Letter to the Editor

SIADH After Influenza Vaccination

Since vaccine is given for disease prevention rather than treatment, it is understandable that the safety requirements for vaccines are high to ensure that the benefits outweigh the risks [1]. Adverse events following immunization may occur due to errors in administration, storage and transport of the vaccine, as well as the inherent vaccine properties [2]. The currently-employed World Health Organization criteria may not be sufficient for determining whether or not an adverse event is truly vaccine-related [3]. Nevertheless, causality is most likely for events that are unusual and closely follows vaccination [1]. Here, we report an elderly woman who developed syndrome of inappropriate antidiuretic hormone (SIADH) shortly after influenza vaccination.

Mrs. M was an 81-year-old lady with history of hypertension and minor stroke. Her medications included aspirin, famotidine and lisinopril with no recent change in the dosages. She had not taken any herbs or over-the-counter drug. She had received trivalent inactivated influenza vaccine (Vaxigrip; Sanofi Pasteur, Lyon, France) as part of the territory-wide vaccination program 2 days before she was hospitalized for headache, malaise, myalgia, nausea, and vomiting once of undigested food.

On admission, she was euvolemic with no tachycardia. Her blood pressure was 165/66 mmHg. There was no focal neurological sign. The laboratory data on admission is shown in the Table. SIADH was diagnosed and fluid restriction of 1 L/day was implemented. Spot morning cortisol was 990 nmol/L. Thyroid function test, chest X-ray and plain computed tomography of the brain were normal. Serum sodium (in mmol/L) rose to 121, 124 and 130 on days 3, 5 and 7 of hospitalization, respectively. Her symptoms subsided by day 7 and she was discharged without sequelae. Her serum sodium level remained normal 3 weeks after discharge.

Vaxigrip is an inactivated influenza vaccine containing three strains of influenza viruses—A/Brisbane/59/2007 (H1N1)-like strain, A/Brisbane/10/2007 (H3N2)-like strain and B/Brisbane/60/2008-like strain (B/Brisbane/60/2008—or the year 2009 to 2010 [4]. Common side-effects after influenza vaccination include local reactions such as pain, erythema and edema that occur in up to 57% of patients, but which usually disappear spontaneously within 1–2 days [4–6]. Systemic reactions such as fever, malaise, myalgia and arthralgia occur in 26.4–52.3% of individuals [5,6].

Our patient developed systemic upset after influenza vaccination. She had hypotonic hyponatremia on admission. Although she had vomited once before admission, she was clinically euvolemic. Her normal hematocrit, normal serum urea and markedly elevated urinary sodium level spoke against a hypovolemic state.

Headache occurs in up to 10% of patients after influenza vaccination [7], but serious neurological complications such as Guillain-Barré syndrome [8–10], acute demyelinating encephalomyelitis [8] and chronic inflammatory demyelinating polyneuropathy [11] are rare. Hyponatremia or SIADH in the absence of a neurological syndrome has, however, not been reported. Given the myriad of neurological symptoms that may occur after influenza vaccination, it would be rational to add influenza vaccine to the long list of medications that may cause SIADH [12].

Our case may be categorized as being possibly vaccine-related, although it has been emphasized that adverse events temporally associated with vaccination might not necessarily be caused by the vaccine [13]. Case reports like ours, in principle, do not fulfil the requirements for hypothesis testing [2]. Faithfully adopting the current World Health Organization criteria in determining if an adverse event is truly vaccine-related is, however, unlikely to be sufficient. Therefore, we consider vigilant post-marketing surveillance and an effective reporting system to be of importance in building up the risk and safety profile of individual vaccines. Effectively conveying the risks and benefits of vaccination to the general public should be part and parcel of a mature health care system.

Table. Laboratory data on admission

Hematocrit	34.7%
Plasma levels of	
Urea	2.8 mmol/L
Creatinine	59 μmol/L
Sodium	117 mmol/L
Potassium	3.5 mmol/L
Glucose	6.3 mmol/L
Serum osmolality	251 mOsm/kg of water
Urine osmolality	361 mOsm/kg of water
Urine sodium	118 mmol/L

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References

1. Griffin MR, Braun MM, Bart KJ. What should an ideal vaccine postlicensure safety system be? *Am J Public Health* 2009;99(Suppl 2): S345–50.
2. *The Weekly Epidemiological Record (WER), 23 March 2001, Vol. 76 (pp. 85–92).* Geneva: World Health Organization. Available at http://www.who.int/wer [Date accessed: November 8, 2009]
3. Kavadas FD, Bitnun A, MacGregor D, Heurter H, Ford Jones EL. Acute neurological events associated with influenza vaccination: are the WHO criteria for assessing causality adequate? *Scand J Infect Dis* 2008;40:565–70.
4. *Vaxigrip Product Monograph.* Toronto, Canada: Sanofi Pasteur Limited, 2009.
5. Lopes MH, Mascheretti M, Franco MM, Vasconcelos R, Gutierrez EB. Occurrence of early adverse events after vaccination against influenza at a Brazilian reference center. *Clinics (Sao Paulo)* 2008;63:21–6.
6. Jansen AGSC, Sanders EAM, Smulders S, Hoes AW, Hak E. Adverse reactions to simultaneous influenza and pneumococcal conjugate vaccinations in children: randomized double-blind controlled trial. *Pediatr Allergy Immunol* 2008;19:552–8.
7. Hsiao JY, Hsin SC, Hsieh MC, Hsia PJ, Shin SJ. Subacute thyroiditis following influenza vaccine (Vaxigrip) in a young female. *Kaohsiung J Med Sci* 2006;22:297–300.
8. Izurieta HS, Haber P, Wise RP, Iskander J, Pratt D, Mink C, et al. Adverse events reported following live, cold adapted, intranasal influenza vaccine. *JAMA* 2005;294:2720–5.
9. Haber P, DeStefano F, Angulo FJ, Iskander J, Shadomy SV, Weintraub E, et al. Guillain-Barre syndrome following influenza vaccination. *JAMA* 2004;292:2478–81.
10. Kuwabara S. Guillain-Barre syndrome: epidemiology, pathophysiology and management. *Drugs* 2004;64:597–610.
11. Brostoff JM, Beitverda Y, Birns J. Post-influenza vaccine chronic inflammatory demyelinating polyneuropathy. *Age Ageing* 2008; 37:229–30.
12. Ellison DH, Berl T. Clinical practice. The syndrome of inappropriate antidiuresis. *N Engl J Med* 2007;356:2064–72.
13. Huynh W, Cordato DJ, Kehdi E, Masters LT, Dedousis C. Post-vaccination encephalomyelitis: literature review and illustrative case. *J Clin Neurosci* 2008;15:1315–22.