

Case report

Report of two rare complications of pandemic influenza A (H1N1)

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Abstract

Novel influenza A (H1N1) has created a major worldwide health problem within a short time after its emergence. This infection is often self-limited, but sometimes can cause severe and fatal complications. In this study, we present two rare complications of pandemic influenza A, who were referred to Razi University Affiliated Hospital in northern Iran. The first case was a 30-year-old man with severe headache and high fever accompanied with chills, generalized myalgia, and arthralgia. Cerebrospinal fluid analysis was consistent with aseptic meningitis. The second case, a 25-year-old pregnant woman with high fever, chills and severe fatigue and malaise, developed tachypnea, tachycardia, respiratory distress, cyanosis and loss of consciousness a few hours after admission. Echocardiography reported myopericarditis. The patient was transferred to the intensive care unit and mechanical ventilation was begun. The next day, the patient started vaginal bleeding which progressed to spontaneous abortion three days later. Diagnosis of novel influenza A (H1N1) was confirmed using real-time reverse-transcriptase PCR of a pharyngeal swab.

Key words: influenza A (H1N1); influenza complication; meningitis; myocarditis

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Introduction

Novel influenza A (H1N1), which is also called human influenza virus with swine origin, has created a major worldwide health problem within a short time after its emergence [1]. This infection is often self-limited but sometimes can cause severe and fatal complications [2,3]. In this study, we present two cases with rare complications of pandemic influenza A, who were referred to Razi University Affiliated Hospital.

Case 1

During the last days of fall 2009, a 30-year-old male was admitted to the emergency ward at Razi University Affiliated Hospital because of severe headache and high fever. He was in good health until three days before admission, when he suddenly experienced headache and back pain. During the next hour, high fever and chills developed along with generalized myalgia and arthralgia. Sore throat, nausea, vomiting, diarrhoea, abdominal pain, and urinary symptoms were absent. The severity of his fatigue and malaise prevented him from working.

He was a construction worker, he was married, and he had a five-year-old child. He never smoked or used any illicit drugs. His medication history was

recent use of dexamethasone and diclofenac injection, prescribed by his family physician the previous day. In the morning of the day of admission, he developed severe headache, vertigo and recurrent vomiting, along with high body temperature. He was therefore referred to the emergency ward.

The patient was admitted to the infectious disease ward with initial suspicion of influenza A. At the time of admission, he was severely ill but still conscious of place and time. The vital signs were satisfactory, except for oral temperature of 38.9 C and tachycardia (PR: 100/min). Physical examinations revealed neck stiffness but kernig and brudzinski signs were normal. Additional examinations were normal except for mild pharyngeal erythema. Biochemical laboratory results are presented in Table 1.

To rule out bacterial meningitis, lumbar puncture was done. Cerebrospinal fluid (CSF) was clear with normal pressure. CSF analysis was as follows: white blood count (WBC): 380, P 12%, L 88%; red blood count (RBC): 0; protein: 66 mg/dl; glucose: 48 mg/dl.

Results of Gram smear, bacterial culture, Venereal Disease Research Laboratory (VDRL) test, Wright and Herpes simplex virus (HSV) 1 and 2 PCR, were all negative.

Table 1. Biochemical laboratory study of case 1

CBC	WBC	8.8 ×10 ³ /μl	FBS	120 mg/dl
	RBC	5.49×10 ⁶ / μl	BUN	33 mg/dl
Hb		15.3 gr/dl	Creatinin	0.8 mg/dl
	PLT	211×10 ³ /μl	Na	131meq/l
	PMN	62.2%	K	4.2meq/l
	LYMPH	37.8%	ESR	3 m.m
			CRP	0
	SGOT	20 IU/L	CPK	85 IU/L
	SGPT	25 IU/L	LDH	234 IU/L
	ALP	73 IU/L	amylase	114 IU/L
Urine analysis		Normal	Wright	Negative
Urine culture		Negative	Ca	9.8 mg/dl
Blood culture		Negative	phosphor	4mg/dl

Brain computed tomography (CT) scan with IV contrast was normal. Blood cultures were obtained and a pharyngeal swab specimen was sent to the reference laboratory at Tehran Health School for viral culture and RT-PCR for testing for influenza virus. Intravenous ceftriaxone was prescribed and after 48 hours novel influenza virus (H1N1) by RT-PCR of pharyngeal swab and cerebrospinal fluid (CSF) specimen was confirmed.

Tamiflu 75 mg every 12 hours along with diclofenac 25 mg every 8 hours were begun, while ceftriaxon was discontinued. Fever diminished over the next 48 hours and headache recovered in 72 hours. After 10 days, the patient was discharged in good health with a final diagnosis of aseptic meningitis due to novel influenza (H1N1) virus.

Case 2

A 25-year-old woman presented to us because of high fever, chills and severe fatigue and malaise which had begun two days previously. The patient was in her third month of pregnancy (G₂P₁LC₁). She had travelled to Syria with her husband and five-year-old son two weeks before admission. On the way back to Iran, her husband and their child got sick with the same signs and symptoms as her present illness. Both of them recovered well. She was in good health for almost two days and did not use any medication except folic acid daily. In admission, she complained of generalized myalgia, nausea, vertigo, mild sore throat and dry cough. Physical examinations showed

oral temperature of 38°C; pulse rate: 96/minute; respiratory rate: 16/minute; blood pressure: 110/70; and pharyngeal erythema without exudates. Her neck was supple, both lungs were clear, and the other examinations were normal.

She was admitted to the infectious disease ward and oseltamivir (Tamiflu) was prescribed after obtaining a pharyngeal specimen for pandemic influenza (H1N1). Initial laboratory test results are presented in Table 2.

Pelvis sonogram showed a viable fetus with gestational age of 14 to 15 weeks. Electrocardiogram revealed sinus tachycardia.

A few hours later, she developed tachypnea, tachycardia, respiratory distress, and cyanosis along with loss of consciousness. The patient was transferred to the intensive care unit and mechanical ventilation was begun. In addition, IV infusion of dopamine was begun because of refractory hypotension to IV fluid therapy.

Emergency echocardiography reported myopericarditis. A broad spectrum antibiotic (Ceftriaxone, 1 g every 12 hours) was prescribed, and the dosage of Tamiflu was increased to 150 mg every 12 hours. A diagnosis of H1N1 was received 48 hours later.

The day after, the patient started vaginal bleeding. A medical team consisting of an infectious disease specialist, cardiologist, anesthesiologist, gynecologist, nephrologist and physiotherapist were conducting the patient's care and treatment at the time. Vaginal

Table 2. Initial laboratory tests of case 2

CBC	WBC	9.3 ×10 ³ /μl	PT	12 second
Hb		14 gr/dl	INR	1 IU
	PLT	222×10 ³ /μl	BUN	20 mg/dl
	PMN	76%	Creatinin	0.7 mg/dl
	Lymph	22%	CPK	473 IU/L
	Mono	2%	LDH	528 U/L
			ABG Pao ₂	92 mmHg
LFT	SGOT	89 IU/L	Paco ₂	24 mmHg
	SGPT	50 IU/L	O ₂ saturation	90.2%
	ALP	61 IU/L	PH	7.31
	FBS	95 mg/dl	HCO ₃	11.9
Ca		9.2 mg/dl	Urine analysis	Normal
	P	6.3mg/dl		
Alb		2.9 gr/dl		

bleeding progressed to spontaneous abortion three days later. Therapeutic curettage was done to control the continuous bleeding.

Respiratory distress continued during the next two weeks. After three weeks mechanical ventilation was discontinued and the patient was referred to the infectious disease ward for completion of treatment.

The patient was discharged after 24 days in good health with a diagnosis of complicated pandemic influenza with myopericarditis and spontaneous abortion.

Discussion

In April 2009, the Centers for Disease Control (CDC) confirmed two cases of human infection with novel influenza with swine origin for the first time [1]. The 2009 H1N1 virus contained a unique combination of gene segments that had not previously been identified in humans or animals [2]. In a short time, many cases of the disease were reported in the United States, Mexico, and other countries worldwide, and the World Health Organization eventually declared it to be the first pandemic in the new millennium [3]. Like other influenza viruses, 2009 H1N1 spreads from person to person through coughing, sneezing, and occasionally through touching objects contaminated with the virus. The incubation period of the infection is estimated at two to seven days. Infection usually involves healthy, young and middle-aged people.

Symptoms include abrupt onset of fever, chills, headache, sore throat, malaise, coryza, non productive cough and occasionally nausea, vomiting and diarrhoea. The disease is often self-limited in a one-week period, although dry cough or weakness can continue up for to two to four weeks. Some patients have greater risk for complications or death, including pregnant women, very obese people, children younger than five years old, regular aspirin consumers, and patients with immunosuppression or chronic diseases [4].The most common complications of infection are related to the respiratory system, including primary viral pneumonia, secondary bacterial pneumonia, otitis media, acute sinusitis, croup, and exacerbation of a chronic lung disease. Non-respiratory complications that occur uncommonly are encephalopathy, encephalitis, transverse myelitis, Guillain Barré Syndrome, toxic shock syndrome, myositis, myoglobineuria, Reye’s syndrome, myocarditis and pericarditis [5,6].

Our first case was a 30-year old man who presented with the signs and symptoms of pandemic influenza along with signs of meningitis. CSF analysis suggested aseptic meningitis. Based on the positive results of the SCF specimen for H1N1, diagnosis of aseptic meningitis secondary to H1N1 influenza virus was confirmed. According to the literature, this virus is accepted as a rare etiologic agent of aseptic meningitis. Few reports of H1N1 aseptic meningitis

have been reported so far, and to the best of our knowledge this is a rare case of influenza A (H1N1) aseptic meningitis. Nevertheless, our patient recovered rapidly without any sequela. This case underlines the importance of considering CNS complications in influenza (pandemic or seasonal) cases, and of considering influenza in every case of aseptic meningitis, especially during pandemics.

Our second case was a 25-year-old pregnant woman who developed myopericarditis and spontaneous abortion after influenza A infection. Myocarditis is a well-known but uncommon complication of influenza. Although a few cases of influenza myopericarditis have been reported in the literature [7-9], we still do not know the true prevalence. In a 2009 study of 34 pregnant women that was conducted between 15 April and 18 May and reported to the CDC, six deaths occurred; all the women who died had developed pneumonia and subsequent acute respiratory distress syndrome requiring mechanical ventilation [10]. There are several reports of pandemic influenza A case series in pregnant women but none of them report myocarditis [10-13]. To the best of our knowledge, this is the first case of myocarditis in pregnancy from new influenza A (H1N1).

Pregnant women have an increased risk of complications from pandemic H1N1 virus infection [13] and myopericarditis should be considered in every patient who becomes acutely more breathless or hypotensive during infection with influenza.

This case highlights the importance of considering possible complications in pregnant patients with influenza, and the urgency in initiating treatment with anti-influenza drugs promptly.

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