Neuropsychiatric Disturbances and Hypopituitarism After Traumatic Brain Injury in an Elderly Man

Yi-Cheng Chang, Jui-Chang Tsai,¹,² Fen-Yu Tseng*¹

Neuropsychiatric or cognitive disturbances are common complications after traumatic brain injury. They are commonly regarded as irreversible sequelae of organic brain injuries. We report a case of hypopituitarism in a 77-year-old man who presented with long-term neuropsychiatric disturbances, including cognitive impairment, disturbed sleep patterns, personality change, loss of affect, and visual and auditory hallucinations after a traumatic subdural hemorrhage. The treatment response to hormone replacement therapy was nearly complete. Hypopituitarism is rarely considered in patients who sustain traumatic brain injury and the neuropsychiatric manifestations of posttraumatic hypopituitarism have rarely been reported. This case highlights the importance of hypopituitarism as a potential reversible cause of neuropsychiatric disturbances after traumatic brain injury. [J Formos Med Assoc 2006;105(2):172–176]

Key Words: hypopituitarism, neuropsychiatric symptoms, traumatic brain injury

Traumatic brain injury (TBI) is an ongoing pandemic with an annual incidence of 1.5–2.0 million in the U.S.¹ The incidence of neuropsychiatric disturbances after TBI is also high. Depending on the study, 10–80% of people who sustain TBI suffer from a psychiatric disturbance at some point in their recovery period.² Researchers have consistently suggested that the neuropsychiatric problems of individuals who sustain TBI may actually be the major challenge facing rehabilitation. However, neuropsychiatric or cognitive disturbances after TBI are commonly regarded as irreversible sequelae of organic brain injuries and current therapies for these patients are costly and largely ineffective.

We report a case of hypopituitarism presenting as post-TBI neuropsychiatric disturbance. The neuropsychiatric symptoms resolved almost completely after the initiation of hormone replacement therapy. The importance of hypopituitarism as a potential reversible cause of neuropsychiatric or cognitive disturbances after TBI is discussed.

Case Report

A 77-year-old man had a history of hypertension for many years without medical control. After he fell and hit his head on the ground, his mental status deteriorated rapidly (Glasgow Coma Scale, E1M5Vt). Head computed tomography (CT) revealed right frontotemporoparietal subdural hemorrhage and subarachnoid hemorrhage with mass effect (Figure 1). Emergency hematoma evacuation resulted in excellent neurologic recovery. He could perform normal daily activities 2 weeks after the operation and was discharged.

Two months after the operation, however, he complained of headache and dizziness. Memory
impairment, especially involving short-term memory, developed, and he gradually lost most of his ability to deal with daily affairs, such as the ability to calculate. He had visual and auditory hallucinations, especially at night. Inattentiveness, loss of affect, change in personality characterized by bad temper, disturbed sleep patterns, easy fatigability, and poor appetite with decreased dietary intake also developed. He was, therefore, readmitted for further evaluation.

On neurologic examination, he was awake and alert but with poor attention. He looked apathetic. He was oriented to time and place but was disoriented to people. His speech was coherent and relevant. Short-term memory was impaired. Other physical examinations were unremarkable.

Head CT scan on admission revealed only mild subdural effusion in bilateral frontotemporal areas (Figure 2). Cerebrospinal fluid (CSF) study was normal. Biochemistry studies showed only mild hyponatremia (sodium, 132 mmol/L) and mild hypokalemia (potassium, 3.4 mmol/L). He was hydrated with parenteral fluids for nutritional support and for correction of electrolyte imbalance. However, the neuropsychiatric disturbances persisted. His clinical course during hospitalization was complicated by an episode of nosocomial pneumonia which developed on the 26th hospital day, and mental status deteriorated rapidly to stupor thereafter. Repeat CSF study was negative and repeat brain CT revealed no new findings. The pneumonia gradually subsided after parenteral antimicrobial therapy, but he remained stuporous. Endocrine evaluations on the 40th hospital day showed low serum levels of adrenocorticotropic hormone (ACTH), cortisol, free thyroxine (free T4), high-sensitivity thyroid stimulating hormone (hTSH), total testosterone, luteinizing hormone (LH), follicle stimulating hormone (FSH), and growth hormone (GH), with an elevated prolactin level (Table). Panhypopituitarism after TBI was diagnosed.

Oral prednisolone (5 mg and 2.5 mg twice daily) was prescribed, and his consciousness became clear the following day. Oral levothyroxine (50 μg daily) was subsequently prescribed. He became fully oriented within a few days. He gradually regained most of his ability to perform daily activities. Physical endurance also gradually improved, and he could ambulate independently a few months later. Follow-up endocrine evaluations 2 months later showed normalized free T4, with persistently low serum levels of ACTH and cortisol (Table). Follow-up biochemistry studies showed normalized serum potassium (4.2 mmol/L), sodium (142 mmol/L) and fasting glucose (95 mg/dL) levels.

Discussion

Posttraumatic hypopituitarism is an uncommon disease. Benvenga et al screened the literature from 1970 to 1998 and found only a total of 367 cases of posttraumatic hypopituitarism. It was predominantly a medical problem of young men, with a reported male to female ratio of 5 to 1, and a peak incidence in the 11–29-year-old group. Road acci-

Figure 1. Head computed tomography scan obtained immediately after the fall reveals right frontotemporal subdural hemorrhage and subarachnoid hemorrhage with mass effect.

Figure 2. Head computed tomography scan obtained 2 months after surgery reveals mild subdural effusion in bilateral frontotemporal areas. The pituitary gland could not be clearly demonstrated.
Our patient developed posttraumatic hypopituitarism, which presented with cognitive impairment, disturbed sleep patterns, personality change, loss of affect, and visual and auditory hallucinations 2 months after TBI. The causal relationship between neurropsychiatric disturbances and hypopituitarism was clear, and the response to hormone replacement therapy was prompt and almost complete. The possibility of age-related endocrine alterations in our patient could be excluded based on reference values from previous studies.5–12

Although posttraumatic hypopituitarism is relatively rare, a growing body of evidence indicates that the incidence of hypothalamic or pituitary dysfunction in patients sustaining TBI is high. Many prospective studies13–22 that conducted endocrine evaluations in patients after TBI revealed consistent findings suggestive of pituitary/hypothalamic dysfunction, such as GH deficiency (9–50%),13,14,18,19,21,22 hypogonadotropic hypogonadism (14.0–56.2%),14,17,20,22 reduced LH/FSH response to stimulation test (4.7–30%),13,19,20 secondary hypothyroidism (10–28%)14,15,18,22 or reduced TSH response to stimulation test (4.5–40%),18,19 and elevated prolactin level (3.8–100%).15,17,18,20,22 These endocrine abnormalities were demonstrated even after decades18,19 or in otherwise stable patients.18 In two large series,19,21 the frequency of reduced GH response to stimulation tests (14.6% and 21%) and low insulin-like growth factor-1 levels (18.8% and 11.4%) were strikingly high. Furthermore, autopsy reports of patients who died

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<th>Table. Serum hormone levels</th>
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<tr>
<td>40th hospital day</td>
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<td>Cortisol (8 A.M. μg/dL)</td>
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<td>ACTH (8 A.M. pg/ml)</td>
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<td>Free thyroxine (ng/dL)</td>
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ACTH = adrenocorticotropic hormone; FSH = follicle stimulating hormone; GH = growth hormone; hs-TSH = high-sensitivity thyroid stimulating hormone; LH = luteinizing hormone.

ments accounted for about three fourths of cases, but it may occur after any type of head trauma.5 The majority of patients (71%) developed symptoms of hypopituitarism within 1 year. However, it may become clinically evident at any time after the accident, and 15% of patients were diagnosed ≥ 5 years after the trauma. Skull fractures complicated about half of all cases. In most cases, coma lasted for days or weeks.3 Diabetes insipidus occurred in only about one in three patients with posttraumatic hypopituitarism. Deficiency in FSH and/or LH was reported in almost 100% of cases. TSH and ACTH deficiency occurred in about half of cases (43.3% and 52.8%, respectively). The clinical picture is highly variable because of the wide spectrum of possible endocrine dysfunctions. The most frequent symptoms were hypogonadism in adults (amenorrhea/infertility in women, erectile dysfunction/loss of libido in men).3 Constitutional symptoms, such as weight change, easy fatigability, muscle weakness, nausea, poor appetite, and cold intolerance, are also frequently observed.3,4

Previous reports linking neuropsychiatric disorders with posttraumatic hypopituitarism have been rare. Springer and Chollet reported a case with severe cognitive impairment as the predominant symptom of posttraumatic hypopituitarism, which improved significantly after hormone replacement therapy.5 Endocrinologic evaluation in that case showed only growth hormone deficiency (peak GH concentration < 0.5 mIU/L).
immediately or soon after TBI also showed high incidences of pituitary lesions (28–69.6%) and hypothalamic lesions (42.4%).3,23

The clinical manifestations of hypopituitarism may resemble the long-term neuropsychiatric or cognitive disturbances after TBI. GH deficiency in adults has been reported to be associated with decreased quality of life and impaired psychosocial wellbeing, characterized by decreased vitality and energy, depressed mood, emotional lability, impaired self-control, anxiety, poor concentration, low self-esteem, increased social isolation, and difficulty in maintaining gainful employment.24 Testosterone deficiency has been associated with mood and behavior disturbances, including depression, irritability, insomnia and anxiety, which are improved by hormone replacement therapy.24 Hypothyroid patients may present with fatigue, decreased libido, memory impairment, disruption of sleep patterns, or true organic psychosis.24 Patients with adrenal insufficiency may present with apathy, social withdrawal, fatigue, poverty of thought, and negativism.24 Therefore, it is reasonable to consider posttraumatic hypopituitarism as an important reversible cause of neuropsychiatric or cognitive disturbances in patients sustaining TBI.

If the high incidence of pituitary dysfunction after TBI shown in previous studies13–22 is accurate, the estimated annual incidence of posttraumatic hypopituitarism in the United States would be between 0.13 and 1.2 million a year. However, in a recent review, only 367 cases of posttraumatic hypopituitarism were found after screening the literature from 1970 to 1998.3 This discrepancy between the high incidence of pituitary dysfunction demonstrated in patients sustaining TBI and the relative rarity of reported cases of traumatic hypopituitarism might reflect the fact that pituitary dysfunction after TBI is under-diagnosed. For example, in a clinical study, 125 consecutive TBI cases admitted to a hospital were reviewed, and hormone assays were performed in only two cases.25 Neurosurgeons are familiar with diabetes insipidus associated with TBI, but may not pay enough attention to syndromes of hypopituitarism which may occur months or years after injury. The onset of symptoms of posttraumatic hypopituitarism is insidious, so it may escape the attention of both the physician and patient, or the symptoms may be ascribed to posttraumatic neurosis. Neurosurgeons or rehabilitationists should be aware of this rare but potentially reversible complication of head trauma. This case highlights the potential importance of endocrine evaluation in patients with neuropsychiatric or cognitive disturbances after TBI.

There have been few prospective studies evaluating the potential role of hypopituitarism in patients sustaining neuropsychiatric or cognitive disturbances after TBI. A recent prospective study demonstrated associations between verbal/visual memory and peak GH levels.26 Gonadotropins and testosterone levels were also associated with visuoconstructual abilities. Further research may be needed to clarify the causal relationship between neuropsychiatric disturbances and hypopituitarism after TBI and to evaluate the responses to hormone replacement therapy. The risk factors and screening criteria also need to be defined in future studies.

References


