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Case Report

Occipital Neuralgia after COVID-19 Vaccination: A Report of Two Cases

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ABSTRACT

Background: A wide range of neurological complications has been described following the administration of COVID-19 vaccinations, with headache being the most commonly reported neurological adverse effect, with higher incidence after the second dose. The most common headache is a dull pain or migraine like. Still, two cases of trigeminal neuralgia and a case series of 7 patients with cluster headache who were clinically stable and had a new episode a few days after COVID-19 vaccination have also been reported. Herein, we describe the first two cases of occipital neuralgia developing after COVID-19 vaccination.

Cases presentation: Two cases were observed in the neurology outpatient clinic of a tertiary university referral center in Portugal between October 2021 and June 2022. Both patients developed the headache within 1 to 6 days after the second dose of BNT162b2 (Pfizer). One had no previous history of headaches, and the other had a migraine that was clearly different from the present headache. Each case is described, checked for ICHD criteria for occipital neuralgia, and its temporal relation with COVID-19 Vaccination is reported.

Conclusions: COVID-19 vaccination can trigger various types of headaches, far beyond the most commonly described feature of dull pain, possibly by activating an immune-inflammatory response.

Keywords: Headache; Occipital neuralgia; COVID-19 vaccination; Immune-inflammatory response; BNT162b2

Abbreviations: CBC: Complete Blood Count; CGRP: Calcitonin Gene-Related Peptide; COVID-19: Coronavirus 19; CT: Computerized Tomography; GON: Great Occipital Nerve.

INTRODUCTION

Current Coronavirus 2019 (COVID-19) is a viral disease that has become a global pandemic, causing severe morbidity and mortality. COVID-19 vaccines have been developed to prevent the disease and have been administered to people worldwide. A wide range of neurological complications was observed in these vaccinations, with headache being the most commonly reported neurological adverse effect [1,2]. In the clinical trial of BNT162b2 (Pfizer), mild to moderate headaches have been reported in 25%-52% of patients, with the second dose having higher incidents of headaches than the first one [3]. According to a recent meta-analysis of headache related to COVID-19 vaccination, the most common characteristic of headaches reported is dull pain, but two cases of trigeminal neuralgia had already been reported [3-5].

Moreover, a series of 7 cases of cluster-headache who were clinically stable and had a new episode a few days after COVID-19 vaccination were also described [6]. Herein, we describe the first two cases reported of occipital neuralgia after COVID-19 vaccination. Both were observed in the neurology outpatient clinic of a tertiary university referral center in Portugal between October 2021 and June 2022. Both patients provided informed consent for this report.

CASE PRESENTATION

Case 1

A 39-year-old Caucasian woman was admitted to our hospital in October 2020 with two weeks of bilateral paroxysmal stabbing shock-like pain beginning in the occipital zone, with irradiation to the vertex, front and parietal zones, accompanied by bilateral dysesthesias in these regions. Six days before headache onset, she received the second dose of BNT162b2 (Pfizer) vaccine against SARS-CoV-2, with fever reported on the first day following. She has an unremarkable medical history, without a history of previous headaches, even after any prior vaccination.

The pain features were a bilateral stabling shock-like pain, with an intensity of 8/10, short duration (less than<10 seconds), appearing more than five times per day, and spontaneously triggered by

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touching or brushing the hair. Over time, in the period between the shocks, she starts to feel a dull pain in the vertex and nuchal region, with concomitant dysesthesia in these zones.

On neurological examination, pressure over the emergence of the Great Occipital Nerve (GON) elicited a paroxysm of shock pain, with allodynia on the affected portion of the scalp. Brain Computerized Tomography (CT) and laboratory analysis (Complete Blood Count (CBC), renal and hepatic panel, electrolyte, and C-reactive protein) performed in the emergency department were unremarkable.

Due to the typical features and localization of the pain and the fact of being triggered by the touch in the emergence of GON, the case was considered probable occipital neuralgia, and a bilateral occipital blockage was performed in the emergency department, with significant relief of the pain. Also, she had started gabapentin, up to a total dose of 300 mg/day.

Later performed brain and cervical MRIs were unremarkable. On reevaluation appointment, one month after the first GON blockage, the patient maintained a light dull pain in the vertex and occipital region but without new episodes of shocks. The dose of gabapentin was lowered to 200 mg/day due to hypersomnolence.

After six months, in the following consultation, she reported a reappearance of the shock sensation in the occipital region, accompanied by a worsening sense of constant dull pain in the vertex and associated allodynia in all the scalp. A second bilateral GON blockage had been performed, and amitriptyline had been associated with gabapentin, up to a dose of 25 mg. After one month, the patient reported the shock's disappearance and significant relief from the dull pain and allodynia. She has been clinically stable since this date, with no need for new GON blockage. Nevertheless, the patient chose not to receive the third dose of the vaccine.

Case 2

A 30-year-old Caucasian man with a previous history of episodic migraine with visual aura was admitted to our hospital in June of 2021 with one week of right paroxysmal stabbing shock-like pain beginning in the occipital zone, with irradiation to the vertex. This pain started one day after administering the second dose of the BNT162b2 (Pfizer) vaccine, with no other systemic complaints.

The pain was a right stabling occipital shock-like pain, with an intensity of 9/10, short duration (less than<10 seconds), appearing more than ten times per day, and spontaneously triggered by touching the region. On neurological examination, pressure over the emergence of the right GON triggered a paroxysm of shock pain, with irradiation to the right temporal zone, with associated allodynia on all the right hemicrania. Brain CT and laboratory analysis (CBC, renal and hepatic panel, electrolyte, and C-reactive protein) were unremarkable.

A primary diagnosis of occipital neuralgia was considered, and right GON blockage was performed in the emergency department, with immediate significant relief. Gabapentin (up to a total dose of 300 mg/day) was started. Brain and cervical MRIs were also unremarkable. On reevaluation, after one month, he was clinically stable, with a slight dull pain in the right occipital zone. Three months later, he reported sporadic shocks in the right occipital region, with slight allodynia in this region. GON blockage was not performed at the patient's request (fear of needles). Likewise, the patient chose not to receive the third dose of the vaccine.

RESULTS AND DISCUSSION

These two patients developed a new headache within 1 to 6 days after COVID-19 vaccination. The first case had a previous history of headaches and the second had a migraine that was clearly different from the present headache. None of the patients accepted the third dose of vaccination, and a causal relation can only be established by the close temporal association.

The most common adverse effects of the BNT162b2 mRNA COVID-19 vaccine are injection site reactions (84.1%), fatigue (62.9%), headache (55.1%), muscle pain (38.3%), chills (31.9%), joint pain (23.6%) and fever (14.2%) [5]. These are usually mild or moderate and remitted within a few days after vaccination [2]. According to the data available, the most common neurological symptom is a headache that occurs in over 50% of vaccinated and is even more common after the second dose [2,5]. From the analysis of a multicenter observational study of 2349 participants that had headaches after vaccination against COVID-19 with the BNT162b2 (Pfizer) mRNA vaccine between 8 January 2021 and 26 February 2022, it was found that the onset of the headache had a mean of 18.0 h ± 27.0 h [3]. In less than 10% of the participants, the headaches began more than two days after the vaccination. The mean headache duration was 14.2 h ± 21.4 h, and in 10% of the participants, the headache lasted longer than 36 h. The most common characteristic of the pain was dull pain (40.7%).

Nevertheless, two cases of trigeminal neuralgia after vaccination against COVID-19 had already been reported, both after the first dose of BNT162b2 (Pfizer) and starting on the same day of the administration [4,5]. An immune-mediated inflammatory response was assumed in both cases.

Moreover, it had been described as a series of seven cases of patients with cluster headache that was clinically stable for a long time and had a new crisis of pain within a few times after the administration of COVID-19 vaccination (from a few minutes to 7 days after). In these cases, an inflammation of the trigeminovascular system with Calcitonin Gene-Related Peptide (CGRP) release had been postulated. Alternatively, the authors assumed the vaccine's possible direct central (inflammatory) role [6].

Occipital neuralgia is described as a unilateral or bilateral paroxysmal described like a shooting, stabbing, electric, shock-like or sharp pain in the posterior part of the scalp, involving the greater, lesser, and third occipital nerve distribution, with sudden onset, and immediately spreading toward the vertex [7]. It can sometimes be accompanied by diminished sensation or dysesthesia in the affected area and commonly associated with tenderness over the involved nerves [7,8].

The paroxysms of the pain may start spontaneously or be triggered by brushing the hair, exposure to cold, or neck movements. A dull occipital discomfort may be present during periods between painful paroxysms [9]. On examination, pressure, palpation, or percussion over the occipital nerve trunks may reveal local tenderness, trigger painful paroxysms, worsen the dull pain, or elicit paresthesias along the distribution of the affected nerve [7].

The pathophysiology of occipital neuralgia is yet uncertain but can result from an injury to the C2-C3 nerve roots and occipital nerves through different mechanisms (chronic instability, entrapment,

trauma, inflammation) [10]. Most often, occipital neuralgia is idiopathic [11].

The diagnosis of occipital neuralgia is considered when typical clinical features are present, based on the diagnostic criteria for occipital neuralgia from the International Classification of Headache Disorders, 3rd edition (ICHD-3), and can be confirmed when pain is transiently relieved by a local occipital anesthetic block (Table 1) [8,11].

Table 1: Diagnostic criteria for occipital neuralgia- HIS Classification ICHD-3.

	Diagnostic criteria
A.	Unilateral or bilateral pain in the distribution(s) of the greater, lesser and/or third occipital nerves and fulfilling criteria B-D
	Pain has at least two of the following three characteristics:
	1. recurring in paroxysmal attacks lasting from a few seconds to minutes
	2. severe in intensity
B.	3. shooting, stabbing or sharp in quality
C.	Pain is associated with both of the following:
	1. Dysaesthesia and/or allodynia apparent during innocuous stimulation of the scalp and/or hair
	2. either or both of the following: a) tenderness over the affected nerve branches b) trigger points at the emergence of the greater occipital nerve or in the distribution of C2
D.	Pain is eased temporarily by local anaesthetic block of the affected nerve(s)
E.	Not better accounted for by another ICHD-3 diagnosis.

Relative to both patients, all the criteria for occipital neuralgia are fulfilled, and in the second patient, no characteristic of migraine headache had been detected. The fact that both cases had developed within 1 to 6 days after the second dose of the vaccine for COVID-19 raises the hypothesis that it is a consequence of this vaccination, which was partially later corroborated by an imaging study that does not show any type of lesion at the root level of C2-C3 and the territory of the occipital nerves.

Although according to a recent systematic review and meta-analysis, post-vaccination headache tends to develop within 24-h from injection and usually resolves in less than 24 h, our cases highlight the possibility of persistent symptoms after COVID-19 vaccination [12].

After COVID-19 vaccinations, the exact mechanism for the neurologic involvement is not fully elucidated and attributed to molecular mimicry and immune-mediated inflammatory response. The first one often requires 10-14 days to be developed, but the last requires less time [13]. In both of our cases, we hypothesize that occipital neuralgia had been consequent to an immune-mediated inflammatory response. Also, bilateral pain is unusual in primary occipital neuralgia and the fact that it was bilateral in the first case can corroborate the fact that there was an underlying systemic inflammatory reaction. However, more studies are required to clarify controversial aspects of the pathophysiology of this unknown disease [14].

CONCLUSION

COVID-19 vaccination may elicit many different types of headaches, far beyond the most commonly described feature of dull pain, possibly by activating an immune-inflammatory response. To the best of our knowledge, we report the first two cases reports of occipital neuralgia after this vaccination. More studies are needed to elucidate the potential neurological manifestations of this vaccine.

LIMITATIONS

Despite being two accurate description of occipital neuralgia, the exact mechanisms by which the vaccines for COVID-19 trigger the pain are not yet clear.

CONFLICT OF INTEREST

The authors of this manuscript declare no conflict of interest.

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ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Both patients provided consent for the description of these reports.

CONSENT FOR PUBLICATION

Both patients provided consent for publication of these reports.

AVAILABILITY OF DATA AND MATERIAL

All included references in the present review article are available on the Internet.

COMPETING INTERESTS

There are no competing interests to declare.

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AUTHOR'S CONTRIBUTIONS

S. Malheiro evaluated and managed both patients and wrote the main manuscript text.

D. Costa helped in management of the first patient and reviewed the concept of manuscript.

R. Varela helped in management of both patients and reviewed the concept of the manuscript.

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