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## Penetrating brain injury with hypopituitarism

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### ABSTRACT

A 34-year-old healthy male presented as a trauma activation after sustaining a gunshot wound to his face. CT head imaging was suggestive of a ballistic fragment adjacent to a posterior wall sphenoid sinus fracture with likely a small volume of adjacent blood products. He was ultimately diagnosed with hypopituitarism which included central diabetes insipidus, central hypothyroid, and adrenocorticotropic hormone deficiency secondary to cortisol deficiency. This case illustrates the spectrum of endocrine dysfunction that can occur with skull base injuries, and the appropriate pituitary-function screening and treatment that should be performed if there is clinical concern. Early recognition and prompt treatment of pituitary insufficiency can facilitate overall rehabilitation after TBI.

### Background

Traumatic brain injury (TBI) has an incidence of 2.8 million cases per year in the United States and accounts for roughly 50,000 deaths annually [1]. Over the last 15 years, a high rate of pituitary gland dysfunction has been reported following TBI, revealing post-traumatic hypopituitarism (PTHP) contributes significantly to morbidity and mortality [2]. A 2007 meta-analysis of 19 studies noted PTHP has a prevalence of 27% and is more common with moderate to severe TBI [2]. Hypopituitarism after TBI was first described in 1918 by Cyran et al.; however, non-specific symptomatology and the lack of an agreed approach to screening for PTHP has led to significant under-diagnosis [2]. Injury patterns hypothesized to be associated with PTHP in blunt trauma include mechanisms resulting in direct traumatic injury to the pituitary from base of skull fractures, hypoxia, hypotension, or raised intracranial pressure [2]. While PTHP is most common after blunt TBI, this report describes a penetrating brain injury leading to hypopituitarism, supporting the role for increased vigilance of PTHP in all mechanisms of TBI.

### Case

A 34-year-old healthy male presented after sustaining a gunshot wound to his face approximately 30 min prior to arrival. On initial evaluation, he had a significant amount of bleeding from his mouth. He was hemodynamically unstable with a heart rate in the 140 s. He received 2 units of whole blood with improvement in his hemodynamics. His Glasgow Coma Scale (GCS) was 15 without focal

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neurologic deficits.

Due to significant oro-facial bleeding, ENT performed an awake fiberoptic intubation. On further evaluation, his right maxillary penetrating injury traversed the hard and soft palate involving several teeth and communicated with the nasal floor (Fig. 1). CT head imaging demonstrated a ballistic fragment adjacent to a posterior wall sphenoid sinus fracture in the sella turcica with a small volume of adjacent blood products (Fig. 2). No other acute injury was identified. The wound was packed with kerlix to obtain hemostasis. Additionally, a tongue laceration and upper lip laceration were identified and repaired.

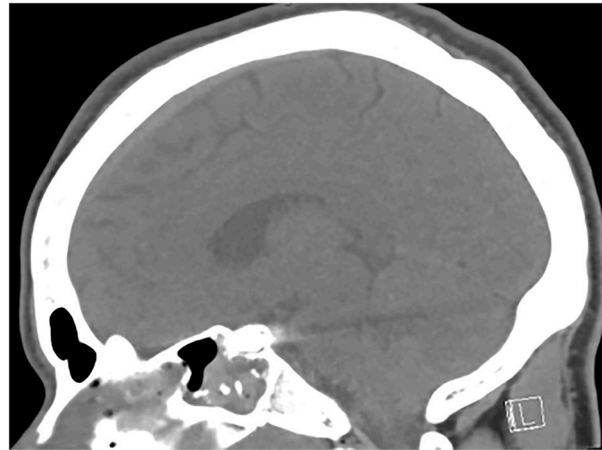
The following day, the patient was noted to have seizure-like activity in the ICU with an associated decline in his GCS from 11T to 3T. A repeat CT head was unchanged from admission. EEG was negative for status epilepticus or seizure. Subsequently, the patient underwent a formal washout, debridement, removal of several teeth, complex laceration repair, tracheostomy, and percutaneous endoscopic gastrostomy tube placement. Post-operatively, his GCS improved to 6T; however, he was noted to have a large volume of urine output. Blood chemistry at that time demonstrated a significant elevation in his sodium level, from 139 to 154 mmol/L, concerning for central diabetes insipidus (DI). Serum osmolality (osm) and urine osm were obtained, revealing 319 mOsm/kg and 245 mOsm/kg, respectively. The patient was treated with 2 mg of IV desmopressin (DDAVP) with improvement in urine output, urine osm, and sodium level.

Endocrinology was consulted and recommended DDAVP dosing to urine output of <300 cc/h with goal decrement in sodium concentration of 8–10 mmol/L over 24 h. He was treated with an additional 1 mg IV DDAVP daily to meet these goals. Due to the location of the bullet and new diagnosis of central DI, Endocrinology recommended evaluation of thyroid stimulating hormone (TSH), free thyroxine (T4) and cortisol. TSH was low at 0.393 uIU/mL (normal 0.450–5.330), free T4 was low at 0.5 ng/dL (0.6–1.4 ng/dL), and cortisol was low normal at 8.8 µg/dL.

Based on these findings, he was diagnosed with hypopituitarism which included central diabetes insipidus, central hypothyroid, and adrenocorticotropic hormone (ACTH) deficiency secondary to cortisol deficiency. Levothyroxine 100 µg IV daily and hydrocortisone 10 mg IV every 8 h were added to his treatment regimen. His GCS ultimately improved to 11T and no source was identified for the intermittent decrease in his responsiveness. His hospital course was complicated by *Streptococcus pneumoniae* pneumonia and bacteremia as well as refractory vasovagal episodes requiring placement of a temporary leadless pacemaker. Removal of the ballistic was discussed with Neurosurgery; however, the risk of removal was ultimately felt to outweigh the benefit. The patient was discharged to follow-up with Endocrinology on desmopressin 0.05 mg PO twice daily, levothyroxine 125 µg PO daily, and prednisone 7.5 mg PO daily. He was seen 11 days after discharge doing well and tolerating oral intake. He declined further facial reconstruction, but did complete testing of his gonadal axis which showed low levels of testosterone consistent with hypopituitarism.



Fig. 1. CT face 3D reconstruction demonstrating extensive facial fracture.



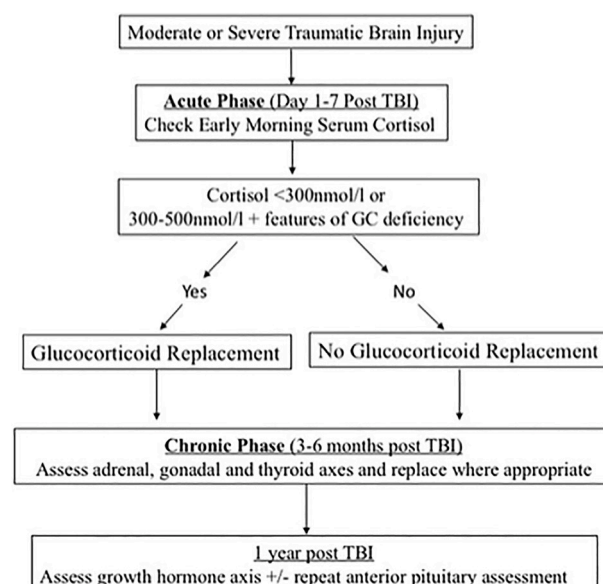
**Fig. 2.** CT head imaging demonstrating a ballistic fragment adjacent to a fracture of the posterior wall of the sphenoid sinus.

## Discussion

PTHP is a common and clinically significant consequence of TBI [2]. The majority of PTHP occurs in the setting of TBI secondary to blunt injury [3]. This case report raises awareness for the potential of penetrating mechanism as a cause of PTHP. Due to the location of the ballistic within the sella turcica, direct trauma to the pituitary gland or secondary injury due to tissue edema were the most likely cause of PTHP.

The hormones underlying PTHP in the ICU include: vasopressin, TSH, and ACTH as well as their target hormones that can be measured via sensitive and reliable immunoassay techniques [4]. Lack of vasopressin can lead to low levels of antidiuretic hormone (ADH), which in turn leads to polyuria and derangements in serum sodium, serum osm, and urine osm. TSH deficiency can be diagnosed using only a thyroid function test. Despite the presence of reduced free thyroid hormones, TSH concentrations that are at or below the normal range implicate dysfunction in the pituitary gland or the hypothalamus [4]. Cortisol levels are normally at their peak in the morning due to diurnal rhythm and it is advisable to measure these concentrations at approximately 8 to 9 am. If the cortisol level is very low or very high then a stimulation test is not needed. [4]. Our patient initially had a derangement in serum sodium and high urine output following his change in clinical status. After further investigation, we additionally found derangements in TSH, free T4, and cortisol. Testing of the gonadal axis should additionally be considered, but is not imperative in the inpatient setting if the patient is critically ill. In the same vein, testing of growth hormone (GH) is critically important in injured children and adolescents [4].

The typical management of the hormone abnormalities of PTHP focuses on addressing each deficiency: ADH, thyrotropin,



**Fig. 3.** Quinn et al. algorithm for the screening and management of post-traumatic hypopituitarism.

corticotropin, gonadotropin, GH, and prolactin. When DI is present, DDAVP can be administered while determining dosing based on the amount of urine and the results of electrolyte levels. In the setting of TSH deficiency, T4 can be administered according to the clinical response and measurement of free T4 concentrations (usually 75 to 125 µg one a day). When administering glucocorticoid, it is desirable to prescribe hydrocortisone at doses of 10 mg, 12.5 mg, or 15.0 mg depending on the clinical response. Under stressful conditions, the dose should be increased to meet the physiologic need [4]. In this case, we initially treated the patient with DDAVP dosing to urine output of <300 cc/h with goal decrement in sodium concentration of 8–10 mmol/L over 24 h, levothyroxine 100 µg IV daily, and hydrocortisone 10 mg IV every 8 h. The patient was ultimately transitioned to desmopressin 0.05 mg PO twice daily, levothyroxine 125 µg PO daily, and prednisone 7.5 mg PO daily with outpatient follow up.

The incidence of penetrating injury to the head involving the sella turcica is unknown and this case report is the first to the authors' knowledge to show PTHP in the setting of a penetrating brain injury. It brings to light the spectrum of endocrine dysfunction that can ensue and the complexity of management. Early diagnosis of hormone deficiency has an important impact on a patients' degree of recovery from TBI [4]. Quinn et al. presents a potential algorithm for early diagnosis and identification of this condition, (Fig. 3) [2]. Hormone replacement therapy has been shown to improve rehabilitation outcomes and quality of life [4]. This case illustrates the need for high vigilance in the setting of a unique presentation of PTHP. The involvement of Endocrinology may be necessary in the acute phase as well as for outpatient management and follow up [3].

## Conclusions

PTHP occurs in the setting of moderate and severe TBI. Early recognition and prompt treatment of pituitary insufficiency can facilitate overall rehabilitation. While this mechanism of injury and associated endocrine dysfunction is rare, this case report brings to light a unique etiology that can impact our trauma patient population.

## Funding

None.

## Statement of consent

Formal consent was not obtained for this case report; however, confidentiality was protected by collecting only the information needed to evaluate this case and minimizing to the fullest extent any information that could directly identify the subject.

## Declaration of competing interest

The Author(s) declare(s) that there is(are) no conflict of interest.

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