

# Pituitary Hemorrhage in Hemolytic Uremic Syndrome

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**A 5-year-old girl with hemolytic uremic syndrome is reported with pituitary hemorrhage in the acute phase. Seizures, hemiplegia, and transient blindness were observed. These symptoms cannot be attributed to the pituitary hemorrhage; however, pituitary hemorrhage should be added to the list of neurologic lesions that can occur in hemolytic uremic syndrome.**

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## Introduction

Neurologic complications of hemolytic uremic syndrome (HUS) include generalized or focal seizures, alterations of consciousness, hemiparesis, and coma [1,2]. Reported computed tomographic (CT) findings range from normal to diffuse cerebral edema, large-vessel infarctions, diffuse, multiple small-vessel infarctions, or hemorrhage [3-6]. The causes of HUS are considered to be multifactorial but, recently, verotoxin-producing *Escherichia coli* infection was proposed as one of the causal factors [7]. We report a girl with HUS probably associated with *E. coli* 0-157:H7 infection. She demonstrated severe neurologic complications with pituitary hemorrhage on CT in the acute phase of HUS.

## Case Report

An epidemic of HUS occurred at a kindergarten in the eastern Tokyo Metropolitan area in October, 1990. During this period we examined a 5-year-old girl who was admitted to our hospital with anuria after

prodromal gastroenterocolitis manifested by watery-loose and bloody stools.

On admission, she was alert with pale skin but without petechiae or ecchymosis. Blood pressure was 110/70 mm Hg. The platelet count was 71,000/mm<sup>3</sup> and fragmented erythrocytes were observed on peripheral smear. Hemoglobin was 10.7 gm/dl, hematocrit 30%, BUN 102 mg/dl, serum creatinine 4.5 mg/dl, serum sodium 139 mEq/L, potassium 4.7 mEq/L, chloride 103 mEq/L, and calcium 7.3 mg/dl. Blood gas analysis disclosed pH 7.32 and bicarbonate 15 mEq/L. IgM antibody assessed by the Widal method against somatic antigen for *E. coli* strain 0-157:H7 was increased on admission (× 320) and decreased 1 month later (× 80). Antiverotoxin antibody concentration determined by the ELISA method revealed high antibody levels of both antiverotoxin<sub>1</sub> and antiverotoxin<sub>2</sub>. Stool culture confirmed the presence of *E. coli* 0-157:H7.

Three hours after admission, she developed generalized tonic seizures with poor response to antiepileptic drugs. Funduscopic examination revealed no hemorrhage and no cotton-wool spots on the retina.

The initial cranial CT on admission disclosed a high-density lesion in the pituitary gland with no evidence of large-vessel infarctions, no hemorrhage in the centrum semiovale, and no cerebral edema (Fig 1). There were no abnormalities of the geniculate bodies, calcarine cortex, or optic radiations.

The child's hospital course was characterized by prolonged oliguria lasting about 1 month, blindness for longer than 2 months, and spastic hemiplegia for 2 months. Continuous, ambulatory, peritoneal dialysis therapy was successfully performed without hypertension or electrolyte imbalance. During the period of blindness, pupillary responses to light were elicited but were slow and incomplete. Three months after admission, she had no neurologic deficits and her renal function was normal.

Serial CT scans obtained weekly in the acute phase revealed a persistent high-density lesion in the pituitary. Magnetic resonance imaging (MRI) performed 1 month after admission demonstrated high intensity in the T<sub>1</sub> image and low intensity in the T<sub>2</sub> image (Fig 2), suggesting hemosiderin deposit in the pituitary.

Two months after admission, endocrinologic studies were performed. Luteinizing hormone and thyrotropin-releasing hormone loading tests



*Figure 1. On admission, unenhanced axial CT (5 mm thick section) demonstrates high-density lesion at the pituitary gland. This high-density lesion remained unchanged for more than 1 month.*

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Figure 2. Sagittal MRI obtained 1 month after admission discloses a hypointense lesion at the pituitary gland by T<sub>2</sub> image.

disclosed a normal response to luteinizing hormone, follicle-stimulating hormone, and thyroid-stimulating hormone. Arginine (0.5 gm/kg) and insulin (0.1 IU/kg) loading tests revealed an inadequate response of growth hormone (3.0 → 9.3; 5.1 → 6.8 ng/ml, respectively). The adrenocorticotrophic hormone (ACTH) and cortisol response to insulin loading also documented an unsatisfactory response: ACTH (31 → 42 pg/ml) and cortisol (7.96 → 17.27 µg/100 ml).

## Discussion

The pathogenesis of neurologic complications of HUS has not been elucidated. Many metabolic disturbances encountered in this syndrome – hypertension, volume overload, hyponatremia, acid-base changes, hypocalcemia, intravascular coagulation, and microthrombi in the central nervous system (CNS) – may be considered to be causal factors. Intravascular coagulation and microthrombi in the kidney are the hallmark of this syndrome; however, these changes have not been consistently present in the CNS in autopsied cases [1,8].

Our patient had a renal disorder; however, because her metabolic disturbance was relatively mild (normal sodium and calcium concentration and normal blood pressure), her neurologic complications cannot be attributed to the metabolic disturbances. Radiologic examination revealed no infarction, but pituitary hemorrhage was observed. Cranial CT changes reported in this syndrome are various [3-6]; pituitary hemorrhage, however, has not been reported.

Clinically, she demonstrated inadequate response of ACTH and growth hormone to anterior pituitary gland stimulation tests. She now has no apparent sign of ACTH or growth hormone deficiency, but is being carefully monitored. Ocular involvement, especially cortical blindness, has been described occasionally in HUS [2,9,10] and retinal thrombi and opacity also have been reported [11]. The blindness usually is transient and no permanent blindness has been described in the literature. Our patient had no retinal lesions or detectable lesions of the optic tract or cortex on CT and MRI. Pituitary hemorrhage can com-

press the optic chiasm and cause a visual disturbance. We could not demonstrate such compression of the optic chiasm on CT or MRI; however, we speculate that her transient blindness may be related to pituitary hemorrhage.

Since the initial description by Karmali et al. [7], the causal relationship between HUS and antiverotoxin-producing *E. coli*, especially *E. coli* 0-157:H7, infection has been suspected [9,12-14]. We are uncertain whether there is any correlation between antiverotoxin-producing *E. coli* infection and pituitary hemorrhage. These two processes may have occurred in this patient coincidentally; however, because verotoxin causes vascular toxicity in the kidney and neurotoxicity in the CNS at the same time [15], we speculate that there may be some correlation between antiverotoxin-producing *E. coli* infection and pituitary hemorrhage pathologically.

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