Pituitary Dysfunction After Traumatic Brain Injury (TBI)

By Arthur Croft, DC, MS, MPH, FACO

Years ago, an internist colleague, Keith Sehnert, and I reported on over 100 whiplash patients who had developed hypothyroidism in the aftermath of acute whiplash injury. In contrast to the more common clinical finding of decreased T4 and an elevated thyroid-stimulating hormone (TSH), we usually found either normal TSH or low TSH, speculating that these cases might be the result of a central (e.g., hypothalamic) form of pituitary dysfunction.¹ These findings are of special interest to me because I developed hypothyroidism following my own mild traumatic brain injury (MTBI).

Nine years after our paper was published, I continue to get the occasional inquiry on this interesting subject for which the literature remains rather scant - just recently from an internist in Israel. Scant though the literature may be, according to the authors of a more recent paper, the first documentation of pituitary failure from TBI goes back to 1918.² Complicating recognition of the connection between injury and the development of hypothyroidism is the thyroid gland’s ability to store up to four months’ worth of hormone, coupled with the fairly common occurrence of the condition among the uninjured.

The association between TBI and various endocrinological conditions seems to be, at least from my experience, not widely appreciated. A question we raised in 1996 was, "How many cases of hypothyroidism (or indeed, any form of hypo- or hyperpituitarism) are the downstream result of TBI and how often is this association not made?" The authors of the present paper also voiced the concern that the signs of hypopituitarism may often go unrecognized and cautioned that clinicians should watch for them in their TBI patients. Even when they are eventually recognized clinically, how often are these conditions attributed correctly to prior trauma? I suspect this attribution is frequently overlooked; MTBI itself is often overlooked by clinicians.

Bondanelli, et al., studied the occurrence and risk factors of pituitary dysfunction, including growth hormone deficiency (GHD), in 50 patients (mean age 37.6 +/- 2.4 years; 40 males, ages 20-60 years; 10 females, ages 23-87 years) with TBI over five years.² According to the Glasgow Coma Scale (GCS), 16 patients had suffered from mild, 7 from moderate, and 27 from severe TBI. The Glasgow Outcome Scale (GOS) indicated severe disability in 5, moderate disability in 11, and good recovery in 34 cases.
The authors demonstrated several cases in which T4 and TSH were low and one case in which T4 was low with a normal TSH. Similar to our own findings, in no cases did they find high TSH. This paper is a good source of references to this interesting literature (although the authors apparently did not find our 1996 paper). They cite studies, for example, that report finding hypopituitarism in 60-69 percent of TBI cases, which supports their own findings.

The symptoms of GHD include significant alterations in body composition, decreased muscular strength, low exercise capacity, and diminished bone mineral content, as well as impairments in the sense of well-being and quality of life. To evaluate this, the authors infused GH-releasing hormone (GHRH) and arginine intravenously and measured the spike in GH at several intervals after that. A GH peak higher than 16.5 Âµg/L was considered normal; less than 9 Âµg/L was considered diagnostic for "severe" GHD. ACTH was normal in all cases. The breakdown of their findings was as follows:

- GHD: 51.8%
- Hypogonadism: 25.9%
- Hyperprolactinemia: 14.8%
- Hypoprolactinemia: 14.8%
- Hypothyroidism: 18.5%

Decreased LH and FSH were found in 22 percent of the test subjects.

Most of these patients were males. There was a relationship to injury severity on the basis of the GCS, although even individuals with MTBI showed abnormalities - but interestingly, not to the appearance on CT. There also was no correlation with GOS (1 = death; 2 = persistent vegetative state; 3 = severe disability; 4 = moderate disability; 5 = good recovery). The authors speculate that the injury might be blamed on hypoxic injury to the hypothalamus or pituitary.

In our previous study, we speculated that the central lesions might be in the region of the hypothalamus that could result in a diminished release of thyrotropin-releasing factor (TRF), which regulates the release of TSH, which, in turn, increases all cellular activity in the thyroid gland and the subsequent release of thyroid hormone. The usual negative feedback between the thyroid gland and TSH is that a drop in thyroid hormone production results in a release of TSH from the pituitary gland. This, in fact, is the most common clinical picture in hypothyroidism today, with laboratory studies typically showing an elevation of TSH and a decrease in thyroid hormone. When TSH is low in hypothyroidism, it may signal the involvement of the hypothalamus and a condition we dubbed "posttraumatic hypothyroidism."
Animal studies of TBI have demonstrated that diffuse axonal injuries resulting from brain acceleration injuries are often found in the hypothalamic region - a finding consistent with CT and MRI findings reported in humans exposed to similar forces. It seems likely that such injuries could adversely affect any hormonal axis associated with the hypothalamus and pituitary gland, although there is not much literature on the subject. Bondanelli, et al., offer further support for such a hypothesis, which Keith Sehnert and I had advanced earlier. I think the take-home points of this discussion should be that (a) many of these conditions occur in the weeks or months following the injury; (b) these conditions are often subtle and may go unnoticed until they become progressively more severe with time; and (c) by the time they are recognized, associations between the initial injury and clinical manifestations are frequently overlooked. Laboratory tests are simple ways of following MTBI patients.

References


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