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Assessment of haematology patients with confirmed H1N1 positivity

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Aim: H1N1 influenza virus infections in immunosuppressive patients cause complications. Clinical and laboratory findings of H1N1 positive haematology patients were evaluated in this study.

Materials and methods: The "H1N1 Swine Influenza Suspicious Case Notification Form and Inpatient Follow-up Form" was prepared for 15 patients with suspected H1N1 infection between October 2009 and May 2010. H1N1 was detected by real-time RT-PCR assay. For all cases medical records were reviewed for clinical, demographic, and haematologic information.

Results: H1N1 positivity was confirmed using real-time RT-PCR in 9 out of 15 patients (11 men, 4 women). One of the 9 patients had been followed up due to aplastic anaemia, 1 due to Evans syndrome, and the remaining 7 due to haematologic malignancy. Among the 9 patients diagnosed with H1N1, 3 had previously undergone autologous haemopoietic stem cell transplantation (HSCT). H1N1 was detected in HSCT recipients in the early post-transplant period (range 7–21 days). The most prominent symptoms were as follows: high fever, cough, vomiting, nausea, and diarrhoea, in descending order. Oseltamivir was given to all patients. Eight patients responded to the treatment and recovered clinically. One patient (57-year-old female with multiple myeloma), required intensive care and she died due to severe sepsis and pneumonia.

Conclusion: Our data show that subjective findings like headache and fatigue often seen in influenza infections were not the dominant clinical presentation in these patients. These infections should be considered in patients with haematological malignancy, and appropriate treatment and prophylaxis should be started early.

Key words: H1N1, haematologic malignancy, HSCT, chemotherapy, oseltamivir

Introduction

The influenza A pandemic, sustained by a new H1N1 variant (H1N1v), started in Mexico and the USA at the end of April 2009, spreading worldwide in a few weeks, and the World Health Organization (WHO) declared a pandemic due to the novel virus on 11 June 2009. In Turkey, the first case of pandemic influenza A H1N1 virus (H1N1) was detected on 15 May 2009, in a person that had travelled from the United States to İstanbul, and then the first local case of H1N1 was detected on 18 June 2009. Activities of confirmed cases of H1N1 showed an increase between the 45th and 52nd week in Turkey. Although H1N1 was not very common until the second week of November, activities of H1N1 were at the top level in the last week of November in our region. H1N1 influenza virus infection has been associated with a worldwide outbreak of febrile respiratory infection and causes serious complications in immunosuppressed patients. Similar to immunocompetent patients, most patients with influenza infection and haematologic malignancies present with symptomatic upper

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respiratory symptoms, consisting of sore throat, nasal symptoms, and/or headache. Morbidity and mortality risks are increased in patients with haematological disorders and are treated with chemotherapy and stem cell transplantation. This study examined the clinical and laboratory findings of haematology patients whose H1N1 positivity had been confirmed while receiving treatment at our clinic.

Materials and methods

The "H1N1 Swine Influenza Suspicious Case Notification Form and Inpatient Follow-up Form" was prepared for all patients with suspected H1N1 infection between October 2009 and May 2010. Nasopharyngeal swabs taken from patients were forwarded to our virology laboratory in viral transport medium (Universal transport medium kit, Copan Diagnostics, Brescia, Italy) within a few hours of collection. Real-time RT-PCR assays were performed as soon as the specimens arrived at the laboratory and the remaining specimens were stored at −80 °C. H1N1 was detected by real-time RT-PCR assay (Influenza A H1N1 primer and probe set, SuperScript™ III Platinum® One-Step qRT-PCR System, Invitrogen, USA) by using the ABI 7500 system according to the manufacturer's protocol. The protocol of this assay has been published online at WHO Global Influenza Programme web site (1).

For all cases medical records were reviewed for clinical, demographic, and haematological information.

Results

Among the 15 patients (11 men, 4 women) with suspected H1N1 infection, H1N1 was confirmed using real-time RT-PCR in 9 patients (7 men, 2 women, age average 49). One of the 9 patients had been followed up due to aplastic anaemia, one due to Evans syndrome, and the remaining 7 due to haematologic malignancy (the underlying conditions are shown in Table 1). Among the 9 patients diagnosed with H1N1, 3 had previously undergone autologous haemopoietic stem cell transplantation (HSTC). H1N1 was detected in HSCT recipients in the early post-transplant period (range 7–21 days).

The most prominent symptoms were as follows: high fever, cough, vomiting, nausea, and diarrhoea, in descending order. Two patients had concurrent bacterial infection, while in 1 patient fungal infection was present and in another patient CMV infection was present.

Interstitial infiltrates were observed in 3 patients and the other 2 patients had areas of ground glass in radiological imaging.

All patients were hospitalised and antiviral treatment was started on average 3.4 days (range 1–7

Table 1. Clinical characteristics of the patients.

Patient no.	Diagnosis	Age	Neutrophil	Lymphocyte	Fever	Coughing	Vomiting	Diarrhoea	Nausea
1	MM	59	2450	410	+	+	–	–	–
2	HL	50	104	140	+	–	+	–	–
3	EVANS SYN	83	15700	748	+	–	–	–	–
4	MM	57	3780	57	+	+	–	–	–
5	NHL	52	19	10	+	–	+	+	+
6	MM	50	3030	1450	+	–	–	+	+
7	AA	20	940	490	+	+	–	–	–
8	CML	22	174000	3500	+	–	–	–	–
9	NHL	68	8160	240	+	+	+	–	–

MM: Multiple myeloma, HL: Hodgkin's lymphoma, EVANS SYN: Evans syndrome, NHL: Non-Hodgkin's lymphoma, AA: Aplastic anaemia, CML: Chronic myeloid leukaemia.

days) after the onset of symptoms. All patients were treated with oseltamivir at a dose of 75 mg twice daily (10 days for patients with pneumonic infiltration, 5 days for the other patients). Oseltamivir was well tolerated by all patients. Seven patients received systemic antibiotics in addition to influenza treatment (Table 2). Eight patients responded to the treatment and recovered clinically in 3–4 days. An autologous HSCT patient, a 57-year-old female with multiple myeloma, required intensive care and she died due to severe sepsis and pneumonia.

Discussion

Before WHO declared a pandemic due to the novel virus, in our region respiratory syncytial virus was isolated frequently in children and adenovirus in adults. After WHO raised the pandemic alert level to the highest phase on 11 June 2009, in patients with acute respiratory tract infection the same pathogen was also isolated up to the last week of October 2009. The clinical spectrum of illness due to H1N1 infection in patients with cancer is still being defined; several studies have reported cases of severe disease among patients with cancer and HSCT recipients as well as development of oseltamivir resistance among immunosuppressed individuals, but it remains unclear whether these are representative of the entire population of cancer patients and HSCT recipients (2–6).

Our data show that subjective findings like headache and fatigue often seen in influenza infections were not the dominant clinical presentation in these patients. It is remarkable that nausea and diarrhea, which are prominent findings in H1N1 infections, have also rarely been detected in these patients. Similar to our patients, the first symptom is fever and cough in children with haematologic malignancy (7–9). Ljungman et al. (10) reported data on 286 HSCT (222 had undergone allogeneic and 64 autologous) recipients with pandemic H1N1 infection. Their data showed that the most common symptoms of H1N1 infection were fever and cough. We found no article about H1N1 infections in cancer patients. However, these patients arrive with an attack of fever assessed as febrile neutropenia directly, and this type of viral infection in febrile neutropenic episodes does not make much sense.

Being familiar with the radiological findings of the chest in patients with H1N1 infection is important for early diagnosis and effective treatment planning in these patients. Although chest radiographic findings of H1N1 are described thoroughly in the literature, there are few reports on thorax computed tomography (CT) findings in patients with presumed or confirmed H1N1 infection (11).

Radiological findings were obtained in 5 patients, but the possibility of infiltration of the lungs not appearing on chest X-rays should be kept in mind in neutropenic patients. Chest X-ray findings of our cases were similar to those of cases in the literature. Because of similar radiological findings, some patients with a prior diagnosis of fungal infection were given antifungal treatment in these studies (10–13).

Table 2. Concomitant infections, co-morbid disease status, and treatment of patients.

Patient no.	Treatment	Concurrent infection	Co-morbid conditions	Active smokers	Radiographic findings
1	Chemotherapy	Fungal pneumonia			Ground glass infiltrates
2	Chemotherapy		Type 2 DM		Ground glass infiltrates
3	Corticosteroid	*Staphylococcus aureus*	Type 2 DM		
4	APSCT				Interstitial infiltrates
5	APSCT				
6	APSCT	*E. coli*			
7	Corticosteroid				
8	No treatment			Yes	Interstitial infiltrates
9	Chemotherapy	CMV		Yes	Interstitial infiltrates

APSCT: Autologous preripheral stem cell transplantation

Most of our patients recovered with intensive support and anti-viral treatment. However, 1 patient, a 57-year-old with severe pneumonia, died during the clinical course. Ljungman et al. (10) found lymphopenia and age to be risk factors for pneumonia, mechanical ventilation, and death. Lymphopenia has been identified as a risk factor for low respiratory tract disease, both for influenza and for infections with other respiratory viruses (14).

Vaccination is recommended by health authorities and scientific organisations (15). Despite abnormalities in immune function, vaccination has been shown to be effective in HSCT patients and in those receiving chemotherapy or corticosteroid therapy (16).

Associating unaccountable high fever with the currently seen infections and early sampling can be life saving and clinicians should be aware of potential pandemic influenza H1N1 in patients with haematological disorders.

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