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(CASE REPORT)

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Addison's disease: A case report

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Abstract

Addison's disease, a rare endocrine disorder, presents a myriad of symptoms that can often be nonspecific and challenging for diagnosis. We present a case of an 11-year-old male child born out of 5th degree consanguineous marriage, who presented with multiple symptoms over a period of months. The patient initially complained of blackish discoloration of nails for 4 months, which was followed by a fall from steps 2 months prior to admission. Subsequently, he experienced generalized weakness, loss of memory, and froathing 1 month prior to admission. Most concerning, the patient developed fever and loss of consciousness in the last day before presentation to the hospital. The patient was diagnosed with Addison's disease, an uncommon disorder in pediatric populations. This case highlights the complex presentation of Addison's disease in pediatric patients and underscores the importance of considering this diagnosis in cases of unexplained hyperpigmentation and systemic symptoms, especially in consanguineous populations, even in the absence of typical signs. This report aims to increase awareness among healthcare providers regarding the diverse presentations of Addison's disease, particularly in pediatric patients, to facilitate prompt diagnosis and management.

Keywords: Addison's Disease; Primary Adrenal Insufficiency; Hyperpigmentation; Consanguinity; Pediatric.

1. Introduction

Primary adrenal insufficiency, another name for Addison's disease, is an uncommon but dangerous disorder in which the adrenal glands fail to produce enough hormones. This illness, which bears the name of the doctor Thomas Addison who initially identified it in 1855, can have a major effect on a person's health and quality of life. It is vital to comprehend Addison's illness, including its symptoms, causes, and therapies. Chronic vomiting, anorexia, hypoglycemia, poor weight gain in children, unexplained weight loss in adults, malaise, fatigue, muscular weakness, hypokalemia, hypotension, hypoglycemia, and most notably, generalized hyperpigmentation are all possible symptoms of adrenal insufficiency. Particularly when fatigue and muscle weakness emerge, these symptoms can provide crucial hints about the underlying disease. The compensatory activation of the hypothalamic-pituitary axis results in elevated levels of MSH and ACTH, which in turn causes "muddy" hyperpigmentation in Addison's disease. On the other hand, the absence of hyperpigmentation may occasionally be caused by a malfunction in the melanocyte response.1

Addison's disease symptoms include generalized weakness, appetite loss, persistently worsening fatigue, hypotension, and weight loss that steadily worsen over time. After at least 90% of the glandular tissue has been damaged, the clinical signs of hypoadrenocorticism truly start to manifest. As a result of elevated levels of beta-lipotropin or adrenocorticotropic hormone, which can both stimulate the production of melanocytes, there is a generalized hyperpigmentation of the skin that is commonly referred to as "bronzing." The hyperpigmentation is typically more

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noticeable on sun-exposed skin and over pressure points, such as the elbows and knees. Skin and mucous membrane hyperpigmentation often develops months to years after other symptoms. Because vitiligo results from the autoimmune loss of melanocytes, it is also possible to observe hyperpigmentation in idiopathic Addison's disease.2

Despite being an uncommon disease, PAI is becoming more common, according to current research. Other iatrogenic conditions, mostly related to pharmacological side effects (e.g., adrenal hemorrhage associated with anticoagulants, drugs affecting glucocorticoid synthesis, action, or metabolism, and some of the novel anti-cancer checkpoint inhibitors), are contributing factors to this phenomenon in addition to the common "classical" causes of PAI, such as autoimmune, infectious, neoplastic, and genetic disorders.2. Owing to the disease's rarity and, at least in its early stages, its sometimes non-specific symptoms, PAI is commonly overlooked, delaying diagnosis. Adequate patient education is the cornerstone of successful therapy for both adrenal crisis prevention and management. The creation of pharmacokinetically improved glucocorticoid formulations and regenerative treatments are two areas of current research attention.3

1.1. Causes of AI

Addison's disease, also referred SAI (secondary adrenal insufficiency) presents either due to deficient adrenocorticotropic hormone (ACTH) secretion as an isolated defect or in combination with other pituitary hormones deficiency with pituitary adenoma being the most common cause. Lastly, abrupt cessation of long-term exogenous steroid use is the most common iatrogenic cause of TAI (tertiary adrenal insufficiency). Numerous variables, including as the glucocorticoid's dose, duration, half-life, strength, and mode of administration, can affect the risk of TAI. Furthermore, medications that modify glucocorticoid metabolism may potentially change the risk of TAI. Lastly, sudden stop of long-term exogenous steroid use is the most common iatrogenic cause of TAI. Numerous variables, including as the glucocorticoid's dose, duration, half-life, strength, and mode of administration, can affect the risk of TAI. Furthermore, medications that modify glucocorticoid metabolism may potentially change the risk of TAI. Up to 29% of patients have been reported to experience opioid-induced AI, an unappreciated adverse effect of long-term opiate medication caused by central inhibition of the HPA axis that results in TAI. It is dose-related and more likely to happen to people taking large amounts of opiates.4

1.2. investigation

Given that AD crises can be quickly lethal, a strong index of concern is required. The patient should be treated as a medical emergency if there are any signs of prolonged vomiting, muscle weakness, dehydration, a low blood pressure headache, excessive tiredness, and shock. If not, you should measure your blood cortisol level at nine in the morning and occasionally, but not usually, you will find low sodium and high potassium levels. You should also measure your urea and electrolytes.5

Serum Cortisol Levels: Typically low in the morning (normal peak is around 6-8 a.m.) and may not rise appropriately in response to stress.The chance of PAI will significantly rise if skin and mucous membrane hyperpigmentation occurs. High levels of ACTH promote hyperpigmentation, which is especially noticeable on skin areas exposed to sunlight and friction. Elbows and knuckles therefore look especially black. Some people have more moderate hyperpigmentation, which is mainly noticeable as dark naevi or areola. Another common feature is a salt appetite, with patients reporting a preference for salty foods such as liquorice, chips, peanuts, and other such items. But until prompted, a lot of people decline to disclose their salt cravings.6

Lack of cortisol and aldosterone lowers blood pressure and may result in symptomatic orthostatism, which the patient often reports as dizziness. In addition, low cortisol may lead to hypoglycaemia, and patients with diabetes become more insulin sensitive. A history of autoimmune disease should also sharpen the suspicion of autoimmune PAI, since the majority have or will develop more than 1 organ-specific autoimmune disease.7

1.3. Management

A morning blood cortisol level below 165 nmol/L (6 μg/dL) is suggestive of adrenal insufficiency, while a reading above 500 nmol/L (18 μg/dL) typically rules out Addison disease. Mineralocorticoid and glucocorticoid hormone replacement therapy is used to treat Addison's disease. Certain Addison disease types also call for specialized care for the underlying ailment, such as antituberculous medications in cases when tuberculosis is the etiology of the disease.8

Basal plasma cortisol measurement is an insensitive screening method. A 250 μg dosage of synthetic adrenocorticotropin 1-24 is an effective dynamic test. The diagnosis is validated by elevated adrenocorticotropin and renin plasma levels.8 The treatment includes with physiologic supply of the missing glucocorticoid and

mineralocorticoid hormones is the treatment for primary adrenal insufficiency. Acute adrenal insufficiency patients should receive intravenous (100 mg per 8 hours) supraphysiologic "stress" doses of hydrocortisone in addition to appropriate medical attention and fluid replacement. Oral hydrocortisone (12 to 15 mg/M2 daily) offers readily diluted and administered glucocorticoid replacement for chronic therapy.9

Adults should take two to three doses of hydrocortisone (15–25 mg/d) or cortisone acetate replacement (20–35 mg/d) daily. Hydrocortisone (about 8 mg/m(2)/d) is advised for children.10

The health-related quality of life in adrenal insufficiency is more severely compromised than previously believed, even with optimized life-saving glucocorticoid replacement and mineralocorticoid replacement therapy. A new treatment called dehydroepiandrosterone replacement may help improve quality of life. When children show with hyperpigmentation, weakness, altered sensorium, and atypical speech patterns, especially in those who are consanguineous, Addison's disease should be taken into consideration in the differential diagnosis. The prevention of potentially fatal adrenal crises depends heavily on early detection and intervention.11

1.4. Mineralocorticoid Replacement (Aldosterone)

If aldosterone is also deficient, fludrocortisone is prescribed. This helps regulate salt and water balance in the body.12

Apart from prevalent auto-immune conditions, individuals must to undergo screening for additional cardiovascular risk factors. To determine the reason for the higher prevalence of reduced BMD at the lumbar spine that has been found, more research is required. Internationally approved long-term management criteria are required.13

Treatment involves urgent administration of IV/IM hydrocortisone and IV fluids. 14

In individuals who are critically ill or undergoing surgery and have healthy adrenal glands, endogenous adrenal secretion is elevated (84). When treating severe feverish conditions, such as Addison's disease, standard steroid dosages should be increased and given over the course of three divided daily doses. IV or im administration of hydrocotisone succinate (Solu-Cortef) and IV hydration should be administered to patients who cannot take oral medication.15

2. Case report

Title: Addison's Disease Presenting with Blackish Discoloration of Nails in an 11-Year-Old Male:

A 11 year old male child born out of 5th degree consanguineous marriage, Chief complaints blackish discoloration of nails from 4 months fall from steps 2 months back, generalized weakness and loss of memory and froath since 1 month. Case of fever and loss of consciousness since 1 day.

2.1. On examination

A pediatric patient was examined presenting with symptoms of irritability. Upon assessment, the child had a high temperature of 105.1°F, a pulse rate of 113 beats per minute, and a blood pressure of 110/70 mmHg. Respiratory rate was elevated at 28 breaths per minute, while oxygen saturation was measured at 98%. Cardiovascular examination revealed normal S1S2 sounds, and the respiratory system exhibited basal crepitations. Abdominal examination was unremarkable with a soft abdomen and no organomegaly noted. Urine output was 1.6 ml/kg/hour, and the blood glucose level was 112 mg/dl. These findings suggest a febrile illness with signs of increased cardiac output, adequate hydration, and normal perfusion. Further investigation and management are warranted to determine the underlying cause of the fever and address the patient's condition effectively.

2.2. Investigations

The provided investigations reveal a comprehensive look into various aspects of the individual's health. The urea level is lower than the normal range at -49, indicating potential issues with kidney function. Creatinine is also below the standard range at -0.57, further pointing to possible kidney impairment. AST is significantly elevated at 120, indicating potential liver damage or inflammation. ALPO4 is also high at 214, which could suggest issues with bone health or liver function. The albumin level is slightly low at 3.8, which may indicate malnutrition or liver disease.

Moving to the metabolic profile, cholesterol is within a healthy range at 157. Cortisol is notably low at -75ug, potentially indicating adrenal insufficiency or chronic stress. Sodium is below normal at 132, while potassium and chlorine levels are also low at 3.3 and 104, respectively, indicating electrolyte imbalances. Calcium is slightly low at 9.5, which could

indicate issues with bone health or parathyroid function. Phosphorus is low at 1.9, which might be related to kidney dysfunction.

In terms of thyroid function, TSH is within range at 2.13, while T3 and T4 are both below normal levels at 1.15 and 11.1, respectively, suggesting hypothyroidism. Glucose is normal at 98mg/dl. ESR is significantly elevated at 50 and 58 minutes, indicating inflammation in the body. Hemoglobin is low at 11.8, suggesting anemia. WBC count is within normal range at 8.46, while platelets are low at 1.51, potentially indicating a risk of bleeding. CRP is highly positive at 96 mg/l, indicating significant inflammation in the body, which may be contributing to many of the abnormal findings in this investigation panel. These results suggest a complex picture of health concerns, including potential kidney, liver, thyroid, and inflammatory issues, alongside electrolyte imbalances and anemia. A thorough clinical assessment and further testing would be necessary for a more precise diagnosis and treatment

2.3. Diagnosis

Based on investigations, the patient presents with an active cough for the past three days, accompanied by sputum production. There is a history of fever two days prior to presentation, along with changes in skin colour noted. Additionally, the patient reports a complaint of lack of consciousness five days ago. These constellations of symptoms and history lead to the diagnosis of Addison's disease. Although Addison's disease frequently manifests as gastrointestinal symptoms, the nonspecificity of these symptoms may cause a delay in diagnosis.

2.4. Treatment

The patient, weighing 19 kgs, is currently on nothing per oral (NPO) status. Intravenous fluids of dextrose normal saline (DNS) are being administered a" a rate of 50 ml/hour, along with 3% normal saline (NS) at a dosage of 0.5 ml/kg/day. Antibiotic therapy includes injection ceftriaxone at 100 mg/kg/day. Additionally, the patient is receiving intravenous Pantoprazole at a dosage of 20 mg. For fever management, injection paracetamol (PCM) is administered at 10 mg/kg/dose. Intravenous midazolam is available for sedation at 2cc initially followed by 3cc normal saline as needed. To manage Addison's disease, the patient is receiving intravenous hydrocortisone with a dosing regimen of 50 mg initially, followed by 25 mg, and then another 25 mg.

A 19 kg patient presented with a history of active cough for 3 days, sputum production, a fever 2 days prior, changes in skin colour, and a loss of consciousness 5 days ago. Based on these symptoms, the patient was diagnosed with Addison's disease. The patient was not consuming anything orally and was receiving intravenous fluids at 50 ml/hour of IVF DNS and 0.5 ml/kg/day of IVF 3% NS. They were also administered injections of ceftriaxone at 100 mg/kg/day, pantoprazole at 20 mg IV/OF, paracetamol (PCM) at 10 mg/kg/dose, and midazolam 2cc + 3cc NS/IV/SOS. Additionally, the patient received a tapering dose of hydrocortisone starting at 50 mg, then 25 mg, and finally 25 mg.

3. Discussion

The presented case of an 11-year-old male child born from a consanguineous marriage highlights a constellation of symptoms culminating in the diagnosis of Addison's disease. Addison's disease, or primary adrenal insufficiency, is a rare endocrine disorder characterized by the inadequate production of cortisol and often aldosterone by the adrenal glands. This case underscores the importance of recognizing the varied clinical manifestations of Addison's disease, especially in pediatric patients. The treatment approach consisted of addressing the adrenal insufficiency with intravenous hydrocortisone, which is the mainstay of acute management. In addition to hydrocortisone, broad-spectrum antibiotics such as ceftriaxone were administered to cover potential bacterial infections due to the patient's presenting symptoms. Pantoprazole was given to prevent potential gastrointestinal bleeding, a common concern in patients receiving high-dose steroids. Intravenous fluids were administered to maintain hydration and correct electrolyte imbalances. IVF DNS and IVF 3% NS were used to provide both dextrose and saline solutions to support the patient's fluid and electrolyte needs. Paracetamol (PCM) was given for fever management, and midazolam was available for sedation if needed.16

This case presents a pediatric patient with Addison's disease exhibiting classic symptoms such as cough, sputum production, fever, changes in skin color, and loss of consciousness. Prompt diagnosis and treatment initiation were crucial, involving a regimen of IV fluids, antibiotics, proton pump inhibitors, antipyretics, sedatives, and hydrocortisone. This case highlights the importance of considering Addison's disease in the differential diagnosis of patients presenting with these symptoms, especially in pediatric populations, to ensure timely and appropriate management.

AD is an infrequently occurring mimic of many other more common conditions encountered in primary care. Despite multiple useful reviews of AD in the literature, we have personal recent experience of delays in diagnosis and there

remains a need to raise the clinical profile in primary and secondary care of this highly treatable but life-threatening disease. Research into a formal diagnostic algorithm would be helpful, as would further epidemiological work to examine clustering of cases in time and place. Dental surgeons may be the first medical professionals to encounter Addison's disease since the disease's oral manifestations, notably oral pigmentation, may manifest earlier than its dermatological equivalent. Early diagnosis of the disease is crucial for appropriate medical care.17

When patients arrive with gastrointestinal problems and weight loss, malignancy is a crucial differential diagnosis. Clinical circumstances and substances (antineoplastics, tetracyclines, phenothiazines, zidovudine, antimalarial drugs) that might cause hyperpigmentation.18

4. Conclusion

This case highlights the clinical presentation and treatment of Addison's disease in a pediatric patient. Addison's disease, or primary adrenal insufficiency, results from the insufficient production of adrenal hormones, particularly cortisol and aldosterone. Common symptoms include fatigue, weight loss, hypotension, hyperpigmentation, and electrolyte imbalances. In this case, the patient presented with classic symptoms such as cough, sputum production, fever, skin color changes, and loss of consciousness. Dysphagia, drowsiness weight loss, hypotension, abdominal pain, amenorrhea, nausea, vomiting, thin and brittle nails, and sparse body hair are commonly linked to Addison disease. The classic manifestation of Addison disease is hyperpigmentation brought on by ACTH melanogenesis. The initial indication is the visible and noticeable pigmentation inside the gingival, vermillion border of the lip, buccal mucosa, and palate tongue. Patients with incomprehensible hyperpigmentation or gastrointestinal problems should be evaluated for Addison's disease, which is often idiopathic and manifests in a variety of ways. It is especially important when hyponatraemia and hyperkalaemia are present. A normal basal cortisol level does not rule out the diagnosis, which calls for testing with ACTH stimulation.

The comprehensive investigation reveals a complex array of health concerns for the individual. With indications of potential kidney impairment, liver damage or inflammation, electrolyte imbalances. These findings underscore the need for further testing and a precise diagnosis to guide appropriate treatment strategies. Addressing these multifaceted health issues will require a multidisciplinary approach to ensure comprehensive care and improved health outcomes for the individual. This case underscores the importance of recognizing and promptly treating adrenal crisis in patients with Addison's disease, especially in pediatric populations where the presentation can be subtle and easily missed. Early initiation of hydrocortisone and supportive care with fluids and antibiotics can significantly improve patient outcomes.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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