Late onset adrenal insufficiency and achalasia in Allgrove syndrome

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DESCRIPTION

A 26-year-old man presented with progressive difficulty in swallowing for 2 years and increased skin pigmentation for 1 year. This was associated with a loss of weight despite a preserved appetite. He had a lack of tears since childhood. His parents had a second-degree consanguineous marriage and had four sons. Examination was normal except for increased pigmentation over his lips ([figure 1](#)) and around his joints ([figure 2](#)). His pulse rate was normal; he had asymptomatic postural hypotension (supine 90/70 mm Hg, standing 56/46 mm Hg). Routine blood results including thyroid function were also normal.

A barium study showed dilation of the oesophagus with abrupt narrowing at the gastro-oesophageal junction ([figure 3](#)). Oesophageal manometry showed an elevated lower oesophageal sphincter pressure (47.2 mm Hg), with absent relaxation to swallow and aperistalsis, consistent with achalasia cardia. Fasting serum cortisol was 1.1 µg/dL (normal 5–25 µg/dL); 60 min after an intravenous injection of adrenocorticotrophic hormone (ACTH) (250 µg), it only increased to 1.2 µg/dL (normal increment is >9 µg/dL from baseline), indicating adrenal insufficiency. (It is likely that the patient had primary adrenal failure with excess ACTH leading to an increase in skin pigmentation.) ACTH was not measured as skin hyperpigmentation is not a feature of secondary adrenal failure. Schirmer's test for lacrimation showed total absence of tears. The presence of alacrimia, achalasia and primary adrenal insufficiency corresponded with a diagnosis of Allgrove syndrome. Upper gastrointestinal

Figure 2 Generalised hyperpigmentation over proximal posterior aspect of forearm with marked hyperpigmentation over olecranon.

endoscopy was performed for pneumatic dilation. The patient received steroid replacement with oral hydrocortisone. A complete recovery from dysphagia was observed in a week. The postural fall in blood pressure normalised after 3 weeks of steroid therapy. The patient's 36-year-old brother also had absent lacrimation, dysphagia, skin pigmentation

Figure 1 Generalised hyperpigmentation of face with marked melanin pigmentation over both lips.

Figure 3 Barium study showing distended oesophagus with abrupt narrowing of the oesophagogastric junction.

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and asymptomatic postural hypotension. His oesophageal manometry showed raised lower oesophageal sphincter pressure. He too responded to pneumatic dilation and oral steroid replacement. Two other brothers are unaffected and hence were not evaluated.

In 1978, a syndrome of familial glucocorticoid deficiency associated with achalasia of oesophageal cardia and deficient tear production was described by Allgrove *et al*¹ and was subsequently referred to as Allgrove syndrome (AS). In 1996, Weber *et al*² localised AS to the Achalasia-Addisonianism-Alacrimia Syndrome (AAAS) gene on chromosome 12q13. Mutation of this gene leads

to a presumptive loss of function of the encoded ALADIN (Alacrimia, Achalasia, aDrenal Insufficiency Neurological disorder) protein.

Adrenal insufficiency is usually diagnosed in the first decade of life, but can be delayed until the third or fourth decade of life as observed in our cases and a similar earlier report.³ Undiagnosed adrenal insufficiency is often the cause of death in this disorder, which otherwise carries a normal lifespan. Alacrimia is the most consistent early presenting feature. Other recognised features in AS include neurological involvement in the form of peripheral neuropathy, pyramidal and extrapyramidal involvement, autonomic dysfunction, ataxia, dementia and parkinsonian signs.³ This case highlights the importance of considering AS in children with alacrimia and screening for adrenal insufficiency in adults with alacrimia or achalasia cardia.

Learning points

- ▶ Allgrove syndrome is characterised by alacrimia, achalasia of oesophageal cardia and adrenal insufficiency. It is primarily a disorder of childhood often presenting in the first decade of life but symptoms can develop later.
- ▶ Unrecognised adrenal insufficiency is the most common cause of death; otherwise, AS is associated with a normal life span.
- ▶ This case illustrates the delayed presentation of achalasia and adrenal insufficiency in Allgrove syndrome. Screening for adrenal insufficiency should be considered in patients with alacrimia or achalasia.

Competing interests None.

Patient consent Obtained.

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REFERENCES

- 1 Allgrove J, Clayden GS, Grant DB, *et al*. Familial glucocorticoid deficiency with achalasia of the cardia and deficient tear production. *Lancet* 1978;1:1284–6.
- 2 Weber A, Wienker TF, Jung M, *et al*. Linkage of the gene for the triple A syndrome to chromosome 12q13 near the type II keratin gene cluster. *Hum Mol Genet* 1996;5:2061–6.
- 3 Bentes C, Santos-Bento M, de Sa J, *et al*. Allgrove syndrome in adulthood. *Muscle Nerve* 2001;24:292–6.

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