**Panhypopituitarism due to Transection of the Pituitary Stalk Diagnosed Nine Years after Traumatic Brain Injury**

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**Abstract**

Traumatic brain injury is frequently involved in cases of hypopituitarism. We report a case of panhypopituitarism due to transection of the pituitary stalk that we diagnosed 9 years after the traumatic brain injury. If a patient develops unexplained or non-specific symptoms, the physician should consider the possibility of hypopituitarism.

**Keywords:** Panhypopituitarism; Brain Injury; Trauma

**Key Clinical Message**

Hypopituitarism is frequently associated with traumatic brain injury, usually presenting acutely post-injury. However, it may present some years later. Thus, if a patient has a history of a traumatic brain injury develops unexplained or non-specific symptoms, hypopituitarism should be considered. Prompt investigation and treatment are required for optimal outcomes.

**Introduction**

Traumatic brain injury is frequently associated with the dysregulation of pituitary hormone secretion during the acute phase [1-3]. In addition, more than 35% of patients exhibit some degree of hypopituitarism within three months post-injury [4]. The subsequent decrease in levels of adrenocorticotrophic hormone (ACTH), thyroid-stimulating hormone (TSH), and antidiuretic hormone can be life-threatening. Moreover, the clinical onset can be acute and severe, requiring intensive in-hospital care [5]. However, there have been no reports of panhypopituitarism with non-specific symptoms occurring several years after experiencing a traumatic brain injury. Herein, we report a case of panhypopituitarism due to transection of the pituitary stalk, which we diagnosed 9 years after the patient’s traumatic brain injury occurred. Careful consideration of hypopituitarism is warranted after a traumatic brain injury, even when presenting symptoms are non-specific or when the injury occurred several years prior to presentation.

**Case Report**

A healthy 68-year-old man sustained a serious head injury after he fell from heavy machinery and was caught between the equipment and the ground. He was moved to the hospital, comatose and with severe epistaxis. Computed tomography (CT) of the head revealed a basilar skull fracture, cerebral edema with midline shift, intracranial hemorrhage, and pneumocephalus (Figure 1). The patient did not have diabetes insipidus. His neurological status gradually improved with conservative therapy. He was subsequently transferred to a rehabilitation hospital and was discharged three months later. However, the patient reported fatigue and excessive somnolence, which began after his stay in the rehabilitation hospital. These symptoms led to a diagnosis of higher brain dysfunction. The fatigue worsened in the two months before being hospitalized.

**Figure 1:** Computed tomography of the head revealed a basilar skull fracture, cerebral edema with midline shift, intracranial hemorrhage, and pneumocephalus. (a) Axial view, (b) and (c) Axial image with bone windows.
at our institution, which was nine years after his head injury. He became lethargic five days before hospitalization and was ultimately admitted via the emergency department of our hospital.

His vital signs at presentation were as follows: body temperature 35.1°C, blood pressure 117/77 mmHg, pulse rate 49 beats/min, respiratory rate 18 breaths/min, and SpO2 value 96% in room air. Physical examination revealed a Glasgow Coma Scale score of 14 (E3 V5 M6), with normal pupil size and pupillary light reflex. As sequelae of his previous head injury, he had bilateral ptosis, left ocular medial deviation, visual loss in his left eye, and hearing loss in his left ear. We confirmed negative results for the Barre and Mingazzini tests. Laboratory data were as follows: white blood cell count, 5,440/µL (neutrophils, 30.0%; lymphocytes, 58.0%; monocytes, 5.4%; eosinophil granulocytes, 5.9%; basophils, 0.7%); hemoglobin level, 10.1 g/dL; platelet count, 14.2 × 104/µL; blood urea nitrogen level, 15.7 mg/dL; creatinine level, 0.95 mg/dL; aspartate aminotransferase level, 32 IU/L; alanine aminotransferase level, 12 IU/L; creatine kinase level, 469 IU/L; C-reactive protein level, 0.65 mg/dL; Na level, 133 mEq/L; K level, 3.9 mEq/L; and Cl level, 98 mEq/L. We suspected adenalin insufficiency and hypothyroidism and performed stimulation tests to determine the basal levels of various hormones (Table 1). We assessed the corticotropin-releasing hormone (CRH)-ACTH-adrenal axis; the patient’s plasma ACTH level was < 1.0 pg/mL. The rapid ACTH challenge test demonstrated a poor response in serum cortisol levels. The lack of an adequate cortisol response to ACTH was most likely a consequence of adrenal gland depletion due to longstanding low serum ACTH levels. The CRH challenge test revealed a poor response in ACTH and cortisol levels. The peak plasma ACTH concentration was < 30 pg/mL. We assessed the activity of luteinizing hormone-releasing hormone (LH-RH) and gonadotropin by measuring serum levels of LH, follicle-stimulating hormone (FSH), and testosterone. These levels were 0.1 mIU/mL and 0.5 mIU/mL, and < 10 ng/mL, respectively. The LH-RH challenge test demonstrated poor responses in LH and FSH levels. The TSH level was elevated and there was a response to thyrotropin releasing hormone (TRH), although this was delayed. The prolactin (PRL) level was normal, but displayed a blunted response to TRH. These results suggested tertiary rather than secondary hypothyroidism. The level of serum growth hormone (GH) was < 0.02 ng/mL, and that of serum insuline-like growth factor-1 was 7.2 ng/mL. The GH-releasing peptide-2 test revealed a poor response in serum GH levels. Given all these findings, we diagnosed the patient with panhypopituitarism.

Head CT and horizontal magnetic resonance imaging (MRI) revealed no significant findings. However, sagittal MRI of the pituitary gland revealed an atrophic anterior lobe, an empty sella, a pseudo-posterior lobe of the pituitary gland, and transection of the pituitary stalk (Figure 2). Empty sella syndrome is an anatomical and radiological abnormality that is not always accompanied by hormonal insufficiency. Therefore, we assumed that the cause of the panhypopituitarism was transection of the pituitary stalk resulting from the previous brain injury, and that the hormonal changes observed were of hypothalamic origin. We treated the patient with oral hydrocortisone (15 mg daily), and introduced levothyroxine sodium hydrate (25 μg daily) 1 week later. The patient responded to this treatment and subsequently completed in-hospital treatment with notably increased attention and improved functional ability.

**Discussion**

This case highlights two important clinical issues. First, hypopituitarism due to transection of the pituitary stalk can be diagnosed several years after a traumatic brain injury. Second, hypopituitarism due to transection of the pituitary stalk can develop without significant symptoms of adrenal insufficiency. Hypopituitarism may develop because transection of the pituitary stalk leads to impaired transport of hypothalamic hormones and nutrients through the hypophyseal portal system. Previous studies of patients who sustained fatal traumatic brain injuries revealed varying degrees of hemorrhagic infarction of the pituitary gland in > 70%, and hypothalamic micro hemorrhages in > 40% of such patients. However, pituitary stalk lesions are not typically considered a major cause of brain injury-induced hypopituitarism [6]. In the present case, T1-weighted MRI revealed anterior lobe atrophy and formation of a pseudo-posterior lobe of the pituitary gland, suggesting that the pituitary stalk transection was caused by the head trauma. MRI revealed an association of the post-injury pituitary stalk lesion with the skull fractures and brain swelling. Moreover, although the risk of anterior gland injury is greatest after a basilar skull fracture, the anterior gland can also be injured after any skull fracture or even due to brain trauma in the absence of fracture [7,8].

Traumatic brain injury-related hypopituitarism remains largely

<table>
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<th>Endocrine studies</th>
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<tr>
<td>TSH level (mIU/mL)</td>
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<tr>
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<tr>
<td>fT4 level (ng/dL)</td>
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<td>ACTH (pg/mL)</td>
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<tr>
<td>Cortisol (µg/dL)</td>
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<td>4.5-21.1</td>
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<tr>
<td>Testosterone (ng/mL)</td>
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<td>230-1037</td>
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<tr>
<td>Growth hormone (ng/mL)</td>
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<tr>
<td>Somatomedin-C (ng/mL)</td>
<td>7.2</td>
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**Table 1: Endocrine study.**

Figure 2: MRI of the pituitary gland revealed an atrophic anterior lobe, empty sella, and a pseudo-posterior lobe of the pituitary gland (the arrow indicates the lesion). (a) T2W sagittal view, (b) T1W coronal view, and (c) T1W sagittal view.
under-diagnosed. This is mostly due to a lack of awareness among physicians who are likely to care for the affected patients [7]. Thus, many undiagnosed or misdiagnosed patients with traumatic brain injury-related hypopituitarism exist. These patients likely experience a lower quality of life and shorter life expectancy, compared with patients who are correctly diagnosed. In the literature, approximately 20 % of patients developed pituitary hormonal deficiencies at 6–9 months after a traumatic brain injury [9], and most patients developed hypopituitarism within one year post-injury, with only a few diagnoses confirmed several years post-injury [10]. To the best of our knowledge, this is the first report of panhypopituitarism due to transection of the pituitary stalk that was diagnosed several years after the causal brain injury.

Hypopituitarism due to transection of the pituitary stalk can develop without significant symptoms of adrenal insufficiency, such as hypotension, hypoglycemia, or hyponatremia. In the case presented, diabetes insipidus had not developed in the presence of a pseudo-posterior lobe, because vasopressin secretion was preserved from the transected part of the stalk. The signs and symptoms associated with hypopituitarism often mimic the sequela of traumatic brain injury, and the patient may develop vague symptoms, such as anorexia, malaise, weight loss, lethargy, and nausea. A previous study recommended that patients with more severe forms of brain injury, and especially patients with basilar skull fractures or early diabetes insipidus, be closely monitored for signs and symptoms of endocrine dysfunction [11]. However, symptom severity is not necessarily related to the severity of the injury. The patient’s medical history can provide important clues to support a diagnosis of hypopituitarism due to traumatic brain injury, but patients may not report their history of traumatic brain injury, particularly if they were not admitted to a hospital or if the injury caused only mild-to-moderate damage. Therefore, physicians should obtain a detailed medical history from patients who exhibit unexplained hypotension, weight loss, fatigue, loss of libido, and/or depression. Furthermore, physicians should consider questioning both the patient and their relatives, as well as testing for pituitary hormone abnormalities [12,13].

**Conclusion**

Hypopituitarism due to transection of the pituitary stalk can exist for several years after the causal brain injury without significant symptoms of adrenal insufficiency, such as hypoglycemia or hyponatremia. Therefore, given the high incidence of pituitary dysfunction after traumatic brain injury, physicians should obtain a detailed history-both of the present illness and past medical history-and should perform a detailed examination of the patient. If hypopituitarism is suspected, hormonal testing should be performed as soon as possible to enable early initiation of hormone replacement therapy, for all complicated cases of mild, moderate, or severe traumatic brain injury.

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**References**