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Thyroid Eye Disease, Acute Anterior Uveitis, And Crohn's Disease Flare Following Covid-19 Vaccine: Report of A Case

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Abstract:

A 39-year-old woman with a history of controlled thyroid eye disease (TED) and Crohn's disease (CD) presents with 2 weeks of diarrhea and 3 weeks of proptosis plus anterior uveitis (AU) after receiving her second dose of the bnt162b mRNA COVID-19 vaccine. Eye and gastrointestinal symptoms occurred 4-5 days and 14 days following her second vaccination, respectively. Workup was consistent with concomitant re-activation of thyroid eye disease, Crohn's disease, and anterior uveitis. The timing of her vaccination and symptoms suggests autoimmune/inflammatory syndrome associated with adjuvants (ASIA).

Keywords: Thyroid Eye Disease; Crohn's Disease; Anterior Uveitis; COVID, vaccine

Graves' disease is an autoimmune thyroiditis caused by thyroid stimulating hormone receptor antibodies (TRAbs) causing an excess production of T3 and T4 hormones [1]. Up to 25% of patients with Graves' disease will present with vision loss, dry eye, exposure keratitis, and proptosis of the eyes termed Graves' orbitopathy or thyroid eye disease (TED) [2-3].

Inflammatory bowel disease (IBD) is a diagnosis that includes two disorders: ulcerative colitis and Crohn's disease (CD). CD is an autoimmune disorder characterized by segmental transmural inflammation of the GI tract anywhere from the oral cavity to the anus. Symptoms of CD include abdominal pain, diarrhea, fatigue, and weight loss [4]. IBD can have ocular manifestations in up to 10% of patients and includes episcleritis, scleritis, and uveitis [5]. IBD Patients with HLA-B27 and HLA-B58 genes are thought to have increased risk of ocular manifestations [6]. Uveitis is defined as inflammation anywhere along the uveal tract. The three layers that comprise the uvea are the iris, ciliary body, and the choroid. If the iris or ciliary body are inflamed the condition is termed anterior uveitis (AU).

The COVID-19 vaccines are an essential element in combatting the current pandemic. Overall, the vaccines have been generally well tolerated, [7-8] but reactivation of certain immune disorders have been observed. Reactivation or flare of TED [3] and CD [9] and AU [10] have all been previously reported following COVID-19 vaccination. However, the authors believe the case we describe here presents the first such report where a patient observed a concomitant re-activation of TED, CD, and AU following the bnt162b2 mRNA COVID-19 vaccine.

Case Presentation

A 39-year-old Caucasian female with a chronic smoking history presented to the general ophthalmology service with 4 weeks of complaints of stomach pain, diarrhea, lymphadenopathy, unbearable eye pain, erythema, tearing, photophobia, and proptosis of the right eye. These symptoms occurred after receiving her second dose of the bnt162b2 COVID-19 vaccine.

She had a 5-year history of Graves' disease diagnosed by her endocrinologist after she presented with complaints of weight loss, and alopecia. Workup showed autoimmune

hyperthyroidism. The patient achieved euthyroid state medically with methimazole 5mg three times per week. She also had a 1-year history of Crohn's disease diagnosed by her gastroenterologist via colonoscopy after presenting with chronic diarrhea. Her symptoms for CD were being controlled with adalimumab 40 mg injections subcutaneously every other week. She was seen by the oculoplastic service for the first time 1 month prior to receiving her first dose of bnt162b2 for routine TED examination. Pertinent exam findings that visit showed visual acuity of 20/20 bilaterally (OU) with full ocular motility. Upper eyelid margin reflex distance (MRD1) was 5mmOU without lagophthalmos and healthy corneal exam. Hertel exophthalmometry measured 20mm for the right eye (OD) and 19 mm for the left eye (OS). At this appointment her clinical activity score (CAS) was 1 and her clinical plan was to follow up with ophthalmology annually.

The patient received her first dose of the bnt162b vaccine in August 2021 and reported no symptoms or aggravation of her TED or Crohn's. She then received her second dose of the bnt162b vaccine in September 2021 where she experienced flares of TED, Crohn's, and AU. Eye symptoms occurred 4-5 days post vaccination and gastrointestinal symptoms occurred 14 days post vaccination.

Her next exam with ophthalmology was 4 weeks after receiving the second dose. She reported new-onset diarrhea and abdominal pain with nausea and vomiting for the past two weeks and worsened bulging of the eyes with sensitivity to light and eye pain for the last 3 weeks. Visual acuity was 20/30 OD and 20/20 OS. She had chemosis with ocular injection in the right eye. She reported pain with supraduction OD, along with a trace supraduction deficit. Her MRD1 was 9mmOD/6mmOS with 3mm superior scleral show on the right and 2mm lagophthalmos on the right with superficial punctate erosions noted on the right cornea. Hertel exophthalmometry measured 24mm OD/21mm OS. The anterior chamber was notable for 1+ cell and 1+ flare inflammation without posterior involvement. Dilated fundus exam was normal. The patient was diagnosed with acute anterior uveitis of the right eye and a flare of previously stable thyroid eye disease bilaterally. She was started on 60mg of oral prednisone, prednisolone acetate 1% ophthalmic suspension 1 drop OD 4x/daily, and atropine 1% ophthalmic solution 1 drop OD daily. She was also counseled to use lubricating ointment nightly with sleeping and to lubricate the cornea during the day with preservative-free artificial tears 3-5x/daily as needed.

After 3 days of steroid treatment the orbital exam was improving. Exam showed improved chemosis and injection of the conjunctiva with a quiet anterior chamber. Visual acuity remained at 20/30 OD and 20/20 OS.

8 weeks after receiving the second dose (November 2021), the patient's symptoms were resolved. Visual acuity was 20/20 OU with full ocular motility. Hertel's measured 21mm OD/19mm OS. MRD1 was 6mm OD/5mm OS with resolved lagophthalmos and improved corneal exam. The anterior chamber was quiet. She also related that her GI specialist believed that she had a flare of her previously stable Crohn's disease, however, the oral steroid and continuation of adalimumab had improved her symptoms back to baseline. The plan from both ophthalmology and GI was to continue adalimumab and to taper oral prednisone in a standard fashion. She was tapered off topical therapy by the uveitis specialist in routine fashion as well. Her HLA B27 status was not known at this time.

In November 2021, after relief of her symptoms, the patient received the quadrivalent flu immunization and pneumococcal conjugate vaccine 13 (PCV13). Notably, the patient did not report any post-vaccination symptoms.

Discussion

There have been multiple cases of thyroid dysfunction following COVID-19 vaccination. Iremli et al. reported 3 cases of subacute thyroiditis following the inactivated CoronaVac vaccine. All 3 cases were observed in females ages 34-37 with 2 of the 3 cases presenting with symptoms within 7 days of the second dose of the vaccine and 1 case presenting with symptoms within 4 days of the first vaccination [11]. Lui et al. reported a case of a 40-year-old female with a history of hypothyroidism who developed Grave's hyperthyroidism 5 weeks after her second dose of the BNT162b2 mRNA vaccine [12]. Other authors have described and summarized similar cases of Graves' disease post-COVID-vaccination [10]. All three of these authors have hypothesized that adjuvants in the COVID-19 vaccines are to blame and that these cases of Graves' disease are best explained by Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) [10-12]. There have also been reports of patients developing Graves's disease after being infected by the SARS-CoV-2 virus. The mechanism of this is phenomenon is unknown, but it is hypothesized that the SARS-CoV-2 virus could use agniotesnin-converting-enzyme-2 (ACE2) receptors to infect thyroid cells to trigger an autoimmune response [13]. It is important to note that none of the Graves' disease cases discussed above were associated with proptosis typical of Graves' orbitopathy like the patient in this case report.

The patient in this case report had a reactivation of TED with proptosis without any known thyrotoxicosis, although free T4 and TSH levels were not measured until 8 weeks after initial symptoms. This case is most similar to the case described by Rubinstein. Rubinstein reported a case of a 50-year-old female patient with a history of controlled Graves' disease and TED, who upon receiving her second dose of the bnt162b2, experienced a flare of previously controlled TED. Rubinstein hypothesized that the flare of TED could be explained by a reaction to adjuvants and ASIA [3]. However, this case is different from Rubenstein's and unique in that multiple autoimmune conditions (TED, CD, and AU) were reactivated concomitantly by the vaccine. It is reasonable to suspect that the patient's already dysregulated immune system could have been triggered by adjuvants consistent with ASIA as suggested by other authors [3,10-12].

A recent study looking at side effects of the COVID-19 vaccine in patients with IBD found that 2% (71/3316) of patients who received at least one dose of the COVID-19 vaccine experienced an IBD flare defined as worsening IBD symptoms [9] The relatively low percentage of patients experiencing worsening Crohn's symptoms is reassuring to providers but not insignificant.

The acute AU seen in this patient is best attributed to ASIA. It is possible that the AU could be an extraluminal manifestation of CD, but this is unlikely given that the patient had never experienced AU before taking the vaccine and the low prevalence of uveitis as a

symptom of IBD [5-6]. Other vaccines such as the MMR and HPV vaccines have had reports of AU post vaccination and has been attributed to adjuvants via ASIA [10,14].

It is worth noting that her quadrivalent flu vaccine and PCV13 that the patient received 10 weeks after the second dose of the bnt162b vaccine did not evoke reactivation of TED, CD, or AU. This suggests that the proprietary adjuvants used in the bnt162b vaccine are responsible. It is also worth noting that the acute AU and flares of TED and CD were experienced while the patient was immune suppressed by adalimumab. It is unknown whether adalimumab acted to worsen or benefit the patient. In theory, the use of immune suppressing biologics should have worked to prevent or lessen the extent of ASIA.

It is the belief of the authors that providers should be counseling their patients with pre-existing autoimmune conditions prior to receiving COVID-19 vaccinations, especially those with TED and Crohn's. This is not to discourage these patients from receiving the vaccines, especially since those with autoimmune dysregulation may be at higher risk of complications of COVID-19 infection [15]. Counseling is to provide patients with the data to make informed decisions about their health care and to facilitate closer post vaccination monitoring. Patients should be encouraged to report worsening autoimmune symptoms to their providers to receive appropriate treatment.

Conflicts of Interest

The authors have no conflicts of interest to disclose.

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