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COVID-19

SARS-CoV-2 vaccination, Parkinson's disease, and other movement disorders: case series and short literature review

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Abstract

Background Several neurological complications have been reported following SARS-Cov-2 vaccination, without a clear causal relationship ever being verified, including some cases of worsening of Parkinson's disease (PD) symptoms and new onset of movement disorders in non-parkinsonian patients.

Methods We describe two new cases of PD patients treated with device-aided therapy who developed worsening of parkinsonian symptoms after receiving the third vaccine dose (booster). We also conducted a short review of the cases reported in literature of PD symptoms worsening and new onset of movement disorders in non-parkinsonian patients after SARS-Cov-2 vaccination.

Results The first patient, a 46-year-old man implanted with bilateral Subthalamic Deep Brain Stimulation, experienced temporary motor and non-motor symptoms worsening after mRNA-1273 booster, improved after stimulation settings modification. The second patient, a 55-year-old man implanted with percutaneous endoscopic transgastric jejunostomy (PEG-J) for levodopa-carbidopa intestinal gel (LCIG) infusion experienced severe temporary worsening of dyskinesia and managed through temporary LCIG dose reduction.

Other seven cases of vaccine-related movement disorder are currently reported in literature, four describing PD symptoms worsening and three the onset of new movement disorders in otherwise healthy people.

Conclusion Both our patients and the cases described so far completely recovered after few days with parkinsonian therapy modification, symptomatic treatment, or even spontaneously, underlining the transient and benign nature of side effects from vaccine. Patients should be reassured about these complications, manageable through a prompt evaluation by the reference neurologist.

Keywords Parkinson's disease · Movement disorders · COVID-19 vaccine · Booster vaccination

Introduction

Various neurological complications following SARS-CoV-2 vaccination have been reported, although without clear causal relationship [1], with few cases of Parkinson's disease (PD) symptoms worsening and new onset of movement disorders in non-parkinsonian patients. The Movement Disorder Society (MDS) highly recommended vaccination for PD patients, considering their higher risk for worse clinical outcome, especially reported on patients in advanced therapy, which present an additional risk of vulnerability [2, 3]. Noteworthy, new onset of movement disorders may occur in the context of Coronavirus Disease 2019 (COVID-19) [4].

Here we describe symptoms worsening in two PD patients in device-aided therapy after the third vaccine dose (booster), and briefly review cases reported so far.

Case series and literature reports

The first patient is a 46-year-old man, with a 9-year PD history, successfully implanted with bilateral Subthalamic Deep Brain Stimulation (STN-DBS) in May 2019. In April

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2021, he received two doses of mRNA-1273 vaccine (Spikevax), without experiencing side effects. On December 2021 symptoms were well controlled with levodopa/benserazide 100/25 mg 5 times a day, selegiline 10 mg, and stimulation set at 130 Hz, 60 µs, 3.1 mA (left STN), and 2.6 mA (right STN). The same night of the mRNA-1273 booster he experienced motor and non-motor symptoms worsening (low back pain, insomnia, left foot dystonia), without flu symptoms. He added three night doses of levodopa/benserazide, with onset of dyskinesia but incomplete wearing-off control. Six days later, we evaluated regular DBS functioning: in MED-OFF/STIM-ON condition, the MDS-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) III score was 61, the Non-Motor Symptoms Scale (NMSS) score was 66, and Montreal Cognitive Assessment (MoCA) score was 26. Motor symptoms improved increasing stimulation intensity (left STN 3.4 mA; right STN 2.8 mA): MDS-UPDRS III score decreased to 36 in MED-OFF/STIM-ON, and to 8 in MED-ON/STIM-ON (Video 1). The patient achieved good wearing-off control in the following days, also returning to usual therapeutic regimen: mild dyskinesia resolved after restoring previous stimulation settings.

The second patient is a 55-year-old man with a 13-year PD history, implanted in September 2021 with percutaneous endoscopic transgastric jejunostomy (PEG-J) for levodopa-carbidopa intestinal gel (LCIG) infusion. Prior to implantation, despite low dose of dopaminergic therapy (levodopa/benserazide 750/125 mg and safinamide 100 mg), he suffered from disabling dyskinesia alternated to severe OFF periods, with unsteady gait and necessity to use a wheelchair. The Unified Dyskinesia Rating Scale (UDysRS) score during daily-ON was 55. With LCIG therapy (morning dose 6.7 ml, continuous dose 2.2 ml/h; 16 h per day), the patient experienced good motor control: dyskinesia significantly improved (UDysRS score 16), and he regained autonomy in walking. He received two doses of BNT162b2 mRNA vaccine (Comirnaty) in April 2021 without any side effect. From the same night of the BNT162b2 booster, on January 2022, dyskinesia severely worsened, forcing the patient to use the wheelchair again. Three days later, the UDysRS score was 73, MoCA score was 28, and MDS-UPDRS III score was 14 (Video 2). We reduced continuous dose to 2.0 ml/h, obtaining only partial dyskinesia reduction and re-emergence of OFF periods. Five days later, dyskinesia regressed: previous dose was restored, with good control of OFF periods and only mild, non-disabling, dyskinesia increase.

Few other data are available in literature, with four cases of PD symptoms worsening and three cases of new movement disorders in healthy people (Table 1).

Erro et al. [4] reported a 61-year-old female with an 11-year PD history and a 79-year-old female with a 5-year PD history, who developed severe dyskinesia (in one case associated with delirium) after receiving the BNT162b2 vaccine, which improved after decreasing dopaminergic therapy.

Cosentino et al. [5] presented two cases of PD motor deterioration after the first dose of BNT162b2 vaccine, the first with increased rigidity and gait impairment and the second with tremor worsening. Both patients improved spontaneously.

Two cases of hemichorea-hemiballismus (males, 88-year-old and 84-year-old) arose following first dose of AZD1222 (Vaxzevria), respectively 16 and 40 days after [6]. MRI, cerebrospinal fluid (CSF) analysis, and panel for autoimmune/paraneoplastic encephalitis and vasculitis were normal. Both patients completely recovered after a short course of intravenous steroids.

Another case of hemichorea occurred in an 83-year-old male the day after the second dose of BNT162b2 vaccine [7]. After 1 month, brain MRI and electroencephalography were normal, while brain SPECT showed asymmetrical decrease of perfusion pattern in left thalamus, contralateral to hyperkinesia. Symptoms mostly relieved 2 weeks after starting Haloperidol 0.75 mg BID.

Discussion

COVID-19 vaccines in PD patients showed similar types and incidence of side effects than the general population [2]. EudraVigilance database reported only few cases of transient movement disorders after COVID-19 vaccination (mostly tremor) [4].

Currently, the mechanisms underlying these post-vaccination manifestations are unknown, also considering lack of data for all vaccinations in parkinsonian patients [9]. The systemic inflammatory response, already known as a possible trigger for PD progression [10, 11], may be implicated in the pathogenesis and fast onset of these side effects. Several mechanisms have been considered to contribute to this response during systemic infections like COVID-19, including the release of inflammatory cytokines such as TNF-α. This response could alter the permeability of the blood–brain barrier and consequently modify drug availability, leading, together with a possible striatal glia-mediated inflammatory processes, to the occurrence of symptoms complications [5, 6]. Other intriguing proposals are that circulating cytokines produced during infections may lead to impaired function of dopaminergic receptors and consequent response to dopaminergic drugs, or directly promote neurodegeneration through the activation of quiescent microglia and consequent increase of pre-existing inflammatory processes in the brain of PD patients [11]. Inflammatory cascade could also mediate new onset of movement disorders after vaccination, in this case as an immune-mediated endotheliopathy induced by the spike protein, especially suggested by

Table 1 Clinical features of PD patients worsened and non-parkinsonian patients with new onset movement disorders after vaccination

Report	Age/sex	Type of vaccine/dose	Movement disorder	Latency	Therapeutic intervention	Outcome
Erro et al	61 F	BNT162b2—1st dose	PD—dyskinesia new onset (no other side effects reported)	6 h	LEDD reduction	Dyskinesia disappearance but wearing-OFF reemergence
Erro et al	79 F	BNT162b2—2nd dose	PD—dyskinesia worsening (with fever and delirium)	1 day	Acetaminophen, Levodopa reduction	Residual mild confusion and dyskinesia
Cosentino et al	NA	BNT162b2—1st dose	PD—motor worsening (no other side effects reported)	NA	No intervention	Recovery in few days
Cosentino et al	NA	BNT162b2—1st dose	PD—tremor worsening (no other side effects reported)	NA	No intervention	Recovery in 2 weeks
Matar et al	88 M	AZD1222—1st dose	New onset of hemichorea/hemiballismus (no other side effects reported)	16 days	1 g IV methylprednisolone for 3 consecutive days	Recovery 24 h after starting therapy
Matar et al	84 M	AZD1222—1st dose	New onset of hemichorea/hemiballismus (no other side effects reported)	40 days	1 g IV methylprednisolone for 3 consecutive days	Recovery 3 days after starting therapy
Ryu et al	83 M	BNT162b2—2nd dose	New onset of hemichorea (no other side effects reported)	1 day	Haloperidol 0.75 mg TID	Recovery 2 weeks after starting therapy
Present case/1st patient	46 M	mRNA-1273—3rd dose	PD—motor worsening	12 h	DBS modulation and Levodopa increase	Recovery 5 days after therapy adjustment
Present case/2nd patient	55 M	BNT162b2—3rd dose	PD—dyskinesia worsening	12 h	LCIG continuous infusion reduction	Recovery 5 days after therapy adjustment

PD, Parkinson's disease; *IV*, intravenous; *LEDD*, Levodopa Equivalent Daily Onset; *DBS*, Deep Brain Stimulation; *LCIG*, Levodopa Carbidopa Intestinal Gel; *TID*, two times a day; *NA*, not available

the steroid-responsive cases [7]. The mechanisms involved in the infectious systemic response may overlap with those relating to the vaccine response in the patients described, albeit with a different severity and above all a course that in this case is transient and benign.

No other reports from booster doses are available in literature. Booster dose, with greater immunogenicity than the two-dose primary vaccination, demonstrated a good safety and tolerability profile in clinical trials [12]. Our patients presented a previous history of unstable symptom control, and the vaccine-induced immune reaction may have represented a trigger for the disruption of their frail clinical balance: this resulted in altered efficacy of dopaminergic therapy in both cases, in the first patient partially explainable by general malaise and anxiety exacerbation, less likely by interference with the DBS system.

All cases described completely recovered after few days with parkinsonian therapy modification, symptomatic treatment, or even spontaneously, underlining the transient/benign nature of side effects. Patients should be reassured about these complications and encouraged to receive COVID-19 vaccines and boosters, highly recommended to prevent the risk of worse SARS-CoV-2 infection outcome, especially on patients in advanced therapy in PD [2, 3].

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10072-022-06182-w.

Declarations

Ethical approval. The authors confirm that the approval of an institutional review board was not required for this work.

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

Conflict of interest The authors declare no competing interests.

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