patient was unwilling for insulin tolerance test. We used zero and 30 minutes values of serum cortisol in ACTH stimulation test, to assess the pituitary ACTH reserve. Synacthen 250 mg was given as an intravenous bolus, then serum cortisol levels were measured at 0 and 30 minutes and were found to be 3.5 μg/dl and 9.7 μg/dl, respectively, confirming ACTH deficiency. At present, his AGHDA (Adult Growth Hormone Deficiency Assessment) score [7] is 10, so replacement of GH has not been considered yet.

Discussion

Our patient presented with features of severe anterior pituitary dysfunction due to deficiency of gonadotrophins, TSH, ACTH and GH. Serum PRL and posterior pituitary functions were unaffected. People with pituitary insufficiency after a TBI have a high incidence of GH and FSH/LH deficiency but a low incidence of ACTH and TSH deficiency [2,4]. Agha A et al. [8] studied 102 patients, survivors of moderate to severe TBI. Eighteen TBI patients (17.6%) had GH deficiency, suggested by provocation test, as well as low insulin-like growth factor 1 (IGF-1). Thirteen (12.74%) patients showed significant hypocortisolism. GH or ACTH deficiencies were not related to age, Glasgow Coma Scale score, or the presence of other pituitary hormone abnormalities [P > 0.05]. Twelve patients (11.8%) had gonadotrophin and one (1%) had thyrotrophin deficiencies. Twelve patients (11.8%) had hyperprolactinemia. Twenty-nine patients (28.4%) had at least one anterior pituitary hormone deficiency. Severe anterior pituitary dysfunction after TBI, presenting with deficiency of all hormones, except PRL, has been rarely reported [9]. In various cross-sectional studies, the interval between head trauma and assessment of pituitary functions ranged from three to six months up to 23 years [10,11]. A very recent case report described a patient with hypothalamic hypopituitarism in the absence of neurohypophyseal dysfunction that occurred approximately 31 years after a TBI [9]. In this case, pituitary hormones were secreted in response to exogenous administration of hypothalamic hormones. Our patient was diagnosed 22 years after the TBI. In all these cases, the delay in the diagnosis is due the fact that long-term insufficient release of hypothalamic or pituitary hormones persists after a TBI, which leads to gradual development of symptoms and
signs of single or multiple pituitary hormonal deficiencies. Agha A et al. [8] studied 102 patients, survivors of moderate to severe TBI. Eighteen TBI patients (17.6%) had GH deficiency, suggested by provocation test, as well as low IGF-1. Thirteen (12.74%) patients showed significant hypocortisolism. GH or ACTH deficiencies were not related to age, Glasgow Coma Scale score, or the presence of other pituitary hormone abnormalities (p>0.05). Twelve patients (11.8%) had gonadotrophin and one (1%) had thyrotrophin deficiencies. Twelve patients (11.8%) had hyperprolactinemia. Twenty-nine patients (28.4%) had at least one anterior pituitary hormone deficiency. Severe anterior pituitary dysfunction after TBI, presenting with deficiency of all the hormones, except PRL, has been rarely reported. (see above)

We have not yet considered replacement of GH in our patient despite very low IGF-1, because he has shown remarkable improvement in quality of life with glucocorticoid, androgen and thyroxine replacement therapy and his AGHDA score is 10 (7). Low IGF-1 levels (84 ng/ml) or presence of deficiency of pituitary hormones, other than GH, may have a diagnostic value similar to that of dynamic tests [12]. It has been shown by various cross-sectional and prospective studies that there is a significant prevalence of undiagnosed anterior pituitary hormone abnormalities in survivors of TBI. These hormonal abnormalities are readily treatable, ensuring a remarkable reduction in morbidity and improvement in quality of life. Therefore, regular assessment and monitoring of pituitary functions after severe TBI should always be considered.

References