



Case report

“Marginal keratitis following COVID 19 vaccination”

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ABSTRACT

Purpose: To describe a novel case of marginal keratitis following COVID 19 vaccination.**Methods:** Case report**Results:** A 68-year-old female received the Moderna COVID 19 vaccine. She then developed ocular irritation and peripheral corneal opacities that are characteristic of marginal keratitis. Her symptoms responded well to steroid and antibiotic ophthalmic medications. She received her second dose of the Moderna vaccine while still taking her eye drops and was then able to taper off her drops without a recurrence of symptoms.**Conclusions:** Marginal keratitis represents a localized type III hypersensitivity reaction of the cornea. The SARS-CoV-2 virus that causes COVID 19 gains entry into the cell via binding of the spike protein with the ACE2 receptor. It is this spike protein that is the target for mRNA COVID-19 vaccines, such as the Moderna vaccine, allowing spike protein antigen recognition by the human immune system. The cornea has been found to have significant levels of ACE2 receptors, potentially allowing for the cornea to become a site for the antigen-antibody complex deposition necessary for a type III hypersensitivity response. This reaction should be recognized so that treatment may be provided during the initial episode and the cornea may be monitored following subsequent vaccinations.

Introduction

Marginal keratitis is an inflammatory disease of the cornea characterized by stromal infiltrates in the peripheral zones. Cases typically present with mild to moderate pain, foreign body sensation, photophobia, and conjunctival injection and can progress from isolated corneal opacity to more severe epithelial defects and ulceration [2,3]. On physical exam, stromal infiltrates can be appreciated most commonly 1–2 mm from the corneal limbus, at the intersection of the eyelid margin and the cornea [2]. While there is a strong link between marginal keratitis and blepharoconjunctivitis, particularly due to staphylococcus bacteria, corneal cultures often show no evidence of active bacterial infection [2,3]. Rather, analysis of these marginal infiltrates will demonstrate a sterile neutrophilic response and the immune complex and complement deposition that is classically seen from a type III hypersensitivity reaction [1,2,8]. It is the activation of the complement pathway from immune deposits that are thought to result in the peripheral corneal opacity seen with marginal keratitis [2,5]. Here, we detail a case of marginal keratitis that was triggered by a Type III hypersensitivity reaction to the Covid-19 vaccine. Written informed

consent was obtained by the patient for the publication of this case report with all associated images.

Patient presentation

A 66-year-old female patient presented to the clinic with gradually worsening right eye pain and redness. She described the pain as 5/10 in severity, constant, and unremitting. Symptoms were associated with intermittent blurred vision, tearing, and mild discharge. She denied any history of similar episodes, eye trauma, contact lens wear, or allergies. She denies recent infections and has had no recent sick contacts. She has used antibiotic eye drops without significant improvement in right eye symptoms. The patient notes that she received the first dose of the Moderna Covid-19 vaccine approximately 2.5 weeks prior.

Past ocular history includes surgical removal of a cavernous hemangioma of the left orbit six years prior. Past medical history includes abdominal aortic ectasia, thyroid cancer in remission post thyroidectomy, and a lung mass. Past surgical history includes partial lobectomy, thyroidectomy, hernia repair, and bilateral knee arthroscopy. There is a family history of hypertension and retinal detachment. Her only

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medication is levothyroxine daily. She is a lifetime nonsmoker with no current or past history of illicit drug use.

The external exam showed best-corrected visual acuity of 20/25 and 20/30 in the right and left eyes, respectively. Pupils were 3 mm and reactive bilaterally. Intraocular pressure was 14 mmHg in the right eye and 13 mmHg in the left eye. Extraocular movements and visual fields were full bilaterally. Anterior segment exam of the right eye showed 1–2 + blepharitis and 3 + injection, 1 + chemosis. There was no discharge noted in the fornix. There were 5–6 small, flat infiltrates in the inferior cornea, 1–2 mm from the limbus, and several raised infiltrates superiorly with adjacent peripheral vascularization. The epithelium was intact, without overlying epithelial defects (Images 1, 2, and 3). The anterior chamber was deep and quiet, the iris round and reactive, and the lens showed trace nuclear sclerosis. The anterior segment exam in the left eye was remarkable for 1 + blepharitis. The posterior segment exam was unremarkable bilaterally.

The patient was diagnosed with marginal keratitis of the right eye and started on an antibiotic and corticosteroid combination ophthalmic drop. She also started an antibiotic ointment at bedtime. She was evaluated several days later with significant improvement in discomfort and injection of the right eye. Over the following two weeks, she was slowly tapered off her drops, during which time she also received her second dose of the Moderna COVID-19 vaccine. The patient completed her medication taper and was found at her follow-up visit to have a resolution of her corneal infiltrates and ocular symptoms.

Discussion

The SARS-CoV-2 virus that causes COVID 19 gains entry into the cell via binding of the spike protein with the ACE2 receptor [9]. It is this spike protein that is the target for mRNA COVID-19 vaccines, such as the Moderna vaccine, allowing spike protein antigen recognition by the human immune system [4]. The cornea has been found to have significant levels of ACE2 receptors [10], potentially allowing for the cornea to become a site for the antigen-antibody complex deposition necessary for a type III hypersensitivity response. As previously discussed, type III hypersensitivity reactions occur when antigen-antibody complexes are deposited in tissue and subsequently activate the complement pathway [8]. When this occurs in the cornea, it forms the peripheral stromal opacities seen with marginal keratitis. Type III Hypersensitivity reactions are delayed and may occur between days to weeks following exposure to an antigen [8]. This patient was found to have marginal keratitis 2.5 weeks after her COVID-19 vaccine.



Image 1. A color photograph of the right eye demonstrating significant injection of the conjunctiva and several small, round peripheral corneal infiltrates.

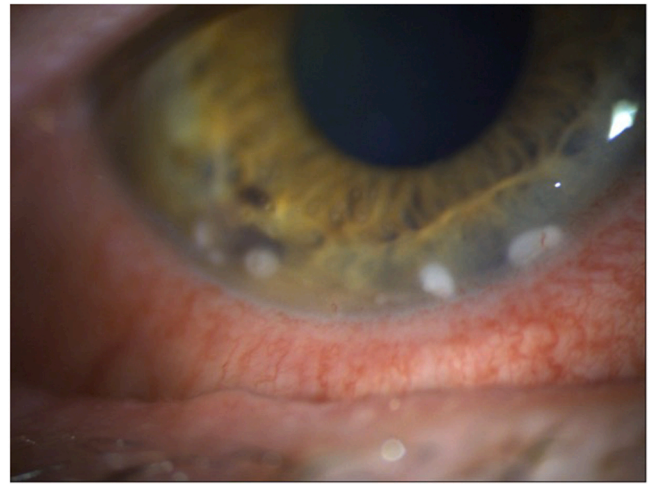


Image 2. A closer look at the inferior corneal infiltrates. A clear corneal zone can be seen between the corneal limbus and the infiltrates.



Image 3. Color photograph of the superior cornea demonstrating peripheral corneal opacity and fine vascularization.

There have been similar reports of marginal keratitis after non-traditional triggers. In 2007, a patient was reported to have bilateral marginal keratitis after stem cell transplant [7]. In 2014, a patient was found to develop marginal keratitis following Ranibizumab injection [6]. In both scenarios new antigens were introduced to the body and both had negative bacterial and viral cultures of the eye [6,7]. These cases support the possibility of a novel vaccine creating a substantial immune response and subsequent type III hypersensitivity reaction to trigger marginal keratitis of the eye.

Due to the pathophysiology of marginal keratitis and the timing of this patient's corneal findings following her vaccination, we believe that these events are possibly correlated. Causality cannot be demonstrated in this case, but it is our impression this is the first report of the COVID-19 vaccine causing marginal keratitis. In terms of potential risk benefit analysis, marginal keratitis would represent a minor complication of vaccination and this case should not deter patients or providers from taking and recommending vaccination against Covid-19. As patients continue to be vaccinated against the virus, clinicians should be aware of this possible ophthalmic scenario.

Ethical Approval

This is a case report that followed all ethical guidelines and principles. All authors agreed to and followed all ethical procedures.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

CRediT authorship contribution statement

Daniel A Farrell: Conceptualization, Investigation, Validation, Resources, Writing – original draft, visualization, **Sara Deacon:** Conceptualization, Resources, Writing – review and editing, **Thomas Mauger:** Writing – review and editing, Project Administration, Supervision.

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