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Associations with hypoglycemia are useful: A case report of Allgrove syndrome

Hipoglisemi ile ilişkili durumlar: Allgroove sendromlu vakanın sunumu

To the Editor,

Allgrove syndrome, also known as triple A syndrome, is a rare autosomal recessive disorder characterized by the triad of adrenocorticotropic hormone (ACTH)-resistant adrenal failure, achalasia of the cardia and alacrima (1). We report a six-year-old boy who presented with recurrent hypoglycemic attacks associated with convulsions. His perinatal history was uneventful. There was no family history of hypoglycemia; his parents were first cousins. His weight and height were at the 25th and 50th percentiles, respectively. He had normal blood pressure and normal male external genitalia. Neurological examination was normal. Electrolytes, 24-hour glucose profile and basal cortisol level were normal. Both short and prolonged ACTH stimulation tests showed subnormal responses (lack of increase in basal cortisol level). Brain magnetic resonance imaging (MRI) was normal. Treatment with oral glucocorticoid was initiated. The patient was lost to follow-up for three years, after which he presented with chronic fatigability and failure to thrive. He had a history of repeated vomiting and progressive dysphagia more to fluids than solids, which is a characteristic finding in achalasia. This raised the suspicion of triple A syndrome, especially when the parents reported that the child used to cry without tears.

On examination, the patient's weight and height were below the 5th percentiles. He had giant café-au-lait patches on the thigh and abdomen with hyperkeratotic skin lesions on the plantar area. He had weakness and wasting of the muscle of the hands with decreased peripheral sensation (peripheral neuropathy). Evidence of autonomic neuropathy was detected in the form of blood pressure fluctuation and diminished heart variations during deep breathing and Valsalva's maneuver. Decreased tear production was documented using Schirmer test. Barium swallow showed dilation of the esophagus with narrowing of its lower end and tertiary contractions. Esophageal manometry showed weak aperistaltic body contractions with incomplete relaxation of the lower esophageal sphincter (LES) (Figure 1). The patient was treated with artificial tears and oral glucocorticoids. Heller myotomy was done together with laparoscopic fundoplication to avoid post-myotomy reflux. There was marked improvement in the dysphagia and the patient began to gain weight.

In Allgrove syndrome, adrenal insufficiency does not occur immediately in the postnatal period, but results from a progressive disorder leading to hypofunction of the adrenal gland at a variable time after birth (2). Our patient presented initially at the age of six years with hypoglycemia. Although his basal cortisol level was normal, the lack of a normal increase in cortisol in response to stimulation tests was diagnostic for decreased adrenal reserve and ACTH insensitivity. Allgrove syndrome must be distinguished from familial glucocorticoid deficiency, as both manifest during the first decade of life with hypoglycemia and hyperpigmentation and are due to ACTH insensitivity (3). However, the presence of additional features, especially alacrima or hypo-lacrima, helps the diagnosis.

Although alacrima started early in infancy, it had been missed by parents and physicians at this sta-

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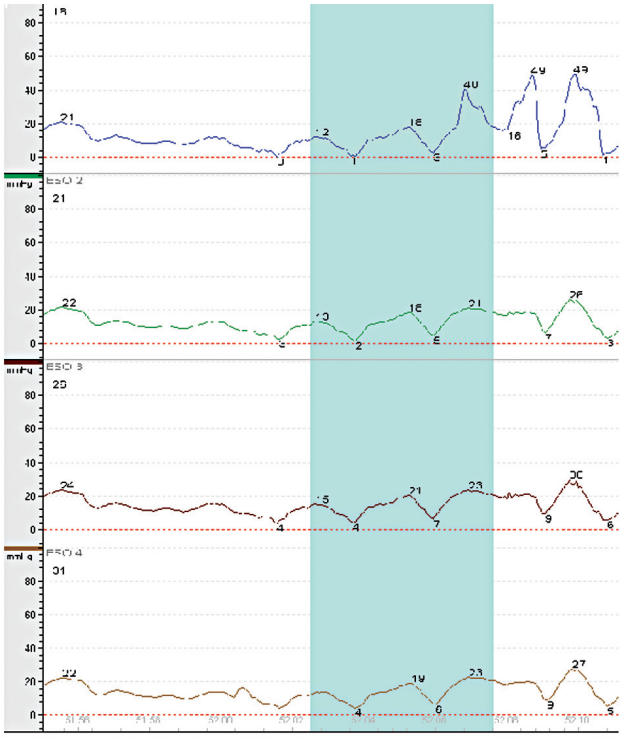

Figure 1. Esophageal manometry shows weak aperistaltic body contractions (ineffective peristalsis).

ge of diagnosis. A similar oversight occurred in many of the reported cases of triple A syndrome (4).

Achalasia of the cardia occurs in about 75% of all cases of Allgrove syndrome, and can be the dominant symptom of this syndrome. The age of presentation may be variable (4). Up to 60% of all patients with Allgrove syndrome have progressive neurological impairment involving the central, peripheral and autonomic nervous systems (5).

Generalized hyperpigmentation has been reported previously; however, to the best of our knowledge, the presence of café-au-lait patches was not reported before in cases of Allgrove syndrome.

Our reported case of Allgrove syndrome was diagnosed three years after his initial presentation. Early recognition of such a rare disorder requires clinicians to have a high index of suspicion and to screen patients for other components of the syndrome. Early management can prevent life-threatening complications such as adrenal crisis and frequent aspiration.

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