

Auto-immune thyroiditis in SARS-CoV-2 exposed twins

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Abstract. – OBJECTIVE: In the coronavirus disease 2019 (COVID-19) pandemic, a spectrum of sequelae affecting different organs has been reported. Of these, the ones affecting the thyroid gland have been reported, especially in the adults.

CASE REPORT: We present previously healthy twin adolescents with no history of thyroid disease, presenting with signs and symptoms of hypothyroidism after recovery from mild COVID-19 infection. Their investigations were consistent with auto-immune thyroiditis with primary hypothyroidism, showing markedly elevated thyroid-stimulating hormone (TSH), suppressed FT4 levels, positive anti-thyroid peroxidase antibody and anti-thyroglobulin antibody titres. They were treated accordingly and showed quick clinical improvement in symptoms.

CONCLUSIONS: This case report demonstrates that COVID-19 infection can be temporally associated with primary hypothyroidism in genetically predisposed children adding more to the growing list of sequelae especially in children.

Key Words:

Autoimmune thyroiditis, SARS-CoV-2, Children.

Introduction

Many cases of adults infected with SARS-CoV-2 who subsequently developed autoimmune diseases are reported¹. This disorder may develop after many viral infections, including SARS-CoV-2. It may also appear after resolution of the respiratory syndrome or in this case as asymptomatic infection. This is the first case report of auto-immune thyroiditis post SARS-CoV-2 infection in children to be reported to the best of our knowledge.

Case Presentation

A 14-year-old girl elder of the twins, born out of *in vitro* fertilization presented to our

Outpatient department with easy fatigability, decreased appetite, and hair loss. The symptoms were insidious in onset. About 8 weeks before presentation, all the family household members were diagnosed by RT-PCR for SARS-CoV-2 infection. All of them had asymptomatic and mild disease lasting for about 2-3 days. The index case and her twin brother had anosmia, mild fever and myalgia during the course of illness. Their anosmia recovered after about 4 weeks. During the last 6 weeks before presentation, she was noticed to be increasingly listless and eating less. Her twin brother was apparently doing well. They had not received any medications, supplements or SARS-CoV-2 or any other vaccinations during this time. The investigations e.g., complete blood count, renal and liver functions, blood glucose levels were normal and IgG for SARS-CoV-2 was positive. The thyroid function test results showed a hypothyroid state with Thyroid Stimulating Hormone (TSH) levels of 16 mIU/mL (up to 4.7 mIU/mL); free T4 of 0.5 ng/dL (0.7-1.8 ng/dL). The Thyroid Antibody profile was positive for anti-thyroglobulin antibodies (Tg) of 252 IU/mL (less than 50 IU/mL) and anti-thyroid peroxidase antibodies (TPO) of 71.2 IU/mL (less than 50 IU/mL). A thyroid ultrasound scan showed the presence of heterogeneous and diffusely hypoechoic tissue. During the same time her twin brother who was apparently normal, when screened also showed features of hypothyroidism with thyroiditis, i.e., TSH – 17.6 mIU/mL; free T4 of 0.6 ng/dL; antibodies, anti-Tg of 152 IU/mL and anti-TPO of 104 IU/mL. His parameters were normal for other screening tests. Both of them were diagnosed with auto-immune thyroiditis with primary hypothyroidism. Both of them started treatment of levothyroxine sodium 25 µg every day. At 6 weeks, the index case reported improvement in fatigue symptoms, hair loss and

better appetite. The thyroid biochemical parameters normalised. Both of them continued to be doing well clinically and biochemically during the last follow-up.

Discussion

In few cases published, sub-acute thyroiditis was the sole symptom of SARS-CoV-2 infection in adults. It should also be noted that cases of primary hypothyroidism related to COVID-19 in adults have been reported in previous studies²⁻⁷. Of interest, cases of sub-acute thyroiditis after SARS-CoV-2 vaccination have also been described^{8,9}.

Other common thyroid manifestations of COVID-19 especially in adults include overt thyrotoxicosis, Graves' orbitopathy, and primary hypothyroidism. A few research papers have even suggested that COVID-19 could be considered as an endocrine disorder, to make sense of the nonspecific response of the immune system to the SARS-CoV-2 virus, which is far different from infections, such as influenza¹⁰. Even in acute COVID-19 in adults, the outcomes of the meta-analysis showed that patients with abnormal thyroid-related hormones had greater mortality¹¹.

Some scholars² have suggested three forms of post-COVID-19 syndrome using the following criteria: acute post-COVID-19, with symptoms from 5 to 12 weeks; long post-COVID-19, with symptoms from 12 to 24 weeks, and persistent post-COVID-19, in which symptoms occur over 24 weeks after the infection.

COVID-19 is associated with a systemic inflammatory and immune response, involving Th1/Th17/Th2 lymphocytes and pro-inflammatory cytokines, which resemble the immune activation that occurs in immune-mediated thyroid diseases¹². The viral infected cell triggers a molecular mimicry, leading to an autoimmune response to the host tissue. The Antigen presenting cells (macrophage), triggered by the auto-antibodies cause epitope spreading and activate the T-lymphocytes, mainly the CD8+ cells^{13,14}. In genetically predisposed children, SARS-CoV-2 infection is likely to establish an environment that promotes autoimmunity. SARS-CoV-2 uses ACE2 as a receptor to infect the host cells and ACE2 is highly expressed by follicular thyroid cells^{2,15}.

Unravelling the pathophysiology of SARS-CoV-2-triggered thyroid dysfunctions may aid

pertinent therapeutic options and management of these patients in both during and post-COVID-19 scenarios¹⁶.

They have been counselled to undergo genetic tests for possible influence of genetic polymorphisms in pro-inflammatory genes that favour chronic inflammatory signalling triggering autoimmune diseases¹⁷.

Conclusions

It has been demonstrated that COVID-19 is a multi-systemic inflammatory disorder. Among other symptoms and late complications of SARS-CoV-2 infection, endocrine dysfunction should be considered. The thyroid disease that developed in the twins after an apparently mild to asymptomatic infection underlines this nature. It is prudent to closely follow-up and keep a high index of suspicion in a particular cohort of paediatric patients (like co-morbidities, significant previous medical histories, etc.) even after an asymptomatic course and performing relevant tests if clinically indicated. The objective of this case report is to sensitize general practitioners and paediatricians to remain updated with these kinds of possibilities in the current COVID-19 pandemic.

Conflict of Interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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Informed Consent

Obtained.

Ethical Approval

This case report is approved by Sarji Ethic Committee.

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