A case of acute areflexic, flaccid quadriplegia resulting from acute hypophysitis

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ABSTRACT

Introduction: Acute flaccid paralysis, though relatively common, can pose a diagnostic challenge because of its varied etiology. Case Report: We report a 42-year-old Afro-Caribbean woman whose third and final admission over a 3-week period was because of acute onset quadriparesis. At the final admission, she had flaccid paralysis, no ankle and knee reflexes, and equivocal plantar responses. Investigations revealed severe hypokalemia and hypernatremia, increased creatinine, and low adrenocorticotropic hormone, cortisol, follicle-stimulating hormone, luteinizing hormone, and thyroid-stimulating hormone. She had marked polyuria and increased plasma osmolality. Atrial natriuretic factor was detected and chest computed tomography showed a dilated esophagus and bilateral acute pulmonary emboli. Magnetic resonance imaging revealed an enlarged 1.2x1.4x1.8 cm pituitary gland showing enhancement, indicating hypophysitis. She was diagnosed with quadriplegia secondary to hypokalemia and neurogenic diabetes insipidus secondary to panhypopituitarism involving the stalk, which is postulated to have resulted from acute hypophysitis. She made a complete recovery following treatment with intravenous potassium, fluids and hormone replacement. Conclusion: Hypophysitis-induced panhypopituitarism with diabetes insipidus remains a rare cause of quadriplegia.

Keywords: Diabetes insipidus, Hypokalemia, Hypophysitis, Quadriplegia

INTRODUCTION

Quadriplegia is rare and can result from a number of conditions, including central nervous system, neuromuscular junction and muscle disorders, Guillain-Barré syndrome, systemic envenomation, and electrolyte disturbances caused by panhypopituitarism [1]. Hypopituitarism, defined as partial or complete deficiency of pituitary hormones [2, 3], can present in many ways depending on the severity and extent of hormone deficiency [4]. Possible causes are isolated hormone deficiencies (hypothyroidism, hypoadrenocorticism) and panhypopituitarism with deficiency of all anterior pituitary hormones and rarely, posterior pituitary hormones [2]. Clinical presentation depends on the hormones involved, patients can be asymptomatic, subclinical, or critical [5]. Adult hypopituitarism can be congenital or acquired. Acquired hypopituitarism has varied etiologies,
including tumors, surgery, inflammation, infection, trauma, radiation, infection, and vascular conditions [2]. The incidence rate is 12–42 new patients per million population per year [6]. Few cases have been reported on panhypopituitarism with resultant quadriplegia, particularly that due to acute primary hypophysitis resulting from an autoimmune inflammatory condition [5, 6]. Hypophysitis incidence is estimated to be 1 in 7–9 million [7]. Cases presenting as quadriplegia are even rarer. We have been unable to find any reports of cases in the Caribbean. The case report that follows highlights a case of quadripareisia, hypokalemia, and neurogenic diabetes insipidus from functional panhypopituitarism with involvement of posterior pituitary hormones—a rare disease with a high mortality—that most likely resulted from acute primary hypophysitis.

**CASE REPORT**

A 42-year-old female who presented with a two-month history of slowly progressive generalized weakness, lethargy, and headaches was treated by a private physician who had also requested a thyroid function test. On review of her condition and results of her thyroid function tests 1 week later, she was found to have a reduced thyroid-stimulating hormone (TSH) level of 0.01 µIU/mL (normal range 0.27–4.2 µIU/mL), with normal free T3 and free T4 values; carbimazole was commenced. The patient was re-admitted that same day with vomiting and diarrhea, treated for gastroenteritis, and discharged 3 days later. About a week later, she returned to the hospital with generalized lethargy and decreased power of the limbs—particularly the lower limbs—which made mobility impossible. She experienced no fever, back pain, or significant weight loss, nor did she have any respiratory, cardiovascular, or gastro-enterology symptoms at that time. Her past medical history was unremarkable. She was a lifelong non-smoker and teetotaler and denied using any herbal or over-the-counter medication. She had no family history of neuromuscular disorders. The patient had no menstrual cycles for a few months. Examination was unremarkable, and platelet count of 268×10^3 µL was normal. Blood tests revealed severe hypokalemia and hypernatremia; Cl 127 mmol/L (98–109 mmol/L); blood urea nitrogen 13 mg/dL (8–26 mg/dL); and creatinine 4.9 mmol/L (1.9–25 mg/dL). Corrected calcium was mildly elevated at 10.76 mg/dL. Monospot testing, tuberculin skin test, and rapid human immunodeficiency virus (HIV) yielded negative results. The aldosterone level was 38 pg/mL (4–31 pg/mL), and renin was 215.4 pg/mL (2.99–23.95 pg/mL). Chest radiograph, electrocardiogram, and non-contrast brain computed tomography (CT) showed no abnormalities. Pituitary screening revealed the following: TSH 0.01 µIU/mL (0.27–4.2 µIU/mL); free T4 (thyroxine) 7.7 µg/dL (5.1–14.1 µg/dL); free T3 (triiodothyronine) 1.5 ng/mL (0.8–2 ng/mL); TSH receptor 0.3 IU/L (positive > 2 IU/L); and anti-TPO (anti-thyroid peroxidase) antibody 113.0 IU/mL (0–35.0 IU/mL). Follicle-stimulating hormone (FSH) was 0.50 mIU/mL (1.2–9 mIU/mL); luteinizing hormone (LH) <0.10 mIU/mL (0–12 mIU/mL); prolactin 96.6 ng/mL (1.9–25 ng/mL); adrenocorticotropic hormone <5 pg/mL (0–46 pg/mL); morning cortisol 4.8 µg/dL (5–25 µg/dL); and beta human chorionic gonadotropin 2.74 mIU/mL (0–5.3 mIU/mL). In addition, growth hormone (GH) was 0.143 ng/mL (0–10 ng/mL); 30-min postprandial (pp) GH 0.204 ng/mL; 60-min pp GH 0.3 ng/mL; 90-min pp GH 0.2 ng/mL; and 120-min pp GH 0.3 ng/mL. The B12 level was >1000 pg/mL (180–900 pg/mL). Blood and urine cultures were negative. Nerve conduction studies and electromyography yielded normal results. Brain MRI one week after admission showed a mildly enlarged (1.1x1.5x2.0 cm) pituitary gland with no obvious discrete pituitary lesions (Figure 1). Spine MRI and MR angiography were normal. Apart from hypokalemia and findings of panhypopituitarism, the patient was noted to be passing large amounts of urine. Her calculated water deficit was 11 L and plasma osmolality was elevated at 403 mOsm/kg/L (reference range: 275–295 mOsm/kg/L). Further investigations revealed an anti-nuclear factor (1/40 dilution) +++ homogenous pattern; anti-DNA antibody-negative, extractable nuclear antigen negative, pANCA 2.95 (<10 µ/mL); cANCA N/A; anti-cardiolipin IgG antibody 40.31 µ/mL (<48 µ/mL); and anti-cardiolipin IgM antibody N/A. Brain MRI 1 month after admission revealed an enlarged 1.2x1.4x1.8 cm pituitary gland with enhancement, indicating possible hypophysitis. Optic chiasm was normal with no compression (Figure 2). Three weeks after admission, CT revealed bilateral pulmonary emboli and a dilated esophagus, but no evidence of malignancy. Upper gastrointestinal endoscopy revealed normal results.

The patient was assessed as having panhypopituitarism with possible involvement of the hypothalamic stalk and resultant decrease in antidiuretic hormone, presenting with hypokalemia, polyuria, and quadripareisia. We suspected acute hypophysitis with...
complications of bilateral acute pulmonary emboli and acute kidney injury.

She was initially managed with intravenous fluids and potassium replacement in the intensive care unit; however, this failed to adequately increase her potassium levels. Intravenous hydrocortisone 100 mg three times daily, subcutaneous desmopressin 1 µg twice daily, and oral thyroxine 50 µg once daily resulted in improvement of the patient’s condition three days later.

Two months later, she resumed her normal activities. Repeat renal (Na 141 mmol/L, K 3.8 mmol/L, and creatinine 0.6 mg/dL) and liver and thyroid function test results revealed normal results, and a repeat MRI performed 9 months after the initial presentation revealed a reduction in the size of the pituitary gland (Figure 3). She continues to attend regular follow-up visits in the endocrinology outpatient clinic and is presently under treatment with oral desmopressin 240 µg twice daily, levothyroxine 50 µg once daily, and prednisolone 5 mg once daily.

**DISCUSSION**

Panhypopituitarism is characterized by a complete or partial deficiency of hormones secreted by the pituitary gland [6]. Its prevalence and incidence were reported to be 45 cases per 100,000 and 4 cases per 100,000, respectively [5]. As the anterior and posterior portions of the pituitary gland receives different blood supplies, panhypopituitarism affects these portions differently; the former is more commonly affected. Panhypopituitarism may result from cranial surgery, radiotherapy and tumors, hereditary causes, infiltrative or infectious diseases, and head trauma [5]. Flaccid quadriaparesis can result from myelopathies, neuropathies, neuromuscular junction transmission disorder, myopathies, brainstem infarction, conversion/factitious disorders, thyrotoxic periodic paralysis, barium poisoning, renal tubular acidosis, licorice ingestion, and gastrointestinal potassium losses [8, 9]. Other differentials such as hypoglycemia, hyperaldosteronism, myositis, neuritis, and Guillain-Barré syndrome [10, 11] were excluded upon the confirmation of normal glucose and aldosterone levels, as well as normal results from electromyogram and nerve conduction studies. The patient had no history of intermittent weakness, making hypokalemic periodic paralysis unlikely. The patient’s initially low levels of TSH, FSH, and LH were more consistent with secondary panhypopituitarism and central hypothyroidism rather than with subclinical hyperthyroidism [12]. Thyrotoxic hypokalemia, the diagnosis made in similar studies, was refuted on the basis of low levels of other pituitary hormones and the absence of elevated thyroid hormones [13–16]. The administration of potassium failed to sustain normal potassium levels. According to Kalra et al. [17], neurogenic diabetes insipidus is diagnosed based on clinical history and examination, as well as the presence of polyuria, serum and urine osmolality, as was found in our case. Although further testing on plasma and urine osmolalities could have been performed, such as the water deprivation test or the desmopressin challenge test, our patient’s severe hypernatremia precluded such assessments. The use of desmopressin was essential for the alleviation of weakness [18], which was demonstrated by our case; the delay in diagnosis and treatment with desmopressin led to the worsening of her condition and ultimately required the use of ventilatory support.
Panhypopituitarism with hypokalemic paralysis and neurogenic diabetes insipidus is rare [18]. From the observation of an enlarged pituitary gland with a thickening of the pituitary stalk found on MRI, one can postulate a diagnosis of acute hypophysitis in the absence of other causative factors [19, 20]; however, a transsphenoidal biopsy remains the best method for the diagnosis of hypophysitis [19, 21]. Our case could, therefore, be attributed to hypophysitis of an unknown etiology.

Hypophysitis is an uncommon sellar condition that presents as inflammatory lesions on structures of the hypophysis, including the pituitary gland and stalk [22]. The condition may affect both men and women and is age-independent [23]. It may be primary or secondary; the former refers to isolated inflammation of the pituitary not associated with medication, systemic inflammatory disorders, infections, or other diseases, while the latter includes cases associated with immunotherapy, rupture of sellar cysts (Rathke’s cleft cysts and craniopharyngiomas), and rarely, pituitary adenomas [7, 24]. However, notably, the condition can be associated with several autoimmune-type complications such as IgG4-related hypophysitis [25] and a CTLA-4 blockade [26]. The clinical presentation ordinarily includes headache, nausea and vomiting, hypopituitarism, and diabetes insipidus [23]. A case series of tumor-like hypophysitis was reported in China; headache was observed in the majority of the seven cases [22]. Notably, our patient developed bilateral acute pulmonary emboli, possibly precipitated by dehydration and immobility, as well as a dilated esophagus, possibly resulting from hypokalemia.

Treatment of hypophysitis depends on endocrine dysfunction with hormone replacement, or manifestation of visual or compressive symptoms with surgical resection of the pituitary gland [27]. The use of steroids, repeat surgery, and radiosurgery are recommended in case of recurrence [27]. Patients tend to live normal lives. Close monitoring will require serial pituitary MRI and endocrinological testing of the hypothalamic-pituitary axis. In addition to regular follow-up in the endocrinology clinic, the patient’s treatment includes desmopressin, prednisolone, levothyroxine, and rivaroxaban. Our patient was weaned off mechanical ventilation and is now able to perform all activities of daily living.

CONCLUSION

The case of quadripleasis represents a diagnostic challenge because of its multidimensional etiology: neurological, metabolic, endocrinical, and biochemical factors. Early investigations accompanied by aggressive treatment must be initiated to treat acute hypophysitis and prevent complications. Although extremely rare, acute hypophysitis must be considered a cause of panhypopituitarism.

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