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Post-COVID-19 polyautoimmunity (pancytopenia, hypothyroidism): A case report

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Core tip

COVID-19 is known to present in heterogeneous and systemic clinical manifestations, similar to systemic autoimmune diseases and several similarities have been reported in the immune responses in both disease conditions. The association of hypothyroidism and pancytopenia has not been previously reported in the literature, either pre- or post-COVID-19. Broadening possible differentials to apprehend other causal factors in the context of COVID-induced pancytopenia is valuable, especially if it uncovers factors specifically related to a marrow-thyroid interaction in the context of COVID-19.

Abstract

Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-associated pancytopenia and hypothyroidism are known but rare complications of COVID-19 syndrome that are not well described in literature, particularly when manifested simultaneously. Severe acute respiratory syndrome coronavirus 2 has shown the potential to affect any organ including the hematopoietic and endocrine system, which then results in a decrease in all three blood cell lines, hyperthyroidism or hypothyroidism. These cases usually resolve with the passage of time and treatment of underlying risk factors. As COVID pneumonia rates continue to increase worldwide, it is crucial to be able to recognize these complications. Additionally, deeper investigation into a patient's response to COVID infection can be complicated by unexpected underlying diseases.

Case summary: An 88-year-old female with underlying hypertension, rheumatoid arthritis, hypothyroidism, chronic kidney disease, deep venous thrombosis, coronary artery disease presented with nausea and myalgias for 5 days. A diagnosis of COVID-19 and new-onset pancytopenia was confirmed on admission. In addition, her previous hypothyroid state had worsened by a markedly high TSH level. She had a rapid recovery (within 4 days) with our locally devised treatment protocol of azithromycin and dexamethasone, as well as a short course (2 days) of filgrastim.

Conclusion: The concurrence of pancytopenia and hypothyroidism have not been previously reported in the literature. We've found that broadening our differentials to apprehend other causal factors in the context of COVID-induced pancytopenia is valuable, especially if we can uncover factors specifically related to a marrow-thyroid interaction in the context of COVID-19. More research is needed to see if this novel virus differs significantly from others in terms of the immunological mechanisms that underlie pancytopenia and hypothyroidism.

Keywords: SARS-CoV-2; COVID-19; Autoimmune hypothyroidism; Pancytopenia; Case report.

Introduction

The Severe Acute Respiratory Syndrome Coronavirus 2 causes COVID-19 syndrome (SARS-CoV-2). COVID-19 infection primarily causes respiratory pathology, particularly the characteristic bilateral multifocal pneumonia; however, the infection can also impact the bone marrow, impairing the hematopoietic system [1]. Lymphopenia, neutropenia, and, in rare cases, pancytopenia may result [2,3]. In October 2020, the first instance of chronic pancytopenia linked to SARS-CoV-2 bone marrow infiltration in an immunocompromised patient was reported, followed by several cases [4,5]. Many case reports have recently emerged showing the presence of hyperthyroidism and hypothyroidism, most notably Subacute Thyroiditis (SAT) following SARS-CoV-2 infection [6]. However, not only could an infection cause SAT, but new vaccines are also suspected of causing thyroid dysfunction [7-22].

Our goal is to discuss the clinical findings of a rare instance of COVID-19-associated pancytopenia and severe hypothyroidism in an immunocompetent individual without underlying thyroid disease. Although our case has some similarities to other reported cases, it also has important variances to examine.

Case presentation

An 88-year-old female presented to the Emergency Room (ER) 5 days after worsening nausea and myalgias which incapacitated her and she was unable to perform daily activities. She was unaware she had COVID-19 until she tested positive in the ER. She had no family history of blood disorders. Her past medical history is relevant for hypertension, rheumatoid arthritis, hypothyroidism, Chronic Kidney Disease (CKD), Deep Venous Thrombosis (DVT) and coronary artery disease. Her home medications at the time of admission were low-dose aspirin, folate, methotrexate, metoprolol and oxycodone. Laboratory results during an office visit 2 months before index hospitalization revealed no discrepancy in her blood lines, as evidenced by a WBC of 10.6 g/dL, HGB 13.2 g/dL, and PLT of 210 x 10^3/L.

Initial investigation with a complete blood count revealed a Hemoglobin (HGB) of 7.9 g/dL, White Blood Cells (WBC) of 0.9 g/dL, and Platelets (PLTs) of 37 x 10^3 /L. Anemia was normocytic (Mean Corpuscular Volume [MCV] 97.8) and normochromic (Mean Corpuscular Hemoglobin [MCH] 32.8). Leukopenia was neutrophil-predominant (58.9% neutrophils, 27.8% lymphocytes, 1.1% eosinophils, 0.0% basophils, and 1.1% monocytes). Blood smear was only remarkable for a low PLT count and morphology. Free T4 (FT4) was low (0.19 ng/dL) and Thyroid-Stimulating Hormone (TSH) was very high (94.498 mc Intl units/mL). The patient was admitted to the medicine ward for blood transfusion, volume resuscitation, and further workup.

Diagnostic evaluation for hypo-proliferation, hemolysis, and malnutrition was initiated. There was concern for a hemolytic process yet bilirubin level was normal at 0.9 mg/dL. Transaminases were elevated with Aspartate Aminotransferase (AST) at 130 U/L, Alanine Aminotransferase (ALT) at 96 U/L, and normal Alkaline Phosphatase (AP) at 53 U/L, findings suggestive of a non hemolytic anemia. A reticulocyte index was not available to assess for hypo/hyperproliferation. Iron panel revealed iron deficiency. Vitamin B12, folate, and vitamin D were normal. The patient was transfused 1 unit of packed red blood cells and had an appropriate rise in hemoglobin to 8.9 g/dL.

We continued our workup with albumin electrophoresis to rule out other possible causes for this presentation. A bone marrow biopsy was deferred for the time being and was started on filgrastim and dexamethasone.

Clinical improvement was observed over the next few days despite the uncertain pathophysiological process of her pancytopenia. Within 2 days of filgrastim therapy, a leukemoid reaction was observed with a WBC of 38.51 g/dL, exhibiting a recovery in bone marrow function, and filgrastim was discontinued the next day. During the next two days after stopping filgrastim, Absolute Neutrophil Count (ANC) and FT4 levels continued to improve, leading to the patient's safe discharge to a skilled nursing facility for continuation of physical therapy the following day.

Patient progressively recovered and the following labs were reviewed at her outpatient follow up back at our clinic, 2 weeks after her discharge: WBC 11.0 g/dL, HGB 10.7 g/dL, PLT 180 x 10^3/L, TSH 36.37 mIU/L, FT4 1.5 ng/dL. She was now asymptomatic and free of COVID-19.

Discussion

The present COVID-19 pandemic has resulted in a plethora of autoimmune outcomes. The infection affects the entire body's systems, in addition to primary pulmonary involvement. SARS-CoV-2 may cause damage to the endocrine system, according to preliminary research published by Somasundaram et al. in June 2020 [23]. The first reports only a few months later confirmed this suspicion [24]. Several mechanisms may have an impact on the thyroid gland.

To begin with, the virus enters human tissues via the Angiotensin-Converting Enzyme 2 (ACE2) cell receptor, which is highly expressed in thyroid cells and can have direct viral cytopathic effects on the thyroid gland [26,27]. Early studies revealed some similarities between amino acid sequences of virus spike glycoprotein subunits S1 and S2, as well as tissue proteins like Thyroid Peroxidase (TPO). This can trigger or aggravate autoimmune activity against thyroid cells [28].

Furthermore, it is thought that SARS-CoV-2 induces myelosuppression by destroying blood cells with autoantibodies [29]. The coronavirus that causes severe acute respiratory syndrome binds angiotensin converting enzyme 2 receptors, which have also been discovered in bone marrow [29]. As a result, binding to these receptors might have negative consequences, such as pancytopenia. In addition, there have been case reports that suggest proinflammatory cytokines can impede hematopoiesis [29]. Pancytopenia can arise from SARS-CoV-2 infection in the lungs, which causes the death of lung hematopoietic progenitors.

Conclusion

The investigation of hematological outcomes and endocrinopathies caused by COVID-19 is still ongoing. We've found that broadening our differentials to apprehend other causal factors in the context of COVID-induced pancytopenia is valuable, especially if we can uncover factors specifically related to a marrow-thyroid interaction in the context of COVID-19.

More research is needed to see if this novel virus differs significantly from others in terms of the immunological mechanisms that underlie pancytopenia and hypothyroidism. Fortunately, it appears that most people with COVID-induced pancytopenia and hypothyroidism restore bone marrow and thyroid function as they recover from COVID-19 syndrome and underlying risk factors are addressed as has been demonstrated in this case report. Future studies should be directed to autoimmune phenomena associated with COVID-19.

Declarations

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Informed consent: The patient was provided verbal consent for submission of the case report provided personal identifiers are not included. All details that might disclose the identity of the patient have been omitted.

Conflict of interest: The authors have no conflict of interest to declare.

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