



A Case Report of Allgrove Syndrome with Neurological Involvement

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Abstract

Allgrove syndrome is a very rare seen disorder with an autosomal recessive trait. The three characteristics of disease are alacrima, achalasia and adrenal failure. Alacrimia is the first manifestation in most cases. Achalasia and adrenal failure are seen later. Neurological involvement is rare and usually occurs in older age. A woman 22 years old admitted to our hospital with adrenal failure crisis. She had alacrimia and used teardrop for many years. Achalasia was diagnosed after evaluation of her dysphagia. Thus, diagnosis of Allgrove syndrome was done. Autonomic cardiac dysfunction and peripheral motor neuropathy were detected. In conclusion, Allgrove syndrome is rare and has life threatening potential due to adrenal failure. Early diagnosis and appropriate treatment may improve life quality and expectancy. Patients with relevant symptoms should be evaluated for autonomic neuropathy.

Keywords: Allgrove; neuropathy; adrenal failure

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Introduction

Allgrove syndrome is a disorder characterized by a mutation in AAAS gene, with autosomal recessive trait which affects many body systems progressing with achalasia, alacrima and adrenal insufficiency [1]. When Jeremy Allgrove first defined the disorder, he described the associations with adrenal insufficiency, achalasia, absence of tears, autonomic signs and genetic aspects [2]. In the following years, after determining that this syndrome was accompanied by autonomic neuropathies, it was proposed to name as 4A syndrome [3]. Neurological disorders are progressive, and it may present with autonomic neuropathy, peripheral neuropathy and involvement in central nervous system. We hereby present our subject of 22 years old case with Allgrove syndrome with autonomic and motor neuropathy.

Case

A female patient of 22 years old admitted to the emergency department complaining with dysphagia, nausea, vomiting, weakness and fatigue. The patient was hospitalized to the intensive care unit with a pre-diagnosed adrenal insufficiency upon detecting hypoglycemia, hypotension and hyponatremia. It was found out from her history that she had been using synthetic tears since childhood due to xerophthalmia. In her history, neither any characteristic feature nor consanguinity between the parents was found. She had a history of progressive dysphagia and sometimes regurgitation for two years. Numbness in her hands and feet were developed recently. She had a nasal voice. During her physical examination, the blood pressure was found as 85/50 mmHg with hyperpigmentation which was more notable on the extensor surfaces (Image-1). Hemogram and the levels of thyroid hormones were found as normal, while other parameters were 63 mg/dl (70–100) for fasting glucose, 110 mmol/L (136–145) for sodium, 0.4 mcg/dl (6.2–19.4) for serum cortisol, 1343 pg/ml (0–46) for ACTH (Adrenocorticotrophic hormone), and 16.86 pg/ml (38.1–313.3) for aldosterone. The patient diagnosed with adrenal crisis and therefore 0.9 % NaCl and 5 % dextrose replacement therapy with intravenous (i.v.) methyl prednisolone at a dosage of 80 mg/day were administered immediately. Two days later when the adrenal crisis recovered, i.v. prednisolone therapy was interrupted and oral hydrocortisone (30 mg/day) and fludrocortisone (100 mcg/day) therapies were started. Cardiac stenosis and esophageal dilatation were detected in esophagus-stomach-duodenum graphy with barium taken due to dysphagia (Image-2). The gastroscopy was

assessed in consistence with achalasia. Osephageal dilatation was not required. The result of Schirmer test was detected bilaterally as <5 mm. An electromyogram examination was performed due to numbness in hands and motor polyneuropathy was found at bilateral upper extremity. The cranial MR imaging yielded normal results. In adrenal imaging, both adrenal glands were found atrophic. The patient reported no history of tuberculosis. Regarding to the current findings, the patient was diagnosed with Allgrove syndrome. Dysautonomia was detected in the patient during cardiac autonomic assessment. Among the cardiac autonomic tests, Tilt test and Holter ECG detected postural orthostatic tachycardia syndrome and resting tachycardia, respectively. The patient was monitorized in Valsalva test. Electrocardiograms were performed during inspiration and expiration. The ratio of Valsalva was measured (the longest R-R/ the shortest RR ratio < 1.1 positive). Valsalva test yielded positive results suggested autonom cardiac dysfunction.



Figure 1. Hyperpigmentation on the extensor surface



Figure 2. Cardiac stenosis and osephagial dilatation in barium graphy

Discussion

Allgrove syndrome is a multisystemic disorder accompanied by autosomal recessive transitive and progressive neurological disorders progressing with achalasia, adrenal insufficiency and absence of tears. This condition generally appears at early ages. In most patients, the first organ involved is lacrimal gland [4]. The lacrimal gland dysfunctions are due to destruction of gland and autonomic involvement. The first diagnosis at our patient was xerophthalmia and when the patient applied to us, she was using artificial tears. Xerophthalmia is determined by Schimer test [5]. The result of Schimer test in our patient was positive. Adrenal insufficiency is the most vital component of Allgrove syndrome [6]. Early detection can be lifesaving. Hyponatremia, hypopotassemia, hypotension and hypoglycemia may be appeared in patients. Hyperpigmentation due to increased activity of melanocytes associated with an increase in beta-lipotropin and ACTH is one of the most notable characteristics. Our patient demonstrated nausea, vomiting, weakness, fatigue, hypoglycemia, hyponatremia and hypotension as well as increased notable levels of ACTH. The patient also showed hyperpigmentation. Another suggestive characteristic of Triple A syndrome was achalasia with a manifestation of dysphagia. It occurs with the destruction of autonomic ganglia more notably in lower esophageal region [7]. Diagnosis can be performed by means of barium graphy and manometry. Our patient was diagnosed with achalasia using barium graphy. Another sort of the disease involvement is the neurological complications which occurs during progressive stage of the disorder and at later ages [8]. Neurological involvement manifests itself as motor and sensory peripheral neuropathy, orthostatic hypotension, light reflex anomalies, xerophthalmia, extrapyramidal symptoms, and cardiac autonomic neuropathy [9]. Cardiac autonomic neuropathy manifests itself particularly as orthostatic hypotension, impaired cardiac reflex, and cardiac arrhythmia [10]. Our patient presented postural orthostatic tachycardia syndrome and resting tachycardia in Tilt test among other cardiac autonomic tests. The result of Valsalva test was positive. Motor peripheral nervous involvement may also occur during Allgrove syndrome [11]. Ulnar peripheral neuropathy was present in our patient. The plurality of achalasia, absence of tears and adrenal insufficiency should consider Allgrove syndrome. A misdiagnosed adrenal insufficiency may lead to death. Patients with Allgrove syndrome should be assessed in terms of neuropathy.

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