INTRODUCTION

Autoimmune polyglandular syndromes are a rare group of polyendocrine conditions that included multiple glandular deficiencies associated with other autoimmune diseases\(^1\), such as hypergonadotrophic hypogonadism, vitiligo, chronic atrophic gastritis, pernicious anemia, chronic autoimmune hepatitis, and celiac disease. Autoimmune polyendocrine syndrome type 2 (APS II) is defined by the presence of Addison’s disease (AD) associated with autoimmune thyroid disease and/or diabetes mellitus (DM) type 1\(^2\). It is a rare condition, affecting approximately 1.4-2 cases/100,000 inhabitants\(^3\). Its least frequent clinical presentation is the combination of Graves’ disease and diabetes mellitus type 1. We present a case of APS II with the complete triad.
**CLINICAL CASE**

We present a 42-year-old woman, who was emigrated from France between age 19 and 36, with a history of total thyroidectomy due to Graves’ disease 11 years ago, DM type 2 with four years of evolution and hypertension, who sought the DE due to a continued condition, with three months of evolution, asthenia, weight loss (12 kg in three months), dizziness, abdominal pain predominantly in the right quadrants, nausea, and vomiting. She reported having suspended anti-hypertension therapy due to hypotension and presented a glycemic record with frequent hypoglycemia. Other medical history included dyslipidemia, asthma, and repeated urinary tract infections (ITUs). She was medicated with 100 mg sitagliptin, 5 mg folic acid, 0.1 mg levothyroxine, 10 mg atorvastatin, 320 µg budesonide+formoterol + 9 µg SOS. She had complementary diagnostic exams from a DE context, from 1.5 months before, due to a similar clinical scenario: analytical assay with slight microcytic anemia, negative CRP (Table 1), abdominal/pelvic/kidney/bladder ultrasound and combur without abnormalities. She was discharged with an indication for symptomatic treatment and an iron kinetics analysis, video colonoscopy, and outpatient EGD. The iron kinetics and video colonoscopy showed no abnormalities. The EGD was still pending completion. Upon physical examination at DE, TA was 104/77 mmHg, without orthostatic hypotension, FC: 83/min, no fever, discolored mucosa, with skin hyperpigmentation (Figures 1A and 1B); the rest of the exam showed no other abnormalities. After suspected suprarenal insufficiency, the examination proceeded. Analytically, there was no leukocytosis, anemia, hypoglycemia, hyponatremia, or hyperkalemia, and CRP was negative. Morning serum cortisol <0.5 ug/dl (4.3-22.4), free cortisol in urine 9 ug/24h (28-214), ACTH 1384 pg/mL (4.7-48.8), aldosterone and renin in an upright position of 0 pg/mL (41-323) and 430.7 IU/mL (4.4-46.1), respectively (Table 1). An additional study was conducted to investigate the cause of primary suprarenal insufficiency. Negative Quantiferon TB, suprarenal computed axial tomography without infiltrations, hemorrhage, or masses. Results for 21-hydroxylase antibodies were positive. After the autoimmune cause was confirmed and with a previous history of autoimmune thyroid disease, the investigation continued with normal vitamin B 12, positive anti-GAD, and negative anti-insulin, anti-IA2, anti-transglutaminase. In this context,

**FIGURES 1A AND 1B. SKIN HYPERPIGMENTATION.**

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**TABLE 1. ANALYTICAL STUDY.**

| Test                  | Results 1.5 months before | Results in hospitalization | Reference values |
|-----------------------|----------------------------|----------------------------|------------------|
| Leukocytes           | 4.8x10^9/L                 | 5.0x10^9/L                 | 4.5 – 11.50      |
| Hemoglobin           | 11.4 g/dL                  | 13.4 g/dL                  | 12 – 15          |
| Glucose              | 171 mg/dL                  | 154 mg/dL                  | 74 – 106         |
| Sodium               | 134 mEq/L                  | 136 mEq/L                  | 136 – 145        |
| Potassium            | 4.3 mEq/L                  | 4.7 mEq/L                  | 3.4 – 4.4        |
| CRP                  | 0.09 mg/dL                 | 1 mg/dL                    | <0.50            |
| AST                  | 56 U/L                     | 3 – 31                     |                  |
| ALT                  | 61 U/L                     | 3 – 31                     |                  |
| Urea                 | 26 mg/dL                   | 47 mg/dL                   | 16 – 42          |
| Creatinine clearance | 0.5 mg/dL                  | 0.7 mg/dL                  | 0.5 – 1.2        |
| Urinary cortisol     | 9 ug/24h                   | 28-214                     |                  |
| Morning serum cortisol | <0.5 ug/dl               | 4.3-22.4                  |                  |
| ACTH                 | 1.384 pg/mL                | 4.7-48.8                   |                  |
| Renin                | 430.7 IU/mL                | 4.4-46.1                   |                  |
| Aldosterone          | 0 pg/mL                    | 41-323                     |                  |
RESUMO

A síndrome poliglandular autoimune tipo 2 (SPGA2) é definida pela presença de doença de Addison (DA) associada à doença tiroideia autoimune e/ou diabetes mellitus tipo 1 (DMT1). Trata-se de uma doença rara, afetando cerca de 1,4-2 casos/100.000 habitantes. A apresentação clínica menos frequente é a combinação de DA, doença de Graves e DMT1.

Apresenta-se mulher de 42 anos, com antecedentes de tiroidectomia total por doença de Graves, diabetes mellitus tipo 2 e hipertensão, que recorre ao SU por quadro arrastado de astenia, emagrecimento, tonturas, náuseas e vômitos. Referia ter suspendido terapêutica anti-hipertensora por hipotensão e apresentava registro glicêmico com hipoglicemias frequentes. Ao exame físico, salientava hiper-pigmentação cutânea. Analiticamente sem leucocitose, anemia, hipoglicemia, hiponatremia ou hipercaliemia, PCR negativa. Cortisol sérico matinal <0,5 ug/dl (4,3-22,4), cortisol livre na urina 9 ug/24h (28-214), ACTH 1.384 pg/mL (4,7-48,8), aldosterona e renina em posição ereta de 0 pg/mL (41-323) e 430,7 uUI/mL (4,4-46,1), respectivamente. Realizado estudo complementar para averiguar causa de insuficiência suprarrenal primária. Quantiferon TB negativo, tomografia axial computadorizada das suprarrenais sem infiltrações, hemorragia ou massas. Anticorpos anti-21-hidroxilase positivos. Foi aprofundada a investigação com vitamina B12 normal, anti-GAD positivo, anti-insulina, anti-IA2, antitransglutaminase, negativos. Nesse contexto, a doente iniciou insulinoterapia e tratamento dirigido para a DA com prednisolona e fludrocortisona, com boa resposta clínica.

Este caso tem como objetivo alertar para a necessidade de elevada suspeição clínica no diagnóstico de DA. Sendo esta uma doença autoimune rara, é importante rastrear outras doenças autoimunes no sentido de excluir SPGA.

PALAVRAS-CHAVE: Poliendocrinopatias autoimunes. Doença de Addison. Diabetes mellitus tipo 1. Doenças da glândula tireoide.
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