Short Stature Due to Growth Hormone Neurosecretory Dysfunction in a Child with Major Depressive Disorder

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Literature indicating clinical growth hormone deficiency due to depression is extremely limited, despite a well-known impaired basal and/or stimulated growth hormone secretion in depressive disorders. In this communication, we present a case of short stature due to growth hormone neuro-secretory dysfunction in a nine year old girl with major depressive disorder.

Key words: *Depression, Growth hormone.*

Many studies have shown impaired basal and/or stimulated growth hormone secretion in depressed individual(1-3). However, clinical consequences of depression in growth hormone secretion and linear growth have not been clearly documented yet. Here we report a child with short stature associated with impaired growth hormone secretion and severe depression.

Case Report

This nine-year-old girl was referred to our clinic with the chief complaint of short stature. She had been healthy and developmentally normal until three years prior to the presentation. She grew very poorly since six years of age, which coincided with the time when her father was murdered and three weeks later and she witnessed her mother's suicide. Subsequently, her paternal uncle adopted her and her five-year old younger brother. She was also noted to be significantly introvert after the loss of her parents

On initial physical examination, her weight and height were 17 kg and 108 cm respectively, both significantly below 5th centile. Her height standard deviation score was –4.0 with a body mass index of 14.6. Her upper-to-lower segment ratio was 1.1. She was prepubertal. The rest of the physical examination was unremarkable.

On laboratory examination, her complete blood count, urinalysis, thyroid function tests and biochemistry screening panel (glucose, BUN, creatinin. Na, K, Cl, ALT, AST, calcium, phosphate, alkaline phosphatase, iron, total iron binding capacity) were within normal limits.

Her bone age was of five years old female. A child psychiatry consultation revealed that she had frequent episodes of sobbing and nightmares, sadness, forgetfulness, irritability; poor appetite and lack of interest and participation in play with peers ever since the loss of her parents. She failed in school in first grade when she was seven years old. However, she was an average student in the following school years. Her score on Child Depression Inventory, adopted for Turkish children was 29(4,5). Diagnosis of major depressive disorder and post-traumatic stress disorder were made according to DSM–4(6). An anti-depressant, fluoxetine at a dose of 10 mg/day was initiated because of anticipated difficulty in follow-up because of the family's remote

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location (approximately 450 kilo-meters to our clinic) and poor therapeutic alliance with new parents. Interview with the adopted parents did not indicate any adverse family situation other than poor economic and educational status. Upon determining an annualized growth rate of 2 cm/year in her six months follow-up visit, two growth hormone stimulation tests were planned. She felt better with anti- depressant treatment during the interval and she self-discontinued the medication three months after the initiation. Psychiatric evaluation confirmed some degree of improvement in her mental health, though she was still depressed. She was urged to restart fluoxetine and return to the child psychiatry clinic in three months.

However, she was lost to follow-up until the age of 11½ year. Detailed interval history revealed that she had never resumed fluoxetine. The poor compliance with the clinical visits and fluoxetine was explained by the family with low income, remote location, perceived improving mental health and growth. On psychiatric evaluation, however, she was essentially the same as the previous visit. She was again recommended to start fluoxetine. At that time, her height was 116 cm (height standard deviation score: –4.6) with a weight of 20 kg (body mass index: 14.9). Her bone age was 7 years. She grew 7 cm in 23 months, which represented a growth velocity of 3.6 cm/year. Two growth hormone stimulation tests with L-dopa and insulin generated the peak levels of 16.6 and 9.6 ng/mL respectively. The insulin like growth factor –1 level was low at 70 ng/mL (normal range: 120-328). Since she passed the tests while growing poorly, a 5-hours nighttime growth hormone sampling via an indwelling catheter every half-hour from 10 PM until 3 AM was performed. Her highest growth hormone peak was 3.6 ng/mL with a mean integrated concentration of 1.1 ng/mL. This was thought to be consistent with growth hormone neurosecretory dysfunction and growth hormone treatment was initiated at a dose of 0.045 mg/kg/day(7). She grew 4 cm during the following six months. This time she complied with both medications. Her psychiatric evaluation was found normal and fluoxetine was discontinued. She regular1y kept her appointments in the pediatric endocrinology: and child psychiatry clinics. At the age of about 13 years on her last visit, her height was 127 cm and her weight was 24.5 kg (body mass index: 15.3). She grew 11 cm in 16 months while on growth hormone treatment, which corresponds to a growth velocity of 8.2 cm/year. Her height standard deviation score improved to –4.0. Her bone age was 8 years with a predicted adult height between 25 and 50th centile. Her depression has not recurred.

Discussion

The appearance of growth failure in this patient coincides to a major psychological trauma, which evidently led to a severe depression. Her history, physical examination and laboratory work-up failed to demonstrate any other medical problem to account for her growth failure and short stature. Therefore, her documented severe and long-standing depression remains to be the only explanation for her growth problem. The underlying mechanism of growth failure in association with depression is unclear. Sub optimal nutrition due to poor appetite, which is common in patients with depression, could not be excluded in this case because of unavailability of the premorbid weight record, even though she maintained a normal and almost constant body mass index while under our care. Her low insulin like growth factor –1 levels, normal growth hormone response to pharmacological stimulation and subnormal basal integrated nighttime growth hormone secretion are consistent with neurosecretory

dysfunction, which refers to a subgroup of short and slowly growing children with normal growth hormone responses to classical stimuli but impaired spontaneous growth hormone secretion with low insulin like growth factor –1 levels(7).

It has been assumed that these subjects have inadequate spontaneous growth hormone secretion due to neuroendocrine abnormalities. The secretion of growth hormone is regulated through a complex neuroendocrine control system, especially by the functional interplay of two hypothalamic hormones, growth hormone-releasing hormone and somatostatin. The two-hypothalamic neurohormones are subject to modulation by a variety of neurotransmitters including norepinephrine and seratonin(8). Lower activities of these neurotransmitters are believed to be associated also with clinical depression(9) .There has been ample evidence in the literature indicating disordered growth hormone secretion in depression. Many studies have shown impaired basal and/or stimulated growth hormone secretion in depressed children and adults(1-3). Of note, in one study, 10 adult subjects with major depressive illness showed a growth hormone secretory pattern consistent with growth hormone neuro-secretory dysfunction(10). However, none of those studies integrated growth data. More-over, there have been no published cases of short stature resulting from growth hormone deficiency due to depression. The reason may be that most depressive episodes in children last too short to cause a clinically obvious growth retardation. However, depression in children, when untreated may last 7-9 months; 6-10% of the cases persist even longer as in the present case(11).

The diagnosis in this case should not be confused with psychosocial short stature. The hallmarks of psychosocial short stature other than short stature abusive home environment and bizarre behavior (*e.g.*, polyuria, drinking from the toilet, stealing food, encopresis, pain agnosia, self-abuse) were not present in this case. Another inconsistent feature is her good response to growth hormone treatment, which is typically not observed in-patient with psychosocial short stature(12). Nevertheless, depression and poor growth rates are the common features between our case and the subjects of Ferholt, suggesting regardless of the etiopathogenesis depression may cause clinically overt growth failure, provided it lasts sufficiently long.

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Polyarteritis Nodosa with Renal Artery Stenosis

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Renal angiographic signs in Polyarteritis Nodosa (PAN) vary from aneursyms of medium and small vessels, perfusion defects and delayed emptying of renal arteries. These vascular changes are usually responsible for the hypertension. In this case study stenosis of a main renal artery, an unusual finding in classical PAN, is believed to be the cause of hypertension. Hence renal angiography is essential to define the renal vascular changes and confirm the cause of hypertension.

Key words: *Polyarteritis nodosa, Renal artery stenosis, Hypertension.*

Polyarteritis nodosa (PAN) is a rare multisystem disease of childhood characterized by necrotising vasculitis affecting medium sized arteries(1). We present a case of PAN with an unusual association *i.e.*, stenosis of a main renal artery.

Case Report

A three-year-old boy, first born to non-consanguineous parents, previously in good health, developed fever which was insidious in onset, low grade, intermittent, for a period of 3 months. The fever was associated with generalized muscle pain and painful swelling of knees and ankles on both sides, severe enough to prevent the boy from walking. This was followed by blackish discoloration of the skin overlying the same joints as well as the tip

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