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Clinical case

Addison's disease diagnosis based on a skin lesion in primary care: Case report

Diagnóstico de doença de Addison por meio de lesão cutânea na Atenção Primária: relato de caso

Diagnóstico de Enfermedad de Addison a través de lesión cutánea en la Atención Primaria: relato de caso

Izabela Dias Brugugnolli[1], Ana Olívia Guedes Leite[1], Giovanna Emanuella Piffer Soares Arantes[2], Leonardo Valentini Arf[1], João Pedro Martoneto Faccioli[1], Luis Gustavo Cunha Claudino[1]

[1]Centro Universitário Padre Albino – Catanduva (SP), Brazil.
[2]Universidade de Marília – Marília (SP), Brazil.

Abstract

Introduction: Addison's disease — also known as primary adrenal insufficiency — is an insidious and rare disease, which can have high rates of morbidity and mortality when its diagnosis is not identified, and treatment is not initiated early. It presents varied symptoms, among which hypotension, skin hyperpigmentation, hyponatremia, and hyperkalemia stand out. When left untreated, it can progress to adrenal crisis and cardiovascular collapse. Addison's disease is diagnosed clinically and through laboratory findings, with high concentrations of adrenocorticotropic hormone and low plasma cortisol concentrations characterizing primary adrenal insufficiency. The treatment depends on the cause and requires a multidisciplinary approach associated with glucocorticoid replacement as well as other hormones, when necessary. **Case presentation:** This article describes a case of Addison's disease diagnosed in primary care, an uncommon situation since the disease has very nonspecific clinical symptoms, especially in its early stages, and is not often considered in the diagnostic process. **Conclusions:** The case did not have a complete resolution at the primary care level; however, the facility successfully fulfilled its role, established in the National Primary Care Policy, as the care coordinator and organizer of health services, embracing the patient and recognizing their needs.

Keywords: Addison disease; Adrenal insufficiency; Cases reports; Primary health care.

Corresponding author:
Izabela Dias Brugugnolli
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Resumo

Introdução: A doença de Addison, ou insuficiência adrenal primária, é uma enfermidade insidiosa e rara, que pode apresentar altas taxas de morbimortalidade quando o seu diagnóstico não é reconhecido e o seu tratamento não é iniciado precocemente. Apresenta sintomas variados, entre os quais se destacam hipotensão arterial, hiperpigmentação cutânea, hiponatremia e hipercalemia. Quando não tratada, pode evoluir com crise adrenal e colapso cardiovascular. O diagnóstico da doença de Addison é feito clinicamente e por meio dos achados em exames laboratoriais, em que concentrações elevadas do hormônio adrenocorticotrófico e de baixas concentrações de cortisol no plasma caracterizam a insuficiência adrenal primária. O tratamento depende da causa e requer abordagem multidisciplinar, associado à reposição de glicocorticoides como também demais hormônios, quando necessário. **Apresentação do caso:** Este artigo descreve um caso de doença de Addison diagnosticada na Atenção Primária à Saúde, situação que não é comum, posto que a doença apresenta sintomas clínicos bastante inespecíficos, principalmente em seus estágios iniciais e, frequentemente, não é um diagnóstico considerado. **Conclusão:** Ao nível da Atenção Primária, o caso não obteve resolução completa, entretanto a instituição cumpriu com êxito o seu papel, firmado na Política Nacional de Atenção Básica, dispondo-se de ser a coordenadora do cuidado e ordenadora dos serviços de saúde, acolhendo o paciente e reconhecendo as suas necessidades.

Palavras-chave: Doença de Addison; Insuficiência adrenal; Relatos de casos; Atenção primária à saúde.

Resumen

Introducción: La enfermedad de Addison, o insuficiencia suprarrenal primaria, es una enfermedad insidiosa y rara que puede presentar altas tasas de morbi-mortalidad cuando su diagnóstico no es reconocido y su tratamiento no se inicia prematuramente. Presenta síntomas variados, entre ellos se destaca hipotensión arterial, hiperpigmentación cutánea, hiponatremia e hiperpotasemia. Cuando no se trata, puede evolucionar una crisis adrenal y colapso cardiovascular. El diagnóstico de la enfermedad de Addison se hace clínicamente y a través de los hallazgos, en exámenes de laboratorio, en el que altas concentraciones de hormona adrenocorticotrópica (ACTH) y bajas concentraciones de cortisol en plasma caracterizan la insuficiencia Suprarrenal Primaria. El tratamiento depende de la causa y requiere un enfoque multidisciplinario, pero en general se hace con reemplazo de glucocorticoides y, en ocasiones, otras hormonas. **Presentación del caso:** Este artículo describe un caso de Enfermedad de Addison diagnosticada en la Atención Primaria de Salud, situación que no es común, ya que la enfermedad presenta síntomas clínicos bastante inespecíficos, principalmente en sus etapas iniciales, y a menudo no es un diagnóstico considerado. **Conclusiones:** En el ámbito de la APS, o en caso de no obtener una resolución completa, sin embargo, la institución cumple con éxito su rol firmado en la Política Nacional de Atención Primaria, que se pone a disposición para ser coordinadora de la atención y organizadora de dos servicios de salud, acomodando o paciente y reconociendo sus necesidades.

Palabras clave: Enfermedad de Addison; Insuficiencia suprarrenal; Informes de casos; Atención primaria de salud.

INTRODUCTION

Primary adrenal insufficiency (PAI) was first described by Thomas Addison in 1855. It is known as a rare disease that affects 0.45 to 11.7 per 100 thousand individuals. According to the Brazilian guideline for the follow-up of people with rare diseases, this type of disease is defined as the one that affects up to 65 per 100 thousand individuals.[1] Addison's disease results from a lesion of adrenal glands, and its etiology involves several conditions, including tuberculosis, hemorrhages, primary neoplasms or metastases, infections (paracoccidioidomycosis, histoplasmosis, cryptococcosis, coccidioidomycosis, cytomegalovirus infection), amyloidosis, hemochromatosis, adrenoleukodystrophy secondary to medications, and congenital adrenal hyperplasia. However, we now know that the most common cause of PAI is autoimmune adrenalitis, which is responsible for 65 to 84% of cases.[2,3]

The disease can be acute or insidious. The acute manifestation can be rapidly fatal if not promptly identified and treated.[4,5] Symptoms are often nonspecific, characterized by asthenia, anorexia, weight loss, myalgia, abdominal pain, and intermittent vomiting, and occur when at least 90% of the adrenal tissue has been destroyed. Skin hyperpigmentation, a typical and specific aspect of PAI, is almost always present.[4] Hyponatremia, with or without associated hyperkalemia, affects 90% of individuals with PAI.[4]

CASE PRESENTATION

C.H.O.C., 25 years old, female, single, student, born in Cuiabá (Mato Grosso), and living in Catanduva (São Paulo). The patient sought the neighborhood health unit, accompanied by her father, with recurrent gastrointestinal complaints.

She declared having severe abdominal pain, nausea, vomiting, diarrhea, and low back pain for approximately seven months, associated with weight loss of about 20 kg in the period. Concomitantly with the symptoms, she reported progressive skin darkening throughout the body, with hyperpigmented spots on the palms of both hands standing out. The patient stated that the gastrointestinal symptoms motivated recurrent visits to the emergency department and also that she had been evaluated by an oncologist due to hyperpigmented macules in her hands.

She denied using continuous medication, pain complaints, and other abnormalities. She graduated high school without difficulties, but did not speak much during the visit, presenting total deafness in the left ear and partial hearing loss in the right ear. The information was imparted mainly by her companion. In addition, she has a history of intrapartum exposure to HIV, having used azidothymidine (AZT) for one year and presenting negative results in subsequent serological tests.

Physical exam

During the visit, she showed good overall condition, healthy skin color, was hydrated, acyanotic, anicteric, eupneic, and had no tactile fever. Her systolic blood pressure was 90 x 60 mmHg. Pulse was 75 beats per minute. Capillary glycemia was 81 mg/dL.

The dermatological examination revealed hyperpigmentation of interphalangeal joints, elbows, back and palms of the hands, face, and scarred areas, as well as hyperpigmented macules on the palms of her hands and mucous membranes, as shown in the following images (Figures 1, 2, and 3).

The images below illustrate other changes specific to the disease (Figures 4, 5, 6, and 7).

Figure 1. Hyperpigmented macules in the buccal mucosa.

Figure 2. Brownish gum macules accompanied by lip hyperpigmentation.

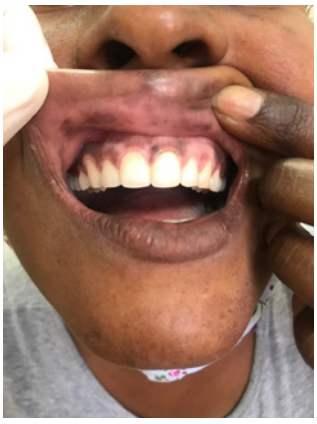

Figure 3. Hyperpigmented macules in the oral mucosa and diffuse hyperpigmentation of face and fingers.

Figure 4. Characteristic hyperpigmentation of elbow and scar site in the left upper limb.

Figure 5. Hyperpigmentation throughout the skin, with emphasis on the greater pigmentation of interphalangeal and metacarpophalangeal joints.

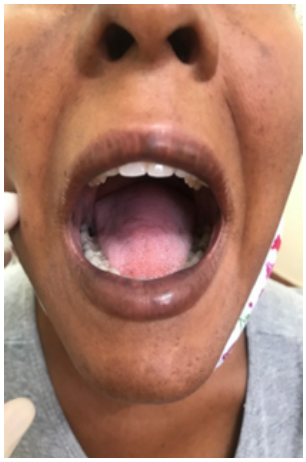

Figure 6. Lip hyperpigmentation.

Figure 7. Hyperpigmented macules on the palms of the hands.

In order to reach a diagnosis, additional tests were requested at the time: complete blood count (Hemoglobin: 12.7|Hematocrit: 35.1|Leukocytes: 6,680|Neutrophils: 30.5|Band neutrophils: 0|Segmented: 30.5|Eosinophils: 8.1|Basophils: 0.6|Lymphocytes: 51.2|Monocytes: 9.6|Platelets: 210,000, erythrocyte sedimentation rate — ESR: 25 (reference value — RV for women: up to 20), renal function (Urea: 37|Creatinine: 0.6|Glomerular filtration rate estimation (method — calculated by the formula Chronic Kidney Disease Epidemiology — CKD-EPI): non-black adult: 127 (RV: above 90), hepatic function (aspartate transaminase — AST: 51 (RV for adult women: 10 to 32 U/L)|Alanine transaminase — ALT: 77 (RV for adult women: 10 to 33 U/L), inflammatory tests (C-reactive protein — CRP: 3 (RV: <5.0 mg/L), stool ova and parasite examination and serological tests had normal results. The initial tests revealed abnormalities only in the thyroid function (thyroid stimulating hormone — TSH: 23.48; free T4: 0.9).

As the patient returned for visits, progressive skin darkening was observed. Thus, the main causes of diffuse skin hyperpigmentation were listed, with the most relevant being: pharmacological, with clofazimine or polymyxin B (however, the patient did not use these medications); some autoimmune connective tissue

diseases (however, the patient's clinical manifestation was not compatible); and hypovitaminosis B12 (vitamin B12 level: 403.2 (RV normal: 197– 771 pg/mL). Cortisol (0.20. Morning RV: 4.82–19.5 mg/dL) and adrenocorticotropic hormone — ACTH concentrations (above 1,250.0. RV: up to 46 pg/mL) showed changes compatible with Addison's disease.

Considering the findings above, the confirmed diagnostic hypothesis was Addison's disease. Since this endocrine-metabolic disease has multisystemic manifestations, a multidisciplinary approach was necessary, maintaining the follow-up at the Primary Health Unit, but including a referral for evaluation in specialized secondary care for adequate endocrine approach and therapy.

DISCUSSION

The nature of Addison's disease fluctuates between subclinical symptoms that progress slowly over years and sudden gland deterioration associated with acute trauma or surgery, which usually accompanies nausea, vomiting, severe hypotension, shock, dehydration, and can even culminate in death.[1-3]

In its chronic manifestation, the disease is insidious. Its peak incidence is around the age of 40, but it can occur at any age. It has varied and nonspecific clinical manifestations, with the most common being fatigue (present in 74% of cases), anorexia (61%), weakness (74%), dizziness (56.5%), and weight loss (78%).[6] In addition, the main dermatological symptom of Addison's disease is skin and mucosal hyperpigmentation (present in 80% of patients), which occurs mainly in joint and palmar creases, scars, oral mucosa, and friction sites due to the increase in melanocyte stimulating hormone (MSH), originating from the ACTH prohormone. Other potential symptoms include postural hypotension (30%) and salt avidity (8.7%). Women may also show pubic and axillary hair loss, absence of pubarche in children, and decreased libido (46%).[7,8]

Laboratory tests revealed hyponatremia (68%), hyperkalemia (79.5%), and renal function abnormalities, which are more common when the adrenal gland has undergone significant deterioration. However, we emphasize that not all patients with Addison's disease develop the classic triad of hyperpigmentation, hypotension, and hyponatremia, making its diagnosis sometimes difficult. Approximately 40% of patients with autoimmune Addison's disease have other associated autoimmune diseases, with Hashimoto's thyroiditis (3.7–32%) being the most frequent. In the case reported, besides the skin lesions, laboratory findings of hyponatremia and hyperkalemia corroborated the diagnosis; the possible association with Hashimoto's thyroiditis was relevant, as the patient presented abnormalities compatible with such diagnosis.

Moreover, the presence of nausea (61%), vomiting (65%), and gastrointestinal complaints (6.5%) delayed the diagnosis since it led the patient to seek care in urgency and emergency departments, and her symptoms might have been mistaken for acute abdomen and other causes of gastrointestinal abnormalities.[4]

This scenario highlights the importance of primary care and its comprehensive approach to the individual as a system organizer and care coordinator. It thus enables early diagnosis by identifying signs and symptoms and appropriately following rare conditions, such as Addison's disease. The clinical manifestation that brought the patient to the health unit several times was the skin lesion — a clinical sign that should therefore be explored in the Family and Community Medicine context since it may be a symptom of other more severe diseases.

In addition, primary health care (PHC) is responsible for the timely referral of the individual with a suspected rare disease to confirm the diagnosis, as well as coordinating and maintaining the care of this patient when referred to other facilities in the system.[1] Although laboratory tests are widely available in

SUS (the Brazilian public health system), the greatest challenge, in this case, was the diagnostic suspicion of Addison's disease, given the nonspecific complaints that the disease may cause.

Initially, routine laboratory tests were performed to investigate the possible diagnosis of adrenal insufficiency, commonly associated with Addison's disease, followed by specific cortisol and ACTH concentration tests. In this scenario, the results of decreased plasma cortisol concentrations and increased ACTH concentrations confirmed the PAI, which, in addition to the patient's clinical manifestation, reinforced the diagnosis of Addison's disease. Regarding the etiological investigation of adrenal insufficiency, other tests can be performed, such as measurement of adrenal antibodies, magnetic resonance imaging, and computed tomography.

Addison's disease requires lifelong treatment with a multidisciplinary approach.[1] It usually involves glucocorticoid replacement with oral hydrocortisone (10 to 25 mg per day divided into two to three doses) administered to mimic the physiological patterns of cortisol secretion. Fludrocortisone (0.10 mg) is administered once a day to replace mineralocorticoid hormones. We underline that glucocorticoid dosages should be adjusted in periods of stress, such as during infections or surgeries, in order to prevent an adrenal crisis.

The prognosis of Addison's disease is considered good since, despite having no cure, it can be well managed with the proper treatment and care to avoid an adrenal crisis, with no implications, in these situations, for life expectancy.[7,8]

In the context of this work, the PHC environment was crucial to reach the final diagnosis since, as the "entry point" of SUS users, it was responsible for the care of this patient based on a horizontal, continuous, and integrated relationship, so as to produce shared management of comprehensive care.[9]

Therefore, although the PHC level could not provide a complete resolution of the case, it was able to create an adequate bond[10] with both the patient and her family, consolidating the PHC role of embracing, diagnosing, and managing people with rare diseases. The trust established between physician, patient, and family was essential — from the diagnostic process to the referral — because it allowed understanding the biopsychosocial profile of the patient and of the environment into which she was integrated. As a result, diagnostic hypotheses could be suggested, the diagnosis was made, as well as properly explained and shared with the patient, who had her doubts solved, and the subsequent goals were traced together.[11]

CONCLUSION

We can conclude that, in this case, PHC successfully fulfilled the role established in the National Primary Care Policy,[9] which states that the main functions of the health care system are: to be a foundation, as the most decentralized modality of care and health services, whose participation in care is always necessary; to be effective, identifying health risks, needs, and demands, using and integrating different technologies for individual and collective care, and being able to build positive bonds and effective clinical and sanitary interventions, aiming at increasing the autonomy of individuals and social groups; and finally, to be the care coordinator and the organizer of health services, recognizing the health needs of the population under its responsibility.[9,11,12]

CONFLICT OF INTERESTS

Nothing to declare.

AUTHORS' CONTRIBUTIONS

IDB: Project administration, Supervision. AOGL: Conceptualization, Data curation, Writing – review & editing. GEPSA: Writing – original draft, Investigation. LVA: Writing – review & editing, Investigation, Methodology. JPMF: Writing – original draft, Software, Funding acquisition. LGCC: Formal analysis, Validation, Visualization.

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