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COVID-19 in a patient with Graves' disease associated with rheumatoid arthritis: the 1st case

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ABSTRACT:

— ***Introduction:*** This article reports the first case of a patient with rheumatoid arthritis (RA) associated with Graves' disease (GD) who evolved with COVID-19 infection.

— ***Case description:*** A 34-year-old male patient who was previously healthy was diagnosed with GD in 2018. After 6 months of GD diagnosis, he started polyarthritis associated with morning stiffness and reduced daily activities. He was treated with 20 m/day of prednisone and hydroxychloroquine 400 mg/day. Laboratory tests showed TSH of 0.09 mcg/mL, positive TRAb, C-reactive protein of 48 mg/L, and positive rheumatoid factor of 32 IU/mL. We initiated methotrexate 15 mg/week plus folic acid 5 mg/week and reduced prednisone to 10 mg/day. He evolved with RA improvement. In February 2022, he started fever, anorexia, severe fatigue, and dry cough. He denied dyspnea. He was diagnosed with COVID-19 infection in the emergency room by rapid test. The patient became asymptomatic after seven days, and RA remained in low disease activity during the COVID-19 infection.

— ***Conclusions:*** It is the first case of a patient with GD who developed RA and COVID-19 described in the literature.

— ***Keywords:*** *Graves' disease, Rheumatoid arthritis, COVID-19, Autoimmune disease, Autoimmunity.*

INTRODUCTION

Some autoimmune diseases are associated with Graves's Disease (GD), such as vitiligo, diabetes mellitus type 1, and Hashimoto Thyroiditis (HT)[1]. Regarding this autoimmune thyroid disease, the literature series varies from 0.5 to 27%[2]. On the other hand, a few previous cases of GD are associated with rheumatoid arthritis (RA). The frequency of this rare association varies from 0.6 to 0.84% in the United States to 1.0 to 1.6% in European countries[3-5]. Analysis of these cases shows that only 101 cases were described with this rare association of GD and RA[2]. Coronavirus disease 2019 (COVID-19) has recently emerged in China, with more than 438.968.263 confirmed cases of COVID-19, including 5.969.439 deaths, reported to WHO. As of 27 February 2022, 10.585.766.316 vaccine doses have been administered[3]. Herein, we report the first case of a patient with RA associated with GD who evolved with COVID-19 infection.

CASE DESCRIPTION

A 34-year-old male patient who was previously healthy was diagnosed with GD in 2018. He had anxiety, tachycardia, sweating, weight loss, and exophthalmia. He received methimazole 20 mg/day and propranolol 40 mg/day. After 6 months of GD diagnosis, he started polyarthritis of his hands (all metacarpophalangeal, proximal interphalangeal, and wrists) associated with morning stiffness and reduced daily activities. He was treated

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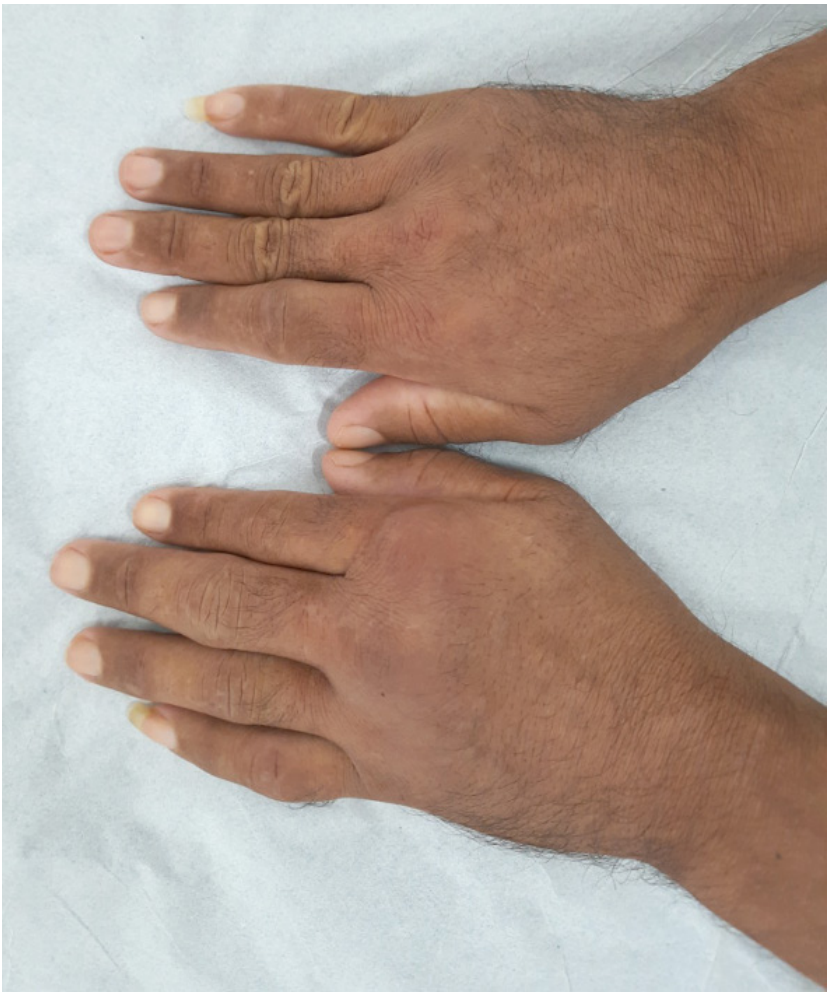

Figure 1. Hand arthritis showing evident edema of the 2nd and 3rd bilateral metacarpophalangeal, left wrist, and 2nd right and 3rd left proximal interphalangeal arthritis.

with 20 m/day of prednisone and hydroxychloroquine 400 mg/day. He came to our private clinic and we confirmed the polyarthritis. Laboratory tests showed TSH of 0.09 mcg/mL [reference value (rv): 0.48-4.5 mcg/mL], free T4 1.31 ng/dL (rv: 0.89-1.76 ng/dL), positive TRAb, C-reactive protein of 48 mg/L [rv: < 3 mg/L], and positive rheumatoid factor 32 IU/mL (nv: < 14 IU/mL). Anti-CCP was negative. 25-OH vitamin D was 22.4 ng/mL (rv: > 30 ng/mL). Antinuclear antibodies were positive with a titer of 1/1280, positive anti-Ro/SS-A, and anti-La/SS-B. Anti-dsDNA and anti-Sm were negative, and complement levels were within the normal range. He denied xerostomia and xerophthalmia; Schirmer and Rose Bengal were negative. We initiated methotrexate 15 mg/week plus folic acid 5 mg/week, reduced prednisone to 10 mg/day, and added vitamin D3 50,000 IU/week. He evolved with RA improvement, reduced polyarthritis (Figure 1) and CRP to 5 mg/L, and normalized vitamin D. In February 2022, he started fever, anorexia, severe fatigue, and dry cough. He denied dyspnea. He was diagnosed with COVID-19 infection in the emergency room by rapid test. Lungs were normal on physical examination, and the X-ray was unmarked. It was suggested to keep social quarantine for 10 days and increase oral hydration. The patient became asymptomatic after seven days, and RA remained in low disease activity during the COVID-19 infection.

DISCUSSION

It is the first case of a patient with GD who developed RA and COVID-19 described in the literature.

Previous studies[4,5] demonstrate an increased prevalence of rheumatic diseases in patients with autoimmune thyroid disease, suggesting similar pathophysiological mechanisms between the two conditions. Genetic and environmental factors are the most studied variables responsible for the appearance of two autoimmune diseases in the same patient. Genes such as HLA and PTPN22 and exposure to tobacco and infections are linked to the two autoimmune diseases described in the present case[4,5].

In this sense, it is suggested to maintain constant surveillance in patients with autoimmune thyroid disease about the appearance of signs, symptoms, or laboratory alterations suggestive of autoimmune rheumatologic disease, mainly Sjogren's Syndrome, Rheumatoid Arthritis, Systemic Lupus Erythematosus, Systemic Sclerosis and Mixed Connective Tissue Disease[6,7].

However, the appearance of polyarthritis in a patient with GD or HT raises a wide range of differential diagnoses and collagen diseases. Musculoskeletal symptoms may be associated with thyroid disease itself. Synovitis, fibromyalgia symptoms, and carpal tunnel syndrome may occur in patients with hypothyroidism and poly-

arthralgia associated or not with periostitis, soft-tissue edema, and digital clubbing in hyperthyroidism[8].

In this context, musculoskeletal symptoms can also be explained by using antithyroid drugs. The occurrence of associated ANCA vasculitis is a relatively rare but well-documented complication with Methimazole and Propylthiouracil, drugs frequently used in treating hyperthyroidism. The clinical picture ranges from cutaneous lesions, arthralgia, or arthritis to life-threatening target organ damage like nephritis and alveolar hemorrhage. It is usually associated with the presence of an anti-myeloperoxidase antibody. High doses of corticosteroids and immunosuppressive agents may be necessary to control vasculitic manifestations. Another condition that is being increasingly recognized is the antithyroid arthritis syndrome, characterized by arthritis that begins after the introduction of antithyroid medications whose treatment consists of stopping them. The absence of ANCA helps differentiate from drug-induced vasculitis[9,10].

The present clinical case presented a patient with a known diagnosis of GD who evolved with symmetrical additive polyarthritis with morning stiffness and elevation of markers of inflammatory activity. The typical clinical picture associated with the presence of positivity for rheumatoid factor and anti-Ro and the excellent response to treatment with Methotrexate even with the maintenance of Methimazole strengthened the diagnosis of Rheumatoid Arthritis.

This case highlighted the first case described in the literature on a patient with Graves's disease associated with RA with COVID-19 infection and had a good outcome.

Ethics Approval:
Not applicable.

Availability of Data and Material:
All material is available upon request.

Conflict of Interests:
The authors declare that they have no conflict of interests.

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J.F. Carvalho: conception, data collection, analysis, writing, submission, supervision.
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