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Case Report

Resolution of Longstanding Unilateral Facial Palsy after Receiving BNT-162b2 Vaccine: off Target Beneficial Effect or Reverse Nocebo Phenomenon?

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Abstract

A patient had complete left facial palsy followed by minimal residual left facial palsy for the next nine years. In anticipation of oncoming waves of new SARS-CoV-2 variants, and after due consideration, he took the BNT-162b2 vaccine. To his surprise his residual facial palsy gradually and almost entirely recovered after completing the two-dose vaccination, with no relapse up to six months' followup. The mechanism and significance of such an off-target beneficial effect is discussed with conceptual projection into the future development.

Keywords: left facial palsy; SARS-CoV-2 variants; BNT-162b2 vaccine

Introduction

The subject of facial palsy in relation to COVID-19 vaccination has been extensively discussed in medical forums and platforms. A Hong Kong study [1] shows that the incidence is slightly but significantly increased after the mRNA vaccine, BNT-162b2 vaccine, at 42.8 per 100,000 person years. The increase is even more significant after the inactivated virus vaccine, CoronaVac, at 66.9 per 100,000. However, the study uses only the available data from the A & E (accident and emergency department) of public hospitals as the population control which amount to 27 per 100,000. Since most patients consider Bell's palsy non-life-threatening and seek treatment only from their own family doctors or traditional herbalists/acupuncturists rather than the A & E departments, such control figures only represent a fraction of the total. On the other hand, most patients would report their post-vaccination facial palsy as there is an established structured system for them to do so, complete with the incentive of financial compensations. If the appropriate adjustment is applied it is conceivable that the small but "significant" increase of Bell's palsy may be wiped out or even reversed. Indeed, most reports show no statistically significant increase nor cause-effect relations between COVID vaccines and facial palsy [2]. There remain some sceptics among the lay population or even some health workers who still hold opposite views. Regrettably, facial palsy has been repeatedly exploited as one of the many excuses put up by vaccine opponents to refuse vaccination. It is not the intention of this paper to enter into such arguments but rather to report objectively the events of a case suffering from facial palsy for nine years and made a gradual improvement of the residual static facial palsy starting from the first dose of BNT-162b2 vaccine and improving further with the second dose. It is believed that such a positive off-target side effect should be reported in full detail so as to give a more balanced picture of the vaccine scenario.

Case report

This is a 47year-old male patient who presented with a past history of complete left facial palsy, in June 2012, for two weeks, treated outside by prednisone with no improvement. His treatment was changed to dexamethasone 10mg and, belatedly, acyclovir was added, 800mg 3 times a day and Vitamins B1,6,12 one tablet a day. His facial palsy was measured by the House-Brackmann score [3] as follows (Table 1).

Date: 2012	Voluntary movements, 2.5mm = 1 point		H-B score	Functional recovery %	Grade	Description
	Eyebrow elevation	Angle of mouth				
Jun 15	0	0	0/8	0	VI	Complete palsy
Jun 22	0	0	0/8	0	VI	Complete palsy
Jun 27	1-2mm (0.5 pt.)	0	<1/8	10%	V	Severe palsy
Jul 18	5mm (2 pts)	2-3mm (1 pt.)	3/8	26%	IV	Moderate palsy
Sep 17	>10mm (4pts)	10mm (4 pts)	8/8	95%*	I	Imperfect recovery*

Table 1: *Progress of patient's left facial palsy as charted by the House-Brackmann (H-B) score*

*Some residual impediment persisted in the form of subtle facial expression, not measurable by House-Brackmann score. This residual facial palsy remained static for the next 9 years. After the first dose of BNT-162b2 vaccine, it started to show an insidious and gradual improvement up to about 70% which further improved to over 80% after the second dose.

Although he appeared recovered by the House-Brackmann score he continued to feel some subjective weakness in left facial muscles especially when it came to certain facial expressions. Furthermore, he experienced on and off abnormal sensations over the left side of the face, (e.g. tightness on left side of the face while protruding the lips, some left-sided headache and some tingling pain over the left ear. Assessment by a neurologist ascribed such symptoms to aberrant nerve regeneration.

The patient was followed up for the next nine years, during which the residual facial palsy remained static. When the pandemic hit Hong Kong in early 2020, his initial decision was to avoid vaccination for fear of worsening or a full-scale relapse of his facial palsy. By mid 2021, it became obvious that the pandemic was not going away very soon. Rather, with successive generations of new variants, it was likely to get worse before it would get better [4]. After a thorough and informed discussion, we decided to let him take the BNT-162b2 vaccine, marketed under the name Comirnaty, at the end of August 2021. Over the next three weeks following the first dose,his residual facial palsy, including the paresthesia, resolved insidiously, gradually and progressively. By the fourth week, he subjectively felt about 70% resolution of his residual 5% facial palsy, and he willingly proceeded to take the second dose on September 22nd. Further improvement followed with almost complete disappearance of the aberrant sensory disturbances except for a trace of occasional left sided "pulling sensation in the head. Another six months passed by, the left residual facial palsy is more than 80% resolved and he is now (mid-March, 2022) scheduled for the third (booster) dose.

The timing of this patient could not have been better. At the time he took the vaccine, the delta variant, with higher reproductive numbers and resistance to naturally acquired or vaccine-generated anti-COVID antibodies, began to take the world by the storm [5], followed by the even more contagious and anti-body-resistant omicron variant [6]. Hong Kong had kept the pandemic at a very low level up to this point. Then, relaxation measures set in, bowing to popular demands, just as the new variants made their landing on this territory. And we paid a high price for our complacency. Over the six weeks since February 1st, the daily new cases, jumped from two digits, mainly imported, to five digits, virtually all of local origin. This patient, protected by his full vaccination, not only remained symptom-free and RT-PCR RNA negative but also in a safer and stronger position to look after his COVID-stricken parents (both had resisted our vaccine drive).

Discussion

This patient's facial palsy was most likely related to herpes simplex virus (HSV) infection, the commonest cause [7]. The clinical course lent support to such a viral etiology. Varicella zoster virus (VZV) is also a possibility, but is less common especially in the absence of skin eruption, conjunctival involvement and more pronounced neuralgia. Moreover, VZV infection would have been less responsive to antiviral drugs when treatment is substantially delayed as in this patient. Like most HSV infections, he did not respond to corticosteroids alone but started to improve after he was started (albeit belatedly) on high dose acyclovir. Today, we would probably have used the prodrug valaciclovir [8] which is far more efficiently absorbed and, on first-pass through the liver converted to the active agent.

It is difficult to understand the way by which the vaccine eradicated the residual facial palsy. The following are speculative attempts to explore the possible mechanisms involved.

First, we may assume that the residual palsy is due to some residual virus in the facial nerve neuron or fibers. The vaccine is capable of eliciting a recall reaction of the immune system to bring on a new wave of antibodies and T-cell and other inflammatory activities. The antibodies would be highly specific to the molecular sequence of the antigen(s) in the vaccine. The cellular response may be less specific. Indeed, anti-coronavirus vaccines have been known to provoke reactions on the skin previously affected by radiotherapy [9].

Second, the residual problem may be one of healing, scarring and/or aberrant nerve regeneration, and the vaccine in some way corrected such a problem, e.g. by activating T-cells, macrophages, monocytes, scavenger cells, fibroblasts and even stem cells to remodel the scarred nerve fibers, clearing undesirable cross connections and fostering correct re-alignments. The significance of T-cell activities has been mentioned in the previous paragraph. More than antibodies, T-cell mediated immunity may extend well beyond a single variant or a single species, and extend certain protection at least against severe or lethal infection of other Beta-coronavirus [10]. It is possible that a high degree of cellular immune activity might cause recall reactions to other previous virus infections.

Third, some ingredients in the BNT-162b2 vaccine could have possessed direct anti-HSV action and mopped up any residual pathogens in the facial nerve. Alternatively, the mRNA itself might modulate the affected neurons and/or virus in such ways as to expedite further clearance of the neuritis.

Fourth, the cause of the residual facial palsy is only functional. He could have recovered completely as shown in the House-Brackmann score, but the impediment lingered on in his mind. After taking the vaccine, his mind was focused on the expectation of relapse of his facial palsy. When this failed to materialize, his mind finally came to terms with the reality that the residual palsy had left him. We often talk of the nocebo effect, that a patient may subjectively notice a symptom because he is expecting to get it. In this patient, the reverse happened and we might call it the reverse nocebo effect.

A fifth mechanism is that this is pure coincidence. It simply takes nine years for this residual facial palsy to recover and, by pure chance, it coincides with the timing of the COVID-19 vaccination.

The true explanation, may lie beyond the above discussion and even beyond our present scope of knowledge. The first lesson we learn from COVID-19 is that there are still many gaps in medical science that we need to fill up. The bottom line is that amid vaccine sceptics' exploiting facial palsy as part of their arguments, here is a real-life example of resolution of a long-standing facial palsy following vaccination. It is hoped that by reporting new, unusual and unexpected findings and openly discussing them we may further advance our knowledge.

Conclusion and projection to the future

This report illustrates a unique off-target benefit on a patient with the COVID-19 vaccine, the almost complete recovery from a nine-year-long facial palsy with taking the BNT-162b2 vaccine. While such an unusual effect is unlikely to be generalized to a large population, it is conceivable that in future other off-target benefits from various vaccines might arise

if we look out for it. If eventually we can work out the mechanism of such "off-target side-effect" we might even convert it into "on-target" therapeutic utility for other diseases.

Limitations

This paper is limited to a single case report. The facial palsy is quantitated by the House-Brackann score which does not provide for measurement of subtle complicated movements of facial expression, for which we have to rely on the patient's subjective assessment. Ideally, we need to collect more cases with persistent static facial palsy to set up a prospective randomized control trial. Such a trial will be difficult as it is difficult to persuade many cases of facial palsy with residual symptoms to take the vaccine. With the pandemic raging, it is unethical to randomize half of the subjects to receive placebo injections instead of an effective vaccine. We have not done any detailed study on the antibody levels, T-cell profile and other immune cell activities, nor the cytokine serum levels or the HSV molecular markers. Granted the present overwhelming wave of omicron virus infection with over 30,000 new cases daily in an overcrowded city, not counting the untested, unreported and unrecorded cases, our medical resources are already stretched beyond their limits and unlikely to accommodate such a kind of research.

Acknowledgement

The patient has agreed on report of his case and promise to cooperate with any further study on him. His generosity is much appreciated. The initial favorable result has been mentioned at various clinical meetings and online discussions, but never in the present detailed and complete format. This paper is the first time the entire clinical picture is presented and its present form is in debt to previous discussions and comments by various learned colleagues.

Declaration of conflict of interest

The author has no conflict of interest to declare. This work is not sponsored or subsidized by any source.

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