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Case Report

Hypothalamic-Pituitary Dysfunctions in An Infant With Streptococcal Meningitis

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Abstract: A six-month-old infant was treated for virulent streptococcal pneumonia and meningitis. He developed diabetes insipidus, hypothyroidism, hypoadrenalism and growth hormone deficiency post infection. Increased awareness and high index of suspicion, of the association of central nervous system infection with hypothalamic pituitary dysfunction will facilitate early diagnosis and could prevent life-threatening sequlae.
Keywords: Meningitis, streptococcus, pneumonia, hypothalamic-pituitary dysfunction.

INTRODUCTION

Hypothalamic-pituitary insufficiency can be caused by diverse etiologies. These include pituitary tumors (glaioma and craniopharyngioma), post-operative and post-radiotherapy states, vascular condition, head injury, and autoimmune diseases, such as hypophysitis [1-3]. Infection and inflammatory conditions are also increasingly being recognized as important causes. The infectious agents that can cause hypothalamic-pituitary insufficiency are *mycobacterium tuberculosis* and non-mycobacterial agents such as other bacteria, as in *streptococcus pneumoniae*, *group B streptococcus* and *haemophilus influenza*, fungi, spirochetes, viruses, and protozoa [4-13]. Hypothalamic-pituitary dysfunction with overt clinical symptoms is not a common consequence of acute central nervous system infection in children and detailed assessment should be reserved for selected cases [14]. However, unrecognized partial or pan hypopituitarism as a part of a critical illness is associated with worse overall prognosis, increases the risk of sever infectious complication, and reduces the survival rate [10].

This report emphasizes the importance of monitoring hypothalamic pituitary functions, during the illness and later in the follow-up of central nervous system infection, as the clinical features are often non-specific and easily confused with the post-encephalopathy picture.

CASE REPORT

In February 2011, an 8 month old Sirilankan boy, who is previously healthy, presented after 48 hours of irritability and fever. He was born to a 30 year old multigravida mother following uncomplicated pregnancy, labor, and delivery; his birth weight was 3,700 grams. He remained well until the onset of this illness. On admission he was irritable, his temperature was 39 C°, pulse 130/min, respiratory rate 30/min. He also developed intractable seizure in the emergency room and treated with multiple antiepileptic medications, namely: phenobarbitone, tegretol, and lamotrigine. Because of his history and examination, bacterial meningitis was suspected and diagnostic CT scan head with lumber puncture was performed. CSF was turbid with polymorph leukocytosis, low sugar level and positive culture. Patient was admitted to pediatric intensive care unit (PICU) because of uncontrolled convulsion and deterioration of the level of consciousness. He had a stormy hospital course; and he stayed in PICU for 45 days. The CT scan showed subdural empyema, which was increasing in spite of treatment with ceftriaxone and vancomycin. The neurosurgeons were involved at that time and evacuation was done under general anesthesia after 10 days of admission. The head circumference increased in size and an MRI was done, which showed hydrocephalus; therefore a ventriculoperitoneal shunt was inserted after a month of admission. He developed

spastic hemiparesis, roving eye movement with bilateral optic atrophy.

The patient was eventually transferred to the pediatric ward after two months of presentation. At that time, the patient developed classic DI with a triad of polyuria with urine output more than 6 ml/kg/hr, low urine osmolality and high blood osmolality and serum sodium 160 mg/dl. The child, therefore, did not require water deprivation test. He received a treatment with oral DDAVP. The anterior pituitary function tests at that time were normal.

At the age of 3 years, he started to gain weight; serum thyroid hormone level (T4) was done and it was low (8 pmol/l) and TSH (1.5 mU/l). We investigated him further for secondary adrenal insufficiency and the results showed low serum cortisol and low ACTH level. So the patient was started on hydrocortisone (6 mg/m^2/day) and thyroxin (37.5/mcg/day) replacement therapies. In the last six months his growth velocity was < 25th centile, IGF-1 was low and formal growth hormone stimulation test was planned to be done. MRI pituitary showed an absent bright spot of the posterior pituitary.

Table-1: Pituitary function tests

(A) Thyroid function tests

T4 (pmol/l)	TSH (mIU/l)
7.720	2.8
9.960	0.14
8.43	0.66
8.5	2.6
17*	0.05*

* With treatment

(B) Cortisol axis functions tests

Cortisol (nmol/l)	ACTH
145	4
45	1.5
24	3

(C) Growth hormone axis tests

IGF-1 level = 55 ng/ml

GH stimulation test: peak GH level below 2 ng/ml with provocation test (Significantly low when the peak level is below 10 ng/ml)

(D) Posterior pituitary function tests

Test	Serum Na (mg/dl)	Serum K (mg/dl)	Blood osmolality (mmol/l)	Urine osmolality (mmol/l)	Specific gravity
Without treatment	164	4.5	330	142	1000
With treatment	139	4	275	450	1010

DISCUSSION

Hypothalamic-pituitary dysfunction can be caused by diverse etiologies. Pituitary tumor, including craniopharyngioma, glaioma and germinoma, post-operative and radiotherapy, vasculitis and vascular condition, and head-trauma are the commonest [1-3]. Infectious causes such as mycobacterium tuberculosis and non-mycobacterial agent, such bacteria, as as *streptococcus pneumonia, haemophilus influenzae* and *group B streptococcous*, fungi, spirochetes, viruses, protozoa are not that uncommon and involve the pia matter, arachnoid and cerebrospinal fluid [4-12].

The mechanism of the pituitary dysfunction after acute meningitis is not clearly defined, but the pituitary hormone deficiency pattern is suggestive of an ongoing dynamic process. It is reasonable to assume that the incidence and the pattern of hormone deficiency may vary with the type of positive causative agent, and the localization of brain lesion, as well as with the severity of the disease as evident by hydrocephalus and cerebritis. Tantivierdi et al [14] postulated that, an autoimmune hypothalamic-pituitary process could be triggered by acute meningitis.

In the previous studies, isolated posterior pituitary insufficiency has been reported post infections, as well as isolated corticotrophin deficiency. The insufficiency of hydrocortisone and thyroid hormone might interfere with the water excretion, and hence mask the clinical picture of diabetes insipidus. Also both prospective and retrospective studies and case reports demonstrated a variable degree of hypothalamic-pituitary insufficiency and also showed that either transit or permanent hormonal deficiency may occur [4-21]. Further extended studies needed to clarify this important issue. In our patient's illness, with its stormy course, we demonstrated a permanent pan hypopituitarism: hypothyroidism, hypoadrenalism, growth hormone deficiency and diabetes insipidus. The scenario suggested that the severity of the disease could be reflected on the degree of hormonal deficiency.

CONCLUSION

As the symptoms of pituitary insufficiency post infections are non-specific, and the sequlae are devastating and can be life threatening, screening for hypothalamic-pituitary dysfunction is warranted in those cases. Further studies are required to evaluate the hypothalamic-pituitary access using dynamic tests and

MRI brain imaging by if needed. Further workup of autoimmunity needs to be explored in future cases.

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