Case Report: Allgrove Syndrome, more than triple A

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Abstract

Allgrove syndrome is a rare autosomal disorder, which is characterized by symptoms of alacrima and adrenal insufficiency. It was first described by Allgrove. It was later, in 1995, diagnosed as a syndrome with variable association of autonomic and neurological manifes-tations. Acutely dangerous in nature, this disorder manifests in the early childhood and of-ten diagnosed along with severe hypoglycemia. Triple A syndrome (All grove syndrome) is a rare autosomal recessive disorder characterized by the clinical triads of adrenal insuffi-ciency, achalasia of cardia and alacrima.

Key words: Autosomal recessive disorder, Alacrima, Allgrove, Hypoglycemia
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Introduction

Allgrove or Triple A syndrome first described in 1978 by Allgrove and his collegues [1], is a rare autosomal reces-sive disorder, characterized by alacrima, achalasia, adre-nal insufficiency resulting from adrenocorticotropic hor-mone resistance. Gazzarian et al later, in 1995, referred it to as 4A syndrome, due to its variable association with autonomic and neurological manifestations [2]. Usually the disease is manifested during the first decade of life with severe hypoglycemia and it can lead to sudden death [1,3, 4]. Hypoglycemia and hyper-pigmentation were the clues for diagnosis in most cases. Alacrima or hypolacrima is probably the earliest and most consistent sign which can aid the diagnosis, which can be easily over looked by the family and physician [4,5]. Achalasia cardia occur in about 75% of patients and may precede adrenal insuffi-ciency by few years [4-6].While adrenal insufficiency begins after dysphagia and develop gradually over the first decade , it can manifest as late as the third decade of life [4-8].Neurological disturbance have progressive course that affect central and peripheral autonomic nerv-ous system with heterogeneity and widely varying mani-festation [2,4,9].

The present case report deals with 14 year old girl who was diagnosed with adrenal insufficiency at the age of four and ten years later she exhibited achalasia with variable neurological manifestations. This highlights the wide variety of clinical manifestation of the disease and its clinical presentation.

Case report

A 14 year old girl was brought at age of four with fre-quent attacks of dizziness and lethargy mainly after pro-longed fasting. She was proved to have hypoglycemia which relieved by frequent feedings. Few months later she was brought again to the emergency room in an uncon-scious state with generalized tonic colonic convulsion. She was found to be hypoglycemic. The blood glucose was l.7mmol/L (normal 2.2-5.8mmol/L). She was immediately treated with intravenous dextrose which subsequently improved her condition. The patient was then admitted to hospital for further investigations.

Since birth she was noted to cry without tears, but she had not shown any sign of eye discomfort. She is the youngest of three siblings of consanguineous family. Her elder sister and brother are healthy. At the age of ten years, she developed recurrent attack of dysphagia but no aspiration. Barium swallow showed typical signs of achalasia where terminal part of esophagus showed beak like narrowing. At the same time she had generalized weakness and

difficulty in walking and the family reported some changes in her gait. Although her school performance was satisfactory ini-tially, she demonstrated remarkable academic deteriora-tion later. Physical examination revealed that her height and weight were at the 50th and 75th centile respectively and blood pressure was 100/60mm. She had generalized hyper-pigmentation which was more pronounced at knuckles and her skin was dry, particularly in hands and soles. There was no dysmorphic features, but the lower limbs were in valgus position with clumsy gait. There was proximal muscle weakness and wasting of thigh muscle with brisk reflexes in both feet. Clinical testing of auto-nomic functions showed inappropriate pupillary response without any postural hypotension. Complete blood count, renal and liver function were normal. However, prolonged fasting induced hypoglycemia with blood sugar 1.5 mmol/L (normal 2.2-5.8 mmol/L) was present. She had very low concentration of serum cortisol of 33nmol /L(normal 140-700) in association with high adrenocorti-cotrophichormone 1300 pmol/L (normal 5-18 pmol). Other laboratories test were growth harmone more than 10mg/ml and T4 15 (10.5-30) mg/dl serum insulin aldos-terone, renine, abdominal ultrasound and skeletal radiog-raphy were normal. The patient started on steroid re-placement therapy with oral hydrocortisone 15mg / m2 /d in two divided doses with poor compliance especially in summer time. There were no more attacks of hypoglyce-mia but there was hyper-pigmentation of the skin in time of poor compliance.

Discussion

The symptoms vary at the time of presentation. The time of adrenal insufficiency varies. It doesn't occur immedi-ately after birth but result from progressive process lead-ing to hypo-function of adrenal gland at variable time after birth (4,10). Although preservation of cortisol secre-tion upto third decade of life has been reported [11], ma-jority of these patients had isolated gluco-corticoid defi-ciency. In about 15% mineral-corticoid production many became impaired later [10]. In our patient, symptoms of hypoglycemia and adrenal insufficiency developed at four years of age and the endocrine study showed low cortisol and high ACTH without mineral-corticoid deficiency. Tests done after prolonged fasting and insulin induced hypoglycemia rather than ACTH stimulation should be used for accurate diagnosis [12]. Alacrima is constant sign in our patient and the mother noticed the baby crying without tears since birth. Achalasia of cardia precedes adrenal insufficiency by about 1-4 years [4 -6]. The eti-ology of achalasia is unknown but may be it is due to de-generation of autonomic plexus. In our patient achalasia appeared ten year after the adrenal insufficiency. At the same time the neurological features appeared and found to be progressive in nature. She had upper and lower mo-tor lesion and autonomic nervous system involvement in the form of proximal muscle weakness, clumsy gait, brisk reflexes, pescavus and inappropriate pupillary response.

It is not definite which will appear first adrenal insuffi-ciency or achalasia. There could be long gap between the occurrence of achalasia and neurological symptoms.

Triple A can be the cause of multi-system neurological diseases like muscle wasting, muscle weakness, brisk re-flexes, clumsy gait, inappropriate pupillary response and intellectual impairment.

Conclusion

There should be high index of suspicion and wide variety of clinical manifestations of the disease. The sequence of clinical presentation of the symptoms has notshown any definite chronological order.

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