Allgrove’s syndrome and oral health care

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Abstract

Allgrove’s syndrome is an uncommon inherited condition. It consists of a triad of congenital defects each of which has a dental relevance in its own right but together can produce major oral health problems for the patient and treating clinician alike. Knowledge of the main aspects of Allgrove’s syndrome will assist the dental team in the provision of oral health care to patients with this condition.

Key words: Allgrove’s syndrome, achalasia, hypoadrenalism, alacrima, xerostomia

Allgrove’s syndrome is an uncommon congenital condition with dental relevance. Also known as Triple-A syndrome, it is characterised by achalasia of the cardia, adrenal insufficiency and alacrima. Early onset of skin pigmentation, hypoglycaemia and impaired cortisol synthesis was described in the 1950s (Shepherd et al., 1959). Allgrove et al. (1978) later described four cases of glucocorticoid failure without any diminution of mineralocorticoid function where achalasia and defective tear production were also features. Autonomic and neurological disturbance such as peripheral neuropathy, spasticity and ataxia, are also described in many cases, leading to suggestions that the syndrome should be renamed Quaternary-A syndrome (Peršic et al., 2001 and Gazarian et al., 2001).

Aetiological mechanisms have been investigated but no auto antibodies to adrenal tissue have been found. Post-mortem studies reveal an absence of the zona fasciculata, while the zona glomerulosa was preserved, hence the presence of mineralocorticoid function but the lack of glucocorticoids. Genetic investigation discovered Triple A syndrome to be an autosomal recessive disorder caused by a mutation at a locus on chromosome 12, which was given the name ALADIN by Houlden et al. (2002).

Achalasia

Achalasia of the cardia is characterised by aperistalsis of the body of the oesophagus and non-relaxation of the lower oesophageal sphincter on swallowing. The oesophagus, above the constriction, becomes dilated and elongated. The primary symptom is dysphagia. Some patients recount symptoms of regurgitation and retrosternal chest pain. Aspiration pneumonia has been reported (Mohan et al., 2001). It is rarely found in children with the condition but develops with age. The underlying pathology is a decrease in the activity of the ganglionic cells in the nerve plexus that supplies the oesophageal wall, which does not relax to allow food and liquids into the stomach. Reflux and aspiration occurs from partially fermented dietary products collecting in the ballooned oesophagus and not from stomach contents (Moazzez et al., 2005).

Reflux of contents from the ballooned oesophagus may reach the oral cavity. Studies have shown that gastro-oesophageal reflux disorders (GORD) increase the risks of erosion of dental hard tissues (Bartlett et al., 1996). Clinicians must be on their guard for any early signs of tooth surface loss in patients at risk of GORD. Serial study models and intra-oral photographs can help to assess any changes in hard dental tissues. Tissue loss can be recorded using standardised indices (Smith and Knight, 1984). Daily fluoride rinses can help to decrease the surface solubility of enamel. Patients presenting with symptoms of achalasia (retrosternal pain, dysphagia, reflux ± dental signs) will require further investigation and should be referred to their physician. Barium oesophagography and endoscopy are common diagnostic investigations and management is by drug therapy, stricture dilatation or surgery.

Adrenal hypoplasia

Hypoadrenalism in this condition is primary and adrenocorticotropic hormone resistant (no secretion of endogenous steroids despite the normal level of ACTH being produced by the anterior pituitary) with a negative Synacthen test. In the Synacthen test the plasma cortisol level is measured before and after administration of tetracosactide. If there is an inadequate rise or no increase in cortisol levels, adrenal failure is present (Kumar and Clark, 2003). This aspect of
the condition is managed with exogenous steroids such as hydrocortisone or prednisolone. These are given in divided doses to mimic the normal diurnal rhythm. However, in situations of stress, such as infection and surgery, these doses may be inadequate and if not increased, an Addisonian crisis may ensue. Patients should be encouraged to wear a medical alert bracelet or carry emergency information about their condition with them. Thus, patients with Allgrove’s syndrome may be on an exogenous dose of corticosteroid that may warrant prophylactic cover prior to dental treatment, since adrenal function may be absent.

Steroid cover is a relatively contentious issue (Key, 2003). A variety of guidelines have been published in the British National Formulary, dental journals and textbooks. The British National Formulary (2005) in its guidance refers to patients that require minor or major surgery under general anaesthesia only. It is this that may contribute to variation in practice between dental schools in patients treated under local analgesia (Perry et al., 2003). Current guidance would require supplementation for stress-inducing operative procedures. This is traditionally reported as including extractions and other surgical procedures. But it is important to assess the patient's anxiety response in relation to the proposed treatment. A synacthen test may be necessary. Dentally anxious people may find many other procedures stressful, not just surgery. Simple anxiety monitoring scales are available such as the modified Corah scale (Corah et al., 1978), to help the clinician assess anxiety responses to dental intervention. Anxiety management techniques such as sedation may be required.

Steroid supplementation regimes vary. Oral dose doubling regimes and low and high dose intravenous regimes have been proposed (Key et al., 2003; Scully and Cawson, 2005). A regime for each individual patient will depend upon the issues already discussed relating to the proposed treatment, level of adrenal hypofunction, level of exogenous steroid supplementation and the anxiety/stress level of the patient. The amount and type of steroid supplementation required for an individual patient may require close liaison with the relevant medical specialist dependant on the nature of the condition, treatment proposed and the dose of exogenous steroid taken. In Allgrove’s syndrome where adrenal hypofunction can be variable, this liaison is of paramount importance. It may be appropriate to refer for assessment of adrenal function by long or short Synacthen test prior to surgical procedures.

Acute hypoadrenalism can present with confusion, weakness, nausea, abdomen pains and signs of acute hypovolaemia with circulatory collapse. It can quickly progress to sudden loss of consciousness with rapidly falling blood pressure. Treatment in the primary care dental setting is to lay the patient flat, apply high flow oxygen by mask (10l/min) and give 100–200mg hydrocortisone intramuscularly or by slow intravenous injection. Monitor the patient, prepare for life support and arrange emergency transfer to hospital. Most texts advocate the inclusion of corticosteroids in dental surgery emergency drug kits and the use of steroids in the acute hypoadrenal crisis (Scully and Cawson, 2005; Addison’s Disease Self Help Group, 2006) but this emergency regime has recently been challenged in primary care with steroid excluded from the emergency drugs kit in one set of guidance (Resuscitation Council of the United Kingdom, 2006).

**Alacrima**

The lacrimal glands sit in the antero-lateral part of the orbital floor. Their innervation originates in the Superior Salivary nucleus of the brainstem, in common with the parasympathetic innervation of the submandibular and sublingual salivary glands. Alacrima results in dryness of the eyes and reports suggest that this is an early manifestation of autonomic dysfunction (Persić et al., 2001). Xerostomia, like alacrima, can be caused by progressive autonomic neuropathy (Dumic, 2000). All cases where dryness of the oral cavity is found in association with achalasia of the cardia, should be investigated and adrenal function measured.

**Xerostomia**

The loss of buffering capacity due to reduced salivary flow leads to an increased risk of caries and periodontal diseases. This must be addressed by preventative measures. Fluoride toothpastes and mouthwashes, meticulous oral hygiene with a low sugar diet are the mainstay of preventive treatment. Adjunctive measures such as fissure sealants are also useful in these ‘at-risk’ groups (Kidd and Joyston-Bechal, 1997). Saliva substitutes may reduce discomfort during speech and mastication. The onset of Allgrove’s syndrome is often at a young age and the need to visit multiple medical clinicians may make oral health care a low priority. This may delay and hamper preventative advice. However, it is vital to emphasise the importance of these measures, along with regular oral health reviews to parents and carers even though they may already feel they have a lot to cope with. The combination of gastric reflux and xerostomia in Allgrove’s syndrome can be devastating to the dentition so it is essential to explain the importance of oral health preventive regimes to the patient in light of the syndrome. Alacrima should be investigated and flow can be assessed with Schirmer’s test. Careful monitoring of ocular function is warranted in alacrima and referral to the appropriate ophthalmology services.

The following is a case description of a patient with Allgrove’s syndrome, who had a history of adrenal crises following dental treatment.

**Case report**

A 61-year-old male with Allgrove’s syndrome attended the Department of Sedation and Special Care Dentistry at
King’s College London Dental Institute for dental treatment. He had been referred to the department following a suspected adrenal crisis during previous dental treatment. His medications included 10mg life-long hydrocortisone (morning and evening) for adrenal insufficiency and Baclofen (a skeletal muscle relaxant) for muscle spasticity. No oral signs of adrenal insufficiency, such as oral pigmentation, were seen.

Although he was not aware of a dry mouth, examination revealed a slight increase in saliva viscosity. In the absence of perceived problems no further formal assessment of salivary function was made. The patient was partially dentate and his remaining teeth were heavily restored, possibly linked to a reduced salivary buffering capacity. He did not report any oesophageal reflux and tooth surface loss due to erosion was difficult to assess due to the number and size of restorations present in his remaining teeth. Similarly, in the absence of any other symptoms of reflux, such as heartburn, further investigations for GORD were not considered necessary.

The patient was mildly anxious about invasive dental treatment but at this treatment episode only preventive and prosthetic treatment was proposed so sedation and steroid supplementation issues did not arise. Initial treatment was aimed at reducing his risk factors for caries. This stabilisation phase included diet and oral hygiene advice and the use of a daily fluoride rinse. Once this phase was completed, partial dentures were constructed.

Important features of this patient’s care were the preparations made for any future, more extensive dental treatment. This required liaison with the patient’s medical specialists. Consultation with the relevant medical specialists allows the dentist to confirm any special supplementation regimes required should any emergency treatment, such as tooth extraction, be required. Results of basic tests can be obtained from the patient’s medical specialists (e.g. urea and electrolytes, plasma cortisol and blood glucose) along with any special test results such as long or short Synacthen tests.

**Summary**

Patients can present with uncommon syndromes that have treatment implications in oral health care provision. All three of the main aspects of Allgrove’s syndrome present dental issues that have to be considered, individually and collectively, in the treatment planning and delivery of care for patients with this condition.

**References**
