

Disease of Addison and Its Impact On Oral Health - A Review

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Aim

To review the manifestations of Addison's disease and its impact on oral health

Objective

To understand the cause and prevalence of the disease and oral health in patients with the disease.

Background

Addison's disease is a rare endocrine disease in which there is inadequate production of glucocorticoid and mineralocorticoid. It is a life threatening disorder which causes premature death. It is seen in all age groups and affects male and female equally. This disease is named after Thomas Addison, who first described patients affected by this disorder. Addison's disease can present as a life-threatening crisis, because it is frequently unrecognized in its early stages. The basis of Addison's disease has dramatically changed from an infectious cause to autoimmune pathology since its initial description. However, tuberculosis is still the predominant cause of Addison's disease in developing countries. In patients with this disease the oral mucosa develops a bluish black plaque which affects the buccal mucosa mainly. Other areas or prevalence are gums, palate and tongue. They are treated with corticosteroids.

Reason

To understand the dental management of patients with Addison's disease

Keywords

Addison's disease, oral health, cortisol, aldosterone, hypoadrenalism.

Introduction

Addison's disease also known as primary adrenal insufficiency or Hypoadrenalism. Addison's disease is a rare disorder of the adrenal gland. Addison's disease affects the production of two essential hormones called cortisol and aldosterone. An early stages symptom of Addison's similar to other more common health conditions such as depression or flu. The main symptoms are fatigue, muscle weakness, low mood, loss of appetite and unintentional weight loss, increased thirst. It also affects the oral health by causing hyper pigmentation. Classically, hyper pigmentation is associated with the disease, and intraoral pigmentation is perceived as the initial sign and develops earlier than the dermatological pigmentation. The symptoms of the disease usually progress slowly and an event of illness or accident can make the condition worse and may lead to a life-threatening crisis. An important distinction for patients is that people with primary adrenal insufficiency usually don't make enough of the hormone aldosterone; so in addition to taking cortisol replacement, they also need aldosterone replacement. People with secondary adrenal insufficiency are only low on cortisol. Cortisol and aldosterone are just two of the more than 50 hormones the adrenal glands generate.

Etiology of Addison's disease

Whereas primary adrenal insufficiency last century was most commonly due to tuberculosis, autoimmune disease currently accounts for most of the cases presenting outside of the newborn period. The various etiologies of Addison's disease can be grouped into three categories: 1] adrenal dysgenesis; 2] adrenal destruction; and 3] impaired steroidogenesis. Congenital adrenal hypoplasia [AHC], mutations of steroidogenic factor-1 [SF-1], and ACTH unresponsiveness can all lead to adrenal dysgenesis/hypoplasia, albeit the latter usually results in isolated deficiency of gluco-corticoids. Autoimmune polyglandular syndrome [APS], adrenoleukodystrophy [ALD], adrenal hemorrhage, adrenal metastases, infections, and amyloidoses can all lead to destruction of adrenal gland. Congenital adrenal hyperplasia [CAH], mitochondrial disorders, the Smith-Lemli-Opitz syndrome [SMOS], an enzyme deficiency in cholesterol metabolism, can all lead to impaired steroidogenesis. The relative frequencies of these different disorders varies markedly according to the age and gender of the patients at their clinical presentation. At birth, adrenal hemorrhage from anoxia/sepsis is most common, adrenal insufficiency from CAH usually presents in neonates, and in older children it often occurs as part of an autoimmune poly-glandular syndrome or APS. In boys, adrenoleukodystrophy, DAX-1-related disorders are increasingly recognized, whereas adults have increasing incidences of infectious and metastatic adrenal failures.

Pathogenesis of Addison's disease

Autoimmune adrenalitis can be divided into stages of progression^{2,3}. As the disease develops, individuals lose adrenocortical function over a period of years. In the first three stages, the human leukocyte antigen genes confer genetic risk; an unknown precipitating event initiates antiadrenal autoimmunity; and 21-hydroxylase antibodies are produced, which predict future disease. The production of these antibodies can precede symptom onset by years to decades, and they are present in more than 90% of recent-onset cases. In the fourth stage, overt adrenal insufficiency develops. One of the first metabolic abnormalities to occur is an increase in plasma renin level, followed by the sequential development of other abnormalities, including a decreased response to adrenocorticotropic hormone [ACTH] stimulation in the fifth stage. If symptoms of adrenal insufficiency are present but go undiagnosed, an Addisonian crisis can occur.

Diagnosis of Addison's disease and its impact on oral health

The diagnosis of chronic primary adrenal insufficiency is frequently preceded by a history of prolonged hyper pigmentation, malaise, fatigue, anorexia, weight loss, gastrointestinal disturbance, and joint and back pain. Patients may crave salt and develop unusual food preferences, such as drinking pickling brine [1]. Hyper pigmentation is the most frequently encountered symptom. It is more easily recognized in the sun-exposed areas of the face, neck and arms, and it also occurs on areas that are subject to trauma, such as the knees and knuckles. However, hyper pigmentation may be more difficult to recognize in darker-skinned races, as the Palmer crease and mucous membranes are often normally pigmented [2]. Extensive or progressive hyper pigmentation at any of these sites should alert clinicians to the possibility of Addison's disease. However, increasing pigmentation of the skin is not diagnostic of primary hypo adrenalism [3]. Scalp hair may also become darker, new naevi may be observed [4] and calcification of the cartilage of the ear may occur [5].

Symptoms for Addison's disease and its impact on oral health

The symptoms of Addison's disease begin gradually, chronic worsening fatigue, loss of appetite, generalized weakness, hypotension, and weight loss. The clinical features of hypoadrenocorticotropism actually don't begin to appear until at least 90% of the glandular tissue has been destroyed. Generalized hyper pigmentation of skin is seen, which is classically described as "bronzing" the hyper pigmentation is generally more prominent on sun-exposed skin and over pressure points, such as the elbows and knees. A primary adrenal failure induces a reduction of the main adrenal hormones, the lack of which triggers an increasing production of adrenocorticotropic by pituitary gland as a part of a feedback mechanism. Increase of ACTH derived peptides stimulates the melanocytes via the skin and mucosa α -MSH receptor [MC1] causing skin and oral mucosa hyper pigmentation. Hyper pigmentation of the mucous membrane and skin usually proceeds over other symptoms by month to year. Vitiligo may also be seen in association with hyper pigmentation in idiopathic Addison's disease due to autoimmune destruction of melanocytes [6, 7, 8]. The symptoms of Addison's disease progress slowly and are usually ignored, an event of illness or accident can make the condition worsen and lead to Addisonian crisis. Sudden penetrating pains in the lower back region, abdomen or legs are symptoms

of Addisonian crisis with severe vomiting and diarrhea, which is followed by dehydration, low blood pressure and loss of consciousness.

Treatment

Glucocorticoid replacement therapy

Patients with Addison's disease require life-long glucocorticoid replacement therapy. This usually takes the form of oral hydrocortisone which is widely available in Europe, the USA, the UK and South Africa [9]. In patients with hypoadrenalism, the most significant barrier to monitoring therapy with glucocorticoids is that no single tests exists that reliably reflects adequacy, over replacement or under replacement. While the 24hrs urine cortisol and plasma ACTH are unreliable in assessing adequacy of glucocorticoid replacement, plasma cortisol day curves have been used, but they require frequent blood sampling and admission to hospital [10]. As salivary cortisol is easily accessible and correlates well with plasma cortisol, it represents an attractive alternative to plasma cortisol measurements. Both, however, demonstrate substantial variability [11]. Both plasma and salivary cortisol monitoring have limited potential to guide doing replacement therapy. There are no specific recommendations about the frequency of monitoring either plasma or salivary cortisol.

Stress dosing of glucocorticoid

Patient should be counseled about the need for stress-dose glucocorticoids for illnesses and before surgical procedures because destruction of the adrenal glands prevents an adequate physiologic response to stress.²⁴ There are many expert recommendations for stress dosing of steroids based on the degree of stress; clinical trials comparing different approaches are lacking in the literature. In our practice, we use a stress-dose strategy for outpatient procedures [e.g., colonoscopy, upper endoscopy] and invasive dental procedures [e.g., root canal] that patients can implement easily. This involves a dose of glucocorticoids three times the maintenance dose the day of the procedure and two days after [i.e., three times three rule for stress-dose glucocorticoids].

For minor illnesses such as influenza or viral gastroenteritis, the patient can take three times the steroid dose during the illness and resume normal dosing after resolution of symptoms. Patients should also have an injectable form of glucocorticoid [intramuscular dexamethasone] available in cases of nausea, vomiting, or other situations when oral intake is not possible. Mineralocorticoid replacement generally does not need to be changed for illness or procedures. However, the dose may need to be adjusted in the summer months when there is salt loss from excessive perspiration.

Mineralocorticoid replacement therapy

Mineralocorticoids are essential for the reversal of aldosterone deficiency. Assessment of mineralocorticoid adequacy is possible by evaluating plasma sodium, potassium and renin activity assays. An elevated plasma renin activity in an Addison's disease patient may indicate inadequate mineralocorticoid substitution, while elevated blood pressure, peripheral edema and sodium retention may indicate over replacement. The usual dose of 9-alpha-Fluor-hydrocortisone is between 50 micro grams per day. Patients are at risk of developing hyperkalemia and hypotension should this be discontinued [12].

Hyper pigmentation treatment

Treatment is sought mainly for cosmetic reasons and includes Q-switched ND: YAG or Q-switched alexandrite laser therapy for bothersome melanosis on the skin [13]. Sun protection is important to prevent reoccurrence. Gyro surgery has also been tried for pigmentation in LHS with good results [14].

Conclusion

Enhanced awareness of Addison's disease is warranted, since prompt institution of replacement therapy is potentially lifesaving. Autoimmune Addison's disease is the most common underlying etiology in South Africa, despite the very high background prevalence of HIV and tuberculosis. Oral naevi and melanomas may also mimic oral Addisonian pigmentation. Oral intra mucosal naevus appears as a brown colored lesion potentially similar to brown maculae of Addison's patients but they are focal and rarely numerous. Generally oral melanoma appears as one isolated brown or black patch with asymmetric and irregular borders. A differential diagnosis with Addison's pigmentation should be considered when clinical features are common to both melanoma and pigmented maculae.

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