Hypothalamic Hypopituitarism following *Shigella* Encephalopathy

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Infectious diseases are one of the possible causes of hypothalamic–pituitary hormone deficiencies [1–3]. Although shigellosis is known to affect the central nervous system, it has not been previously described as an etiologic factor for hypothalamic panhypopituitarism. We present such a case here.

Case Description

A previously healthy 3-year-old boy was admitted because of fever, bloody diarrhea, and generalized convulsions lasting for 10 min. Rectal temperature was 39°C; blood pressure was normal; and there was no respiratory distress, evidence of meningeal irritation, or significant dehydration. The child was lethargic but reacted to painful stimuli. Complete blood count showed 11,400/mm^3 white blood cells, hemoglobin 10.2 g/dl, and platelets 157,000/mm^3. Blood chemistry (SMA-18) was normal. Cerebrospinal fluid tests were normal. Stool cultures grew *Shigella sonnei*.

The child was treated with intravenous ampicillin and fluids. Twelve hours after admission, two short episodes of generalized convulsions occurred and were stopped with diazepam. The patient remained stuporous. Hypertonicity in all four limbs was noted, and mannitol and dexamethasone were added to the treatment. Five days after admission, the child recovered without neurological sequelae.

The child had been growing along the 10th percentile until the acute shigellosis. Following discharge, a decrease in linear growth velocity was noted. At the age of 7 years his height was 4 SDS below the mean for age, weight was in the 5th percentile and head circumference in the 50th percentile. Testicular volume and penile length and diameter were normal. Bone age was 3½ years. Free thyroxine measured 0.3 µg/dl (normal 0.7–2.2 µg/dl), and thyroid scanning showed reduced uptake. After replacement treatment with L-thyroxine, a series of stimulation tests showed blunted response of growth hormone and cortisol, and normal responses of luteinizing hormone, follicle-stimulating hormone and testosterone [Table]. However, stimulation tests for thyrotropin-releasing hormone and growth hormone-releasing hormone were normal. Brain computerized tomography scan and magnetic resonance imaging revealed no abnormalities.

The patient was diagnosed as having multiple hypothalamic–pituitary hormone deficiencies. He was treated with hydrocortisone 10 mg/day, L-thyroxine 0.1 mg/day, and growth

Table 1. Endocrinological tests

Stimulation tests		Hormone tested	Basal level	Peak level	Interpretation
ITT	0.1 U/kg iv	GH (ng/ml)	0.7	1.0	Blunted response
		Cortisol (µg/dl)	7.1	5.9	Blunted response
Clonidine	150 mg/m^2 po	GH (ng/ml)	1.8	3.0	Blunted response
L-dopa	300 mg/m^2 po	GH (ng/ml)	1.6	1.1	Blunted response
GHRH	1 µg/kg iv	GH (ng/ml)	0.9	14.6	Within normal limits
TRH	200 µg/m^2 iv	TSH (mU/L)	7.2	25.1	Normal
		Prolactin (mU/L)	3.8	56	Normal
ACTH	0.25 mg iv	Cortisol (mg/dl)	3.4	9.5	Borderline response
LH-RH	50 µg/m^2 iv	FSH (µg/L)	0.97	1.52	Normal prepubertal response
		LH (µg/L)	1.99	3.67	Normal prepubertal response
HCG	1,500 units im x 3 alternating days	Testosterone (µg/dl)	9	85	Borderline response

ITT = insulin tolerance test; TRH = thyrotropin-releasing hormone; ACTH = adenocorticotropic hormone; LHRH = luteinizing hormone-releasing hormone; HCG = human chorionic gonadotropin; iv = intravenous; po = oral administration; im = intramuscular; GH = growth hormone; TSH = thyroid-stimulating hormone; FSH = follicle-stimulating hormone; LH = luteinizing hormone.

hormone (0.1 U/kg/day). This treatment induced acceleration of growth, and during the 5 years of follow-up he has been growing along the 5th percentile for age.

Comment

Acute shigellosis is associated with central nervous system involvement in up to 50% of patients [4,5], probably due to neurotoxins produced by the bacteria. Besides seizures, which are a common and usually benign complication of shigellosis [4,5], peripheral neuropathy, delirium, coma, and even fatal encephalopathy have been reported [5].

Our patient had acute shigellosis accompanied by encephalopathy and convulsions. Several months later, the child, who was growing along the 10th percentile for age, virtually stopped growing. Subsequent endocrinological investigations revealed panhypopituitarism with growth hormone deficiency, hypoadrenalism and hypothyroidism. On the basis of the normal pituitary hormonal responses to stimulation with hypothalamic hormones (GHRH and TRH), we assumed the disease was caused by a hypothalamic and not a pituitary insult. Acquired hypothalamic–pituitary insufficiency may result from viral or bacterial CNS infection and may present even after a prolonged lag period [2,3]. Possible mechanisms of this complication are inflammation in the hypothalamus or hypophysis, hemorrhage, or increased intracranial pressure resulting in ischemia, infarction, or necrosis [2].

To the best of our knowledge this is the first report of hypothalamic damage resulting in panhypopituitarism due to acute shigellosis associated with encephalopathy. This case emphasizes the need for follow-up of the growth and endocrine functions of children after *Shigella* encephalopathy.

References

1. Hagg E, Astrom L, Steen L. Persistent hypothalamic–pituitary insufficiency following acute meningoencephalitis. *Acta Med Scand* 1987;203:231–5.
2. Kupari M, Pelkonen R, Valtonen V. Post-encephalitic hypothalamic pituitary insufficiency. *Acta Endocrinol* 1980;94:433–8.
3. Pai GK, Rulin HM, Wedemeyer PP, Linarelli LG. Hypothalamic–pituitary dysfunction following group B hemolytic streptococcal meningitis in a neonate. *Pediatrics* 1976;88:289–91.
4. Avital A, Maayan C, Goitein KJ. Incidence of convulsion and encephalopathy in childhood *Shigella* infections. Survey of 117 hospitalized patients. *Pediatrics* 1982;21:645–8.
5. Barrett-Connor E. Extraintestinal manifestations of shigellosis. *Am J Gastroenterol* 1970; 53:234–45.

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