Case Report

H1N1 Influenza Infection Complicated with Diabetic Ketoacidosis

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Abstract

The 2009 H1N1 Influenza virus was the first infectious pandemic of the 21st century which spread rapidly throughout the world. High-risk groups, such as diabetics, suffered more and showed higher hospital admission and death rates due to this virus. Patients with diabetes mellitus (DM) may develop the fulminant picture of their disease after being infected with influenza. From June to December 2009 at Nemazee Hospital, affiliated with Shiraz University of Medical Sciences, two patients with diabetic ketoacidosis (DKA) were admitted. The H1N1 influenza virus triggered DKA and its complications in these patients. Both patients were female, of ages 16 and 40 years. When admitted, they had signs of influenza-like illness (ILI), tachypnea, laboratory confirmation of acidosis, and high blood sugar levels. The 2009 H1N1 influenza viral RNA was detected in their nasopharyngeal specimens by real time polymerase chain reaction (RT-PCR). Both patients received oseltamivir, but eventually both died. This was the first report of an association between DKA and H1N1 influenza in Iran.

Conclusively, rapid diagnosis of influenza by RT-PCR and early treatment with oseltamivir should be considered in diabetics and/or DKA patients with flu-like symptoms.

Keywords: Diabetic ketoacidosis, H1N1, influenza

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Introduction

Shortly after the detection of the H1N1 influenza outbreak, a virus infection that started in Mexico in late March and early April 2009, the world witnessed its first infectious pandemic of the 21st century. Patients with high-risk conditions such as diabetes mellitus (DM), asthma, pregnancy, cardiovascular diseases, immune suppressive status, obesity, and sickle disease suffered more from this pandemic. Hospital admission and death rates were higher in these patients than in the normal population.[1–4]

There are reports about the relation between different infections with the fulminant picture of DM in the medical literature,[5–12] but such reports about 2009 H1N1 influenza are rare.[13] To the best of our knowledge, there is no report that about the association between the influenza virus and diabetic ketoacidosis (DKA) in Iran. Two female cases of the 2009 H1N1 pandemic influenza virus, one adolescent and one adult, both with complications of DKA, are discussed in this article. We aim to help physicians detect and more quickly manage this life-threatening infection and to enable them to become more aware of H1N1 infection when it is masked by diabetes or DKA signs.

Case Reports

Case one

A 16-year-old female with a family history of DM and no major underlying medical conditions presented to Nemazee Hospital, affiliated with Shiraz University of Medical Sciences, because of a decreased level of consciousness. She had been well until 33 days before hospitalization, when she developed chills, fever, anorexia, flank pain, nausea, and vomiting. During that time, she was given common cold medication. After one week, she developed polydipsia. The following week she was admitted in Marvdasht County Hospital with complaints of dyspnea, generalized body pain, and sore throat, but no fever. Routine laboratory investigations were done for the patient (Table 1). On the second day of admission, lab data showed high blood sugar levels and metabolic acidosis. Therefore, her serum ketone level was checked, which was strongly positive and management of DKA was started. On the 18th day of hospital admission, when her DKA was fully managed, she developed respiratory distress and a drop in the Glasgow Coma Score (GCS). She received respiratory support by ventilator in the Intensive Care Unit (ICU). As the patient had a persistent high-grade fever in the hospital, ceftazidime (1 g, IV, tid), gentamycin (40 mg, IV, bid) and vancomycin (500 mg, IV, bid) were administered. After eight days of assisted ventilation in the ICU, her chest X-ray showed lung infiltration. The patient was treated as a case of ventilator-associated pneumonia and she received meropenem (1g, IV, bid). She had decreased urine output and underwent hemodialysis due to high blood urea nitrogen (BUN) and creatinine (Cr) levels. While in the hospital, she developed two episodes of cardiopulmonary and cardiac arrest that responded to resuscitation. She was then transferred to Nemazee University hospital with a GCS score of 4. On arrival, oseltamivir (75mg, PO, bid) was started via nasogastric tube after taking a sample for the detection of 2009 H1N1 influenza. The result of reverse transcriptase-polymerase chain reaction (RT-PCR) for this virus was positive. Routine laboratory tests were done (Table 2). Brain computed tomography (CT) revealed severe brain edema and intracranial hemorrhage of the right frontal and left occipital lobes (Figure 1). High resolution CT (HRCT) of her lungs revealed bilateral alveolar infiltration, severe consolidation, and pleural effusion (Figure 2). A few days after admission to Nemazee Hospital, the patient died.

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Table 1. Laboratory data from case one, a 16 year-old female patient withdiabetes ketoacidosis (DKA) and the 2009 H1N1 influenza infection.

Item	First work up	Last work up
BS	332	141
pH	6.76	7.5
PCO_2	22.3	24.4
HCO_3	4.3	18.8
PO_2	39.9	113
O_2 saturation	41.2%	98.8%
WBC	7600	9500
Hb	14.9	7.9
PLT	336000	215000
Na	136	145
K	4.6	4.2
BUN	11	97
Cr	5.1	4.2
ESR	20	8
PT	13.3	15.3
PTT	>2 minutes	30 seconds
AST	129	441
ALT	43	124
ALP	207	389
Total protein	4.2	5.1
Albumin	2.1	3.6
Total bilirubon	0.9	1.4
Direct bilirubin	0.2	0.3

BS = blood sugar; WBC = white blood cell count; Hb = hemoglobin; PLT = platelet; Na = sodium; K= potassium; BUN = blood urea nitrogen; Cr = creatinine; ESR = erythrocyte sedimentation rate; PT = Prothrombin time; PTT = Partial thromboplastin time; ALT = alanine transaminase; AST = aspartate transaminase; ALP = alkaline phosphotase.

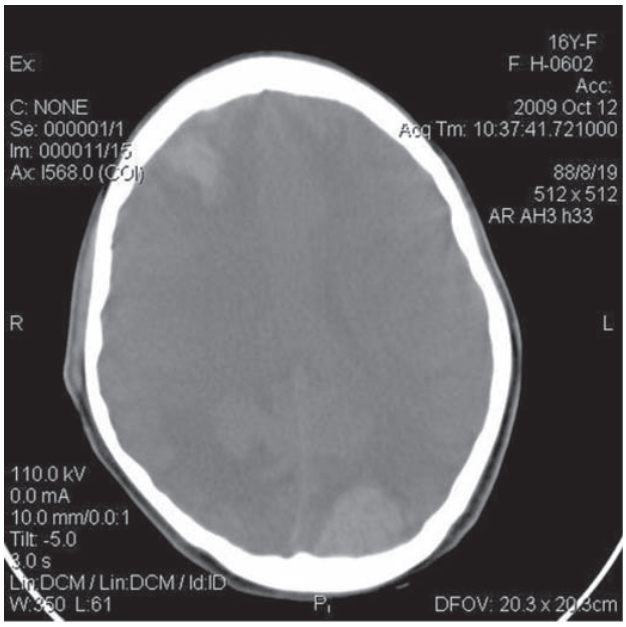

Figure 1. Brain computed tomography (CT) of a 16 year-old female patient who had diabetes ketoacidosis (DKA) and the 2009 H1N1 influenza infection.

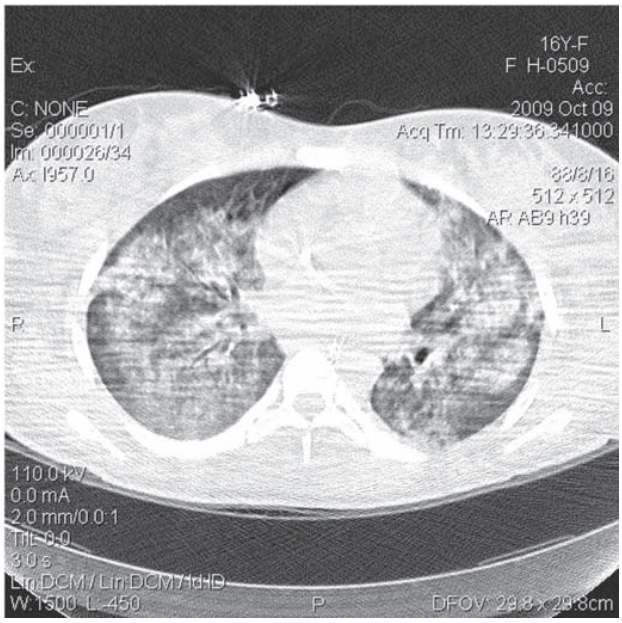

Figure 2. High resolution computed tomography (HRCT) of the lungs of a 16 year-old female patient who had diabetes ketoacidosis (DKA) and the 2009 H1N1 influenza infection.

Table 2. Laboratory test results of case one, a 16 year-old female patient who haddiabetes ketoacidosis (DKA) and the 2009 H1N1 influenza infection.

Urine analysis
Protein: 1+
Glucose: 2+
Ketones: -
Blood: 2+
Red blood cell: 25-30
White blood cell: 4-6
Granular cast: 3-4
Urine culture: Negative
Blood culture: Negative
Calcium: 7.1
Phosphorus: 4.4
C-reactive protein: 12

Table 3. Laboratory data from case 2, a 40 year-old female patient with diabetes ketoacidosis (DKA) and the 2009 H1N1 influenza infection.

Item	First work up	Last work up
BS	776	386
pH	7.31	7.42
PCO_2	28	25
HCO_3	13	16
PO_2	28	52
O_2 saturation	45%	86%
WBC	17800	35160
Hb	11.8	7.5
PLT	248000	185000
Na	125	138
K	5.9	5.8
BUN	28	36
Cr	1.5	1.4

BS = blood sugar; WBC = white blood cell count; Hb = hemoglobin; PLT= platelet; Na = sodium; K = potassium; BUN = blood urea nitrogen; Cr = creatinine

Table 4. Urine analysis and other para-clinical workups of case two, a 40 year-old female patient who appeared with diabetes ketoacidosis (DKA) and the 2009 H1N1 influenza infection.

Urine analysis
Albumin: 2+
Blood: 3+
Red blood cell: 30–35
Ketones: -
Urobilinogen: Trace
Liver function test
Total protein: 7
Albumin: 3.3
AST: 243
ALT: 85
ALP: 348
Direct bilirubin: 0.1
Total bilirubin: 2.01
Calcium: 8.4
Phosphorus: 1.4
PT: 13.5
PTT: 30
ESR: 88
Urine culture
Candida albicans
Colony count: 5000
Sputum culture
Beta hemolytic strep non-A
Colony count: light growth
Echocardiography
Mild left ventricular diastolic dysfunction
Mild right ventricular dysfunction
Mild MS, trivial MR,
Mild TR
Minimal pericardial effusion
Ejection fraction: 65%

AST = aspartate transaminase; ALT = alanine transaminase; ALP = alkaline phosphotase; MS = mitral stenosis; MR = mitral regurgitation; TR = tricuspid regurgitation; PT = prothrombin time; PTT = partial thromboplastin time.

Case two

A 40-year-old female who was a known case of DM for three years, controlled with glibenclamide (80 mg, tid), was admitted to Shahid Faghihi Hospital, affiliated with Shiraz University of Medical Sciences, with complaints of nausea, vomiting, and epigastric pain for four days as well as fever and dry cough for two days. A respiratory rate of 40 per minute, heart rate of 110 per minute, and abdominal tenderness was also detected on admission. There were no other abnormal findings in the physical examination. Routine laboratory studies were performed that revealed high blood sugar levels and acidosis with a low bicarbonate level, indicative of DKA (Table 3). The patient was treated as a case of DKA with the suspicion of the 2009 H1N1 infection. She received oseltamivir (75 mg, PO bid), ceftriaxone (1g, IV, bid), vancomycin (1g, IV, bid), azithromycin (500mg, PO, qd), heparin (5000 units, subcutaneous, bid), and ranitidine (50mg, every 8 hours) as an inpatient. After one day, she developed severe dyspnea, cough, bilateral lung rales, and became unconscious, So intubed with respiratory support. She was sent to the ICU with a GCS of 9 for better management. In the ICU, along with routine laboratory tests (Table 4), a nasopharyngeal swab sampling was taken. One day after ICU admission the patient recovered from DKA, but her general condition had not totally improved. She received the previously mentioned medications with the inclusion of midazolam (5 mg, which was increased to 10 mg per hour, IV). She developed abundant thick lung secretions that were composed of blood clots and pus on the second day of her ICU admission. At this time amikacin (450 mg, bid) was started. RT-PCR a few days after sampling confirmed that she had 2009 H1N1 influenza. Eight days after hospitalization the patient developed cardiopulmonary arrest. Cardiopulmonary resuscitation (CPR) was performed but was ineffective and she died.

Discussion

Human infection with the 2009 H1N1 influenza virus has been reported worldwide. The first cases of influenza-like illnesses were reported in Mexico in March 2009. The disease subsequently spread quickly to the United States and other countries and formed the first pandemic of the 21st century.[14] H1N1 is now in the post-pandemic period (as reported by the WHO on August 10th, 2010). However, localized outbreaks of various magnitudes are likely to continue.[15]

Manifestations of the 2009 H1N1 pandemic influenza are similar to other types of influenza. Patients present with symptoms of acute respiratory illness such as fever, cough, sore throat, rhinorrhea, body aches and headaches. These common, nonspecific symptoms are the cause of difficult differentiation between this virus and other types of flu or the common cold.

The clinical diagnosis may become more difficult in patients with a concurrent disease such as DM. In these patients, symptoms of influenza may be masked and therefore may be overlooked by physicians, which may result in a delay in diagnosis and treatment. These patients are faced with higher morbidity or mortality. Patients with DM have a very high influenza-associated morbidity.[11]

DKA is a life-threatening acute complication of type-1 DM. Although it usually occurs in patients with type 1 diabetes, patients with type 2 diabetes are also susceptible during stressful conditions, such as trauma or infections.[5] Overall, infection is the most common precipitating factor for DKA and is responsible for more than 50% of cases.[16]

This study is the first report association of DKA with the 2009 H1N1 influenza viral infection in Iran. DKA was the initial presenting picture of DM in the first case, as she had no previous diagnosis of diabetes. The second patient was a previously diagnosed case of DM, already under treatment. Both cases had high levels of blood glucose and flu symptoms upon arrival to the hospital. In both patients, it seemed that the H1N1 virus infection was a predisposing factor for the development of DKA, however, the diagnosis of this infection and treatment with oseltamivir were not implemented in the first days of their diseases.

In conclusion, it is essential and lifesaving to act quickly when diagnosing the 2009 H1N1 virus, and to start oseltamivir in the first 48 hours after the appearance of flu symptoms in diabetic patients or those who present with signs of diabetes for the first time.

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