

Onset of Type I Diabetes Followed by Scleroderma Syndrome in a Child After the COVID-19: A Case Report

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Abstract

Morphea, is a chronic inflammatory disease of the dermis and subcutaneous tissue. Research has indicated a connection between morphea and Type I Diabetes (T1D). COVID-19 can cause autoimmune diseases like scleroderma, T1D, systemic lupus erythematosus, and others. A 12-year-old girl with type I diabetes who was on insulin therapy was brought into the clinic for a metabolic evaluation. The patient had induration, skin hardness, and cutaneous erythema upon inspection. The onset of T1D was following a mild COVID-19 infection. Signs of morphea merged 3 months after the onset of T1D. Known as “long-term COVID,” this sickness phase that follows the acute stage of COVID-19 is most likely the result of autoimmune activation. As this patient under evaluation reveals, COVID-19 has been demonstrated in the literature to cause the production of autoantibodies and to either cause or worsen autoimmune disorders in people who have a genetic susceptibility.

Keywords

morphea, type I diabetes mellitus, Covid-19, children, co-existing

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Introduction

Morphea, also called localized scleroderma, is a chronic inflammatory illness of the dermis and subcutaneous cellular tissue that causes atrophy at different levels along with a sclerotic process that causes diffuse thickening and induration of the skin. Although both morphea and systemic sclerosis share physiopathogenic elements, morphea is thought to be a distinct disease that does not progress into systemic sclerosis. Patients with morphea frequently experience extracutaneous disorders, primarily ophthalmic, articular, and central nervous system damage.¹ The pathogenesis of a chronic connective tissue disease with a localized scleroderma or morphea is uncertain.^{1,2}

There are various forms of morphea, and each has a unique clinical presentation and degree of involvement of the connective tissue. Indurative lesions with thicker skin and higher collagen content are indicative of morphea. Linear scleroderma, plaque morphea, deep morphea, bullous morphea, and generalized morphea are the divisions of this entity.¹⁻⁴

Morphea and poor metabolic control in people with diabetes have been linked in numerous studies.⁵ The exact cause of the diabetes-related sclerodermic injuries

pathogenesis remains unknown. It was proposed that collagen fibers' nonenzymatic glycosylation might change how quickly it degrades. According to research by other authors, glucose may promote the growth of fibroblasts and the production of extracellular matrix constituents.^{5,6}

Viral infections and the interferon input are recognized to be triggers for morphea. Viral infections have the ability to induce autoimmunity via a number of different pathways, such as molecular mimicry, interferon-inducible gene activation, apoptosis induction, epitope dissemination, and B-cell activation. Interferon activation can trigger autoimmune dysregulation that quickly develops into autoimmune disorders in those who are genetically prone to them.⁵⁻⁸

The respiratory tract infection known as coronavirus disease (COVID-19) is brought on by the SARS-CoV-2

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Figure 1. Skin lesions caused by morphea.

virus. In select individuals, the acute phase of the infection may be succeeded by a protracted illness phase (long COVID) with an unclear cause that is likely connected in certain cases to autoimmune activation.⁹

COVID-19 has been demonstrated to stimulate the generation of autoantibodies and, in individuals who are genetically susceptible, to either initiate or worsen autoimmune disorders.¹⁰ SARS-CoV-2 is thought to have the ability to cross-react with host cells, impairing self-tolerance and inciting autoimmune reactions. Many people are affected by COVID-19 “long COVID,” which causes late or chronic symptoms that are a topic of intense controversy. The immunological response, clinical symptoms, and response to immunomodulatory treatment of COVID-19 disease are strikingly comparable to those of autoimmune disorders. COVID-19 individuals have been found to exhibit transient autoantibodies, specifically ANA, Anti-Sd70 IgG. In addition, it has been noted that some patients who have COVID-19 infection go on to acquire autoimmune disorders including systemic lupus erythematosus.⁹⁻¹²

We present a case of onset of Type I Diabetes followed by plaque morphea in a child after the COVID-19.

Case Report

A 12-year-old girl with no history of any autoimmune diseases and in good health became sick on the 15th of October 2022 with mild symptoms of a flu-like disease: tiredness, fever, cough, and sore throat. Oropharyngeal swab for SARS-CoV-2 tested positive on the 17th October. The patient was isolated at home and did not need hospitalization. Fifteen days later her fever, cough, and sore throat had disappeared. Six months later (March, 2023), she fell ill with type 1 diabetes, and after another 3 months (June, 2023), she was diagnosed with

plaque morphea, which was treated with low-dose UVA phototherapy 6 sessions (3×/week). The last 6 months of follow-ups patients is in remission.

Medical history: grandmother’s sister suffers from type II diabetes. The course of type I diabetes has a sufficient level of compensation. During the 3 years of the T1D course only 1 episode of ketoacidosis was diagnosed. Has a tendency to hypoglycemia in the evening time.

Objectively: areas of plaque morphea on the abdomen, knee, neck, and arm. The most prevalent kind of localized scleroderma is called plaque-morphea. Multiple indurated plaques, usually symmetrically distributed throughout the trunk, legs, and lumbosacral region, are the hallmark of generalized form of morphea. It is identified as an existence of 4 or more lesions that impact 2 or more anatomic sites, have a diameter of >3 cm. The latter complete the patient’s clinical case as stated (Figure 1).

The following parameters indicate clinical damage: atrophy of the dermis, atrophy of the subcutaneous tissue, hyperpigmentation of the lesion, lesion center with increased skin thickness.

Thyroid gland ultrasound (November, 2023): heterogeneity of the structure - there are single macrofollicles of 1.5 mm in both lobes.

ECG (November, 2023): Middle right atrial irregular rhythm. Heart rate=50-59 bpm, R-R interval=1.21-1.01 second. Normal position of the heart axis: 54°.

Urinalysis (November, 2023): 10 to 12 erythrocytes in hpf.

Serum Biochemical profile (November, 2023): blood protein—64.1 g/L, blood urea—5.6 mmol/L, serum creatinine—70.8 mmol/L, serum cholesterol—4.2 mmol/L, ALAT—11.0 IU, ASAT—14.0 IU, HbA1—8.0%.

Anti-Sd70 IgG—7 AI (June, 2023), 0.85 AI (November, 2023)

The patient is in treatment with bolus-basal insulin injection. According to the latest dermatological consultation, the evolution of skin manifestations was stationary.

Discussion

Morphea is an uncommon inflammatory connective tissue disease that affects 4 to 27 new cases per million individuals each year. Morphea is shown to have 2 incidence peaks: one occurs in the fifth decade of life, and the other occurs between the ages of 2 and 14.^{9,10}

Autoimmunity manifestation and COVID-19 have a complicated and nuanced interaction.⁹⁻¹¹ Problems may arise when morphea is diagnosed via COVID-19. Infection and autoinflammatory response have pathogenesis-based connections. It may be challenging to differentiate between COVID-19-related immune reactions, symptoms, and clinical manifestations and those associated with autoimmune diseases due to the diseases' striking similarities with COVID-19 in terms of pathogenic mechanisms, immune responses, and clinical manifestations.^{13,14}

There are several fascinating parallels between morphea and COVID-19. Potentially these diseases associated with an elevated levels of IL-6, IL-10, and MCP-1 in the bloodstream, and they can potentially be systemic in nature. In addition to morphea, COVID-19 infection can cause endothelial damage, and both conditions are associated with interstitial lung fibrosis.¹⁵

Numerous investigations have documented the phenomena of new-onset hyperglycemia and diabetes after COVID-19 infection. Remarkably, a meta-analysis of 8 trials with almost 3700 hospitalized COVID-19-infected patients from 3 countries revealed a 14.4% pooled incidence of new-onset diabetes (95% confidence interval: [5.9%–25.8%]). Many autoantibodies have been detected in morphea, including ANA, ssDNA, and AHA antibodies.¹⁶

Wang et al assessed the mechanisms that might be in charge of inducing the autoimmune response that results in T1D following Covid-19. T1D may be caused by β -cell injury from viruses, immune-mediated pancreatic β -cell loss, or damage to β cells from surrounding cell infection.¹⁷ According to literature data scleroderma occurs in approximately 2.5% to 3% of patients with diabetes. Scleroderma-like syndromes in the course of long-term diabetes with coexisting complications are observed quite frequently.⁵ Our case describes rare sequence of the disorders, that is, COVID-19, T1D, and morphea.

Conclusion

Thus, the acute phase of infection may be followed by another prolonged phase of illness (long-term COVID) of unknown etiology, probably related to autoimmune activation in some cases. It is known from the literature

that COVID-19 can cause the production of autoantibodies and in genetically predisposed patients can cause the onset or exacerbation of autoimmune diseases, which is the case in the examined patient. This clinical situation requires further research and the search for molecular markers.

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Authors Contribution

Ie.B.—research idea, literature search, paper writing, submission, revision.

I. M.—paper writing, literature search.

O. S.—literature search, work with patient's records.

I. K.—literature search, paper writing.

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Ethical Approval

The local ethics committee of the Bogomolets National Medical University (Kyiv, Ukraine) gave its approval to the study (Protocol no. 142).

Patient Consent

Written informed consent was obtained directly from patient and her parents for her anonymized information to be published in the article.

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Supplemental Material

Supplemental material for this article is available online.

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