Case Report

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Subacute thyroiditis after SARS-CoV-2 BNT162b2 vaccine in a multiple myeloma patient

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Abstract

Viral infections emerge in the pathogenesis of subacute thyroiditis. Aside from this, subacute thyroiditis following vaccines utilizing inactivated viruses has been shown on rare occasions. Due to the COVID-19 pandemic, several vaccines have been developed all over the world; mass and unprecedented vaccination has thus been initiated. However, it is known that cases such as subacute thyroiditis have been reported, albeit rarely, after administration of COVID-19 vaccines. In this case report, we present a 59-year-old patient with multiple myeloma developing subacute thyroiditis following BNT162b2 vaccine. Patient had swelling in the neck, and his symptoms were controlled with non-steroidal anti-inflammatory drugs. Subacute thyroiditis following administration of the COVID-19 vaccine is rare; however, it is likely an under-reported condition that is difficult to detect. Clinicians should stay informed and have increased awareness of post-COVID-19 vaccine subacute thyroiditis.

Keywords

Subacute thyroiditis, coronavirus vaccine, COVID-19, SARS-CoV-2

Introduction

Subacute thyroiditis, also known as De Quervain's thyroiditis, is a benign self-limiting disorder of the thyroid.[1] In clinical presentation, the thyroid gland is usually enlarged with pain radiating to the neck, throat, and jaw being observed. Fever and other symptoms of infection could be seen.[2] Several viral infections have been associated with subacute thyroiditis.[3] Subacute thyroiditis has also been reported after vaccination for viral disease.[4–6]

The COVID-19 disease caused by the SARS-CoV-2 virus has resulted in a global pandemic. This pandemic has brought an enormous burden upon people and caregivers, and more importantly, caused many deaths.[7] With the progression of the COVID-19 pandemic, the development of many vaccines has accelerated. Thanks to these developments, we have watched many vaccines being approved for emergency use and entered our daily life. Vaccination with Coronavac, which is an inactive virus vaccine, started in Turkey and then continued with the BNT162b2 (Pfizer-BioNTech) vaccine.

In addition, it has been shown that COVID-19 infection is more severe and fatal in patients with hematological malignancy.[8,9] Multiple myeloma, which is the second most common hematological malignancy, is characterized by production of malign plasma cells.[10] Due to the nature of the disease, there is an increased risk for infections, and COVID-19 may become more serious in these patients.[11,12] Infections are a major cause of morbidity and mortality in patients with multiple myeloma;[13] there is an increased risk for bacterial and viral infections in multiple myeloma patients when compared to healthy controls.[14] Therefore, vaccination is mandatory for multiple myeloma patients as the disease itself affects antibody-producing plasma cells, impairing T cell and B cell functions, thus causing an immunosuppressive state.

In this case report, we aimed to present a 59-year-old male patient with multiple myeloma who developed subacute thyroiditis after vaccination with Pfizer-BioNTech (BNT162b2) messenger RNA (mRNA)-based vaccine.

Case presentation

Anemia and hypercalcemia were present in the evaluation of a 59-year-old male patient who arrived with complaints of fatigue and bone pain. An IgA Lambda Multiple myeloma diagnosis is present with his detailed work-up that includes a

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bone marrow biopsy. He had no comorbid conditions, and his Eastern Cooperative Oncology Group (ECOG), performance status was 0. He was Stage 1 for International Staging System (ISS) and Stage 1 for revised International Staging System (R-ISS) prognosis classification.[15] The patient is fit for chemotherapy and eligible for autologous hematopoietic stem cell transplant (ASCT). Planned for induction were four cycles of the CyBorD regimen, which is a combination of bortezomib–cyclophosphamide–dexamethasone.[16,17] A very good partial response has been achieved at the end of the treatment according to the International Myeloma Working Group (IMWG) consensus criteria for response.[18]

Mobilization of stem cells was performed with cyclophosphamide 3 gr/m^2, and after that, the patient underwent a successful ASCT. Lenalidomide 10 mg for maintenance therapy was added after the third month of ASCT. Six months after the ASCT, the first dose of mRNA-based BNT162b2 vaccine (Pfizer–BioNTech) was administered to the patient.

He presented with fever, neck pain, swelling in the neck, and fatigue 10 days after receiving the first dose of BNT162b2 vaccine. Upon physical examination, there was swelling and tenderness in his right thyroid lobe. Other bodily functions were normal. In a laboratory work up, a slightly elevated ESR (erythrocyte sedimentation rate) 95 mm and CRP (C-reactive protein) level 158.5 mg/L was observed. His complete blood cell count and other biochemical tests were normal. There was no infiltration on his chest X-rays. His blood and urine cultures were negative. In thyroid function tests, thyrotropin (TSH): 0.02 mU/L (normal = 0.5–4), free T3: 5.14 pg/mL (normal = 2.3–4.2), and free T4: 200 ng/dL (normal = 0.8–1.8) were found. Anti-TPO (thyroid peroxidase) and anti-Tg (thyroglobulin) antibodies were negative.

A thyroid ultrasound revealed an enlarged right lobe of the thyroid and heterogeneous echogenicity. Decreased blood flow, especially in the right lobe, was also found on color Doppler. Technetium-99m (99m Tc)-pertechnetate scintigraphy were performed and demonstrated markedly reduced uptake in the thyroid gland which supports subacute thyroiditis (Figure 1). The patient was evaluated as subacute thyroiditis with clinical, laboratory, and imaging findings. Diclofenac potassium 2×50 mg/day oral treatment was started. At the end of the second week, the pain in the neck completely regressed according to all clinical parameters. His laboratory parameters returned to normal, and diclofenac potassium treatment was stopped. (The course of laboratory parameters at the time of diagnosis and during follow-up is summarized in Table 1.) We performed the Naranjo Adverse Drug Reaction Probability Scale and BNT162b2 vaccine was the probable cause for subacute thyroiditis with a score of six.[19] We have also obtained written informed consent/permission to publish the case report from the patient.

Discussion

Infections are the main causes of death, and one of the major obstacles in care, where multiple myeloma patients are concerned.[20] In addition, infections could also result in early mortality multiple myeloma.[13] Multiple myeloma could, in other words, cause premature mortality, and it has also been

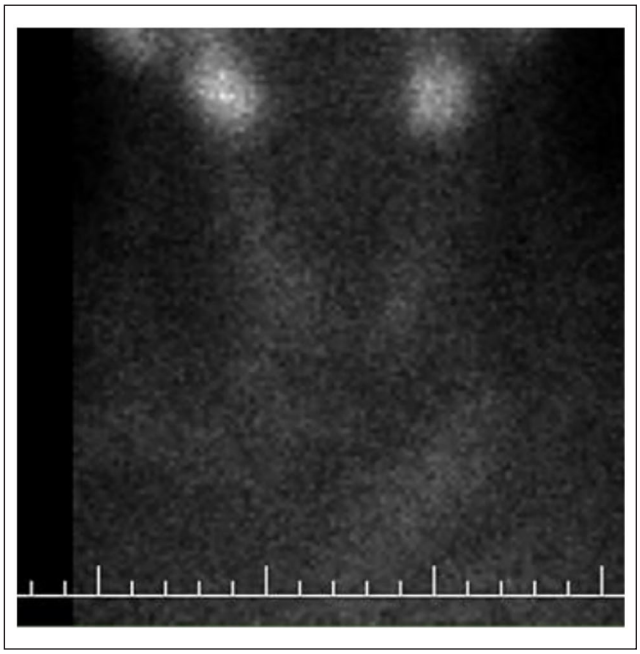

Figure 1. Technetium-99m pertechnetate scan showing decreased and heterogeneous radiotracer uptake in both lobes of thyroid gland.

Table 1. Laboratory findings during the disease course.

	At diagnosis	Follow-up first week	Follow-up second week	Follow-up fourth week
TSH (mU/L)	0.02	0.03	0.05	0.56
fT4 (ng/dL)	2.02	2.46	1.79	0.96
fT3 (pg/mL)	5.14	3.98	2.56	2.24
ESR (mm/h)	95	37	17	14
CRP (mg/L)	158.5	68.6	15.2	3.5
Hemoglobin (g/dL)	10.5	10.9	11.6	12.4
WBC ($\times 10^9$/L)	3.9	4.2	4.8	4.5
Thrombocyte ($\times 10^9$/L)	176	211	209	198

CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; fT3: free triiodothyronine; fT4: free thyroxine; TSH: thyroid-stimulating hormone; WBC: white blood cell count.

observed in a nationwide analysis study.[21] In our routine practice, vaccination of multiple myeloma patients against various viruses and bacterial pathogens is recommended.[22] An intensive vaccination schedule is also advised for patients undergoing ASCT.[22] However, impaired responses to mRNA COVID-19 vaccines in multiple myeloma patients have been reported.[23] Intensive vaccination and even booster doses are expected to continue, as vaccines are our strongest weapon against this deadly enemy.

The exact cause of subacute thyroiditis is unknown, but subacute thyroiditis following several viral infections, as well as[3] subacute thyroiditis following inactivated virus vaccines in healthy people have been described.[4,6] In history, it was associated with the mumps virus outbreaks.[24] In the era of COVID-19, subacute thyroiditis developed after COVID-19 disease and after SARS-CoV-2 vaccines were reported.[25–34] The SARS-CoV-2 virus, which affects many of our systems, also affects our endocrine system. Thyroid gland is one of the most affected endocrine organs. Direct and indirect effects of the SARS-CoV-2 on the thyroid glands could cause thyroid dysfunction. It can lead to changes in the structure or function of the thyroid gland.[35] Subacute thyroiditis is thought to be a post-inflammatory syndrome of viral infections.[29] It usually appears 2–8 weeks following viral infections. In cases that develop subacute thyroiditis after vaccine administration, the time between the vaccine and subacute thyroiditis is usually 5 days to 2 weeks. In our case, the interval time was 10 days. Subacute thyroiditis after SARS-CoV-2 vaccine is usually has a mild prognosis and could be treated clearly.[36]

In recent years, autoimmune/inflammatory syndrome (ASIA) induced by adjuvants which are used for augmenting immunogenicity of vaccines have been suggested.[37,38] It has also been proposed that subacute thyroiditis is also a phenomenon of ASIA. It is also known that ACE2 (angiotensin-converting enzyme 2) receptors play a profound role in the pathogenesis of SARS-CoV-2 in penetrating cells.[39] Aside from the lungs, the thyroid gland is another one of the organs that carry ACE2 receptors.[40] In this setting, ACE2 receptors may be a clue to subacute thyroiditis following COVID-19 infections and vaccines.[41] In addition, a possible cross-reaction and antigenic mimicry between thyroid cell antigens and the spike protein of the coronavirus have been suggested.[42] However, the precise mechanism of subacute thyroiditis developing after the COVID-19 vaccine has not been understood now.

Subacute thyroiditis usually starts with a sudden onset of neck pain; on laboratory findings, it starts with a transient thyrotoxic phase, and is usually followed by an also transient hypothyroidic phase, with an eventual recovery with euthyroid state occurring.[2] Treatment is often targeted to alleviate symptoms. Non-steroidal anti-inflammatory drugs (NSAIDs) are given for controlling pain. Prednisone can be started when NSAIDs are not helpful for symptoms. Usually, NSAIDs are the first choice and cause a dramatic response as in our case.

Conclusion

To our knowledge, this is the first report of a multiple myeloma patient developing subacute thyroiditis following SARS-CoV-2 BNT162b2 vaccine. With developing vaccination rates all over the world, and subacute thyroiditis cases reported after both mRNA-based vaccines and inactivated virus vaccines, we can suggest that there may be an increase in cases of subacute thyroiditis, clinicians should stay informed and have increased awareness of post-COVID-19 vaccine subacute thyroiditis. However, we should keep in mind that this is a mild and transient side effect, and this should not discourage from getting vaccinated.

Declaration of conflicting interests

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Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

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Informed consent

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Supplemental material

Supplemental material for this article is available online.

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