Vaccine 37 (2019) 4864–4866

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Short communication

Case report: Recurrent peripheral facial paralysis following two influenza vaccinations in 2009 and 2016

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ARTICLE INFO

Article history:
Received 25 May 2019
Received in revised form 30 June 2019
Accepted 6 July 2019
Available online 13 July 2019

Keywords:
Influenza vaccination
Peripheral facial paralysis
Adverse effects

ABSTRACT

A 57-year-old female experienced two successive peripheral facial paralysis (PFP) episodes following influenza immunization in 2009 and 2016 with two different vaccines. The similarity of chronology and semiology between the two events and the absence of alternative etiology plead for intrinsic accountability. Extrinsic accountability relies on previous case reports of PFP related to flu vaccination (26 cases in the French pharmacovigilance database and 4 cases in the medical literature).

1. Introduction

Each year, the influenza outbreak involves in France >2 million people and is responsible for an increase in deaths estimated to 14,400 in 2016–2017 [1]. These deaths concern mainly the most fragile patients (elderly people over 65, patients with chronic diseases, immunosuppressed patients) [1]. Since the A/H1NIpdm09 outbreak, controversies about the benefit/risk ratio of the flu vaccine are common in France [2]. The rare neurological side effects of the flu vaccine contribute significantly to the fears of patients relative to this immunization and explain partly the low adhesion of at-risk populations of this vaccine [1]. In this report, we describe the case of a fragile patient who exhibited two successive episodes of peripheral facial paralysis (PFP) following immunization with two different flu vaccines.

2. Case report

A 57-year-old female with a history of type 2 diabetes mellitus, hypertension, dyslipidemia, obesity (BMI = 31) and Meniere's disease received on the 23rd of November 2009, a recommended administration of influenza vaccination (PANDEMRIX® H1N1, adjuvant AS03, GSK). On the 24th of November, she experienced a dysgueusia (metallic taste). The following day, she experienced weakness on the right side of her face, a loss of sensation on the left side of her face and asthenia. A physical examination performed by an otolaryngologist revealed a right PFP with loss of upper and lower facial muscle motor function of her. The remainder of the physical examination was normal. Brain magnetic resonance imaging (MRI) and magnetic resonance angiography were normal on the 27th of November. No laboratory sign of inflammation was recorded. The search for biological stigmata of sarcoidosis (angiotensin-converting enzyme, serum calcium and phosphorus) was negative. The patient was admitted on the 28th of November in the Department of the University Hospital of Saint-Etienne and physicians performed a spinal puncture on the 1st of December. Cerebrospinal fluid analysis showed a high-level protein (0.73 g/L) with only 1 erythrocyte and 1 leucocyte/mm^3. Molecular tests for detecting the genome of herpes simplex virus, varicella-zoster virus and enterovirus were negative. Serology of Lyme disease, syphilis, HIV infection, and infection with other rarer neurotropic viruses were negative. Mumps and EBV serology was in favor of a past immunity. The electromyography performed on the 3rd of December confirmed right PFP with a normal motor and sensory conduction for the left side of her face and for lower and upper extremities. The somatosensory evoked potentials were also normal. The patient was treated with prednisone and valaciclovir for 10 days. After 30 days, clinical examination showed a total resolution of the PFP.

The patient was not vaccinated against influenza from 2010 to 2013. In 2014 and 2015, she received the seasonal flu vaccine without adverse effect. In October 2016, the patient, now 64-year-old,

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https://doi.org/10.1016/j.vaccine.2019.07.025
0264-410X/

Table 1
Cases of peripheral facial paralysis following flu immunization notified between 1985 and 2017 by the French Centre national de pharmacovigilance (p) or through the medical literature (ref).

Case number (reference)	Age (years)	Gender	Underlying diabetes	Vaccine name (brand)	Date of immunization	Time (days) between vaccine and symptoms	Treatment	Evolution (number of days for total resolution)
1p	25	M	No	Mutagrip (Sanofi-Pasteur)	10/01/1985	9	NA	Favourable (>30)
2p	80	F	NA	Tétagrip (Sanofi-Pasteur)	11/06/1987	NA	NA	NA
3p	20	M	No	Mutagrip (Sanofi-Pasteur)	11/10/1989	1	Corticosteroids	NA
4p	76	M	NA	Vaxigrip (Sanofi-Pasteur)	10/08/1999	21	NA	Neurological sequels
5p	50	F	No	Vaxigrip (Sanofi-Pasteur)	10/03/2001	2	NA	Favourable (>12)
6p	66	F	No	Mutagrip (Sanofi-Pasteur)	10/21/2005	2	Corticosteroids	Favourable (90)
7p	50	F	No	Vaxigrip (Sanofi-Pasteur)	11/24/2005	2	Corticosteroids/aciclovir	Favourable (14)
8p[a]	33	M	No	Vaxigrip (Sanofi-Pasteur)	11/18/2006	1	Corticosteroids	NA
9p	40	M	No	Vaxigrip (Sanofi-Pasteur)	11/30/2006	9	NA	Significant improvement (NA)
10p	67	F	No	Influvac (Solvay)	10/13/2008	7	Corticosteroids/valaciclovir	Favourable (35)
11p	2	F	No	Mutagrip (Sanofi-Pasteur)	09/29/2009	3	NA	Favourable (15)
12p	NA	F	No	Pandemrix (GSK)	10/13/2009	19	Aciclovir	Favourable (45)
13p	51	F	No	Pandemrix (GSK)	11/18/2009	5	Corticosteroids	Favourable (8)
14p	41	M	No	Pandemrix (GSK)	11/21/2009	1	Corticosteroids/vasodilator	Favourable (21)
15p[b]	57	F	Yes	Pandemrix (GSK)	11/23/2009	3	Corticosteroids/valaciclovir	Favourable (21)
16p	54	F	No	Pandemrix (GSK)	11/26/2009	1	Corticosteroids	Favourable (21)
17p	33	F	No	Pandemrix (GSK)	12/03/2009	19	Corticosteroids	Slowly improving (NA)
18p	14	F	No	Pandemrix (GSK)	12/21/2009	3	Corticosteroids	Favourable (>7)
19p	52	M	No	Pandemrix (GSK)	01/05/2010	8	Human immunoglobulins	Persistence of symptoms for >10 months
20p	29	F	No	Vaxigrip (Sanofi-Pasteur)	01/06/2011	4	NA	Favourable (60)
21p	24	M	Yes	Vaxigrip (Sanofi-Pasteur)	02/14/2011	7	Valaciclovir	Favourable (>14)
22p	66	M	No	Vaxigrip (Sanofi-Pasteur)	12/02/2013	2	Corticosteroids/valaciclovir	Favourable (7)
23p	61	F	No	Vaxigrip (Sanofi-Pasteur)	11/19/2014	3	Corticosteroids	NA
24p	38	F	No	Vaxigrip (Sanofi-Pasteur)	11/27/2014	2	None	NA
25p	57	M	Yes	Vaxigrip (Sanofi-Pasteur)	12/01/2015	1	Corticosteroids	Favourable (NA)
26p[a]	62	M	No	Vaxigrip (Sanofi-Pasteur)	02/10/2016	21	Physiotherapy	Favourable (>90)
27p	70	F	No	Influvac (Mylan)	10/13/2016	33	Corticosteroids/valaciclovir	Favorable (30–60)
28P[b]	64	F	Yes	Influvac (Mylan)	10/17/2016	2	Corticosteroids/valaciclovir	Favorable (15)
29 (7)	9	M	No	Monovalent H1N1 vaccine (no brand mentioned)	2009	9	Corticosteroids	Significant improvement (8)
30 (8)	30	M	No	Vaxigrip (Sanofi-Pasteur)	2005–2006	10	Corticosteroids/vitamin B complex/ artificial tears	NA
31 (8)	80	M	Yes	KKB/KI-Flu(Adimmune Corporation)	NA	3	Corticosteroids/vitamin B complex/ artificial tears	NA
32 (9)	15	F	No	Monovalent H1N1 vaccine (no brand mentioned)	2009	3	Conservative treatment	Favorable (17)

NA: not available.
[a] Two previous cases having exhibited recurrent paralysis (only the second episode was declared).
[b] Case described herein with recurrent paralysis (the two episodes were declared).

was vaccinated with INFLUVAC® (AH1N1/H3N2 and B, MYLAN). Three days later, she experienced symptoms similar to those of the first episode including dysgueusia, asthenia and complete left PFP. She was not hospitalized. She was tested negative for Lyme disease. Physicians decided that spinal puncture was not required. The brain imaging focused on the facial nerves showed a gadolinium-enhancing aspect of left geniculate ganglion. Treatment was the same as in 2009. Sixty days later, the physical examination showed that the patient's left PFP had completely resolved. In December 2016, the case was reported with the patient consent to the Pharmacovigilance department of the University Hospital of Saint-Etienne and was registered by the French national center of pharmacovigilance (CNP).

3. Discussion

These two successive right then left episodes of PFP following the administration of two flu immunizations using different vaccines question accountability. French pharmacovigilance distinguishes intrinsic accountability that relies on chronology and semiology from extrinsic accountability that refers to the finding of similar cases in the medical literature [3].

The chronology analysis takes into consideration the time having occurred between the administration of the medication and the two episodes of PFP after vaccination (3 days in the present case, which is very favorable to accountability). The semiology analysis considers the mechanism of action, the favoring factors and the differential diagnoses. The mechanism of action has still not been cleared up. The activation of Bell's palsy does not seem to be due to a direct toxic effect from the vaccine, but rather to an autoimmune disorder or a reactivation of herpes simplex virus isoform 1 (HSV-1) and/or varicella zoster virus (VZV) from the geniculate ganglia [4]. Hypertension and type 2 diabetes may also be considered as potential risk factors, even if evidence seems to be modest [5]. For the first episode, the search for a differential diagnosis was extensive. The more frequent cause of PFP is idiopathic Bell's palsy that could be discarded herein in this case report due to the presence of sensitivity lesions of the left hemiface. The laboratory investigations were able to discard the more frequent etiologies of PFP, including Lyme disease, zoster, syphilis and sarcoidosis. The complementary investigations were not in favor of an acute polyneuritis or a Guillain-Barre syndrome. The similarity of the second episode in terms of chronology, semiology and imaging led to limit the investigations to a Lyme serology that was negative.

Concerning extrinsic accountability, the French CNP has recorded 26 similar reports of PFP after flu immunization since 1985. As shown in Table 1, a female predominance was noticed with a mean age of 47.5 years (range: 2–76). The time between immunization and symptoms ranged from 1 to 33 days (median of 3 days). When available, the time for recovery ranged from 15 days to >10 months; sequels were observed in a single case. Three patients exhibited type 2 diabetes in their medical history. With regards to the vaccines that had been used, 8 were A/H1N1pdm09, 16 were inactivated fragmented seasonal vaccines and 3 were subunit seasonal vaccines expressing surface antigens. In the two cases recording 2 successive episodes of PFP following flu immunization, the first episode had not been notified, as in our case report.

An extensive review of the cases of PFP following flu immunization through Medline database identified 4 case reports [6–8]. The main data concerning these 4 cases are summarized in Table 1. In addition, studies from the USA, Taiwan and Switzerland mentioned an increased risk of PFP after intramuscular flu immunization [9,10].

This study is the first to alert on the risk of recurrent PFP after two successive immunizations against flu. Intrinsic and extrinsic factors plead for accountability. This case report could incite to better signal PFP cases occurring after flu immunization. Enhancing transparency should reduce vaccine hesitancy often based on conspiracy theory [11]. These rare events do not impair the favorable benefit risk of influenza vaccination, even in patients with autoimmune disorders or type-2 diabetes. However, the occurrence of a PFP episode after flu vaccination may counter-indicate further flu immunizations whatever the vaccine.

Contribution

Xavier Gocko had the idea of the paper.

Xavier Gocko and Bruno Pozzetto wrote the paper.

Xavier Gocko and Sylvain Poulteau conducted the review from Medline and Cochrane database.

Marie-Noëlle Beyens and Sylvain Poulteau analyzed data of pharmacovigilance.

Pierre Bertholon, a facial paralysis specialist, expertize clinical observation.

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