H1N1 Influenza in an Irish Population: Patterns of Chest Radiograph Abnormality in Patients Testing Positive

Abstract:
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Abstract
The winter of 2010/2011 saw a second peak in the number of H1N1 cases detected in Ireland. The purpose of this study was to investigate the radiological characteristics of patients diagnosed during this period. A retrospective analysis of these cases was performed. Chest radiographs were classified as normal or abnormal. A total of 37 patients were included. Of these, 22 (59%) of chest radiographs were abnormal and 15 (41%) were normal. In the 7 paediatric patients, 4 (57%) had a perihilar distribution of disease, 2 (28%) had peripherally based disease with 1 (14%) having a mixed distribution. A series of radiographs was available for 9 patients, 6 of these showed a radiographic deterioration from the initial study. The majority of chest radiographs of patients with confirmed H1N1 infection will be abnormal. In children, disease is more likely to be perihilar in distribution. Chest radiography is an important initial investigation in patients with H1N1 infection and is useful to track progression of disease in the subset of patients requiring hospitalization for severe disease.

Introduction
Novel influenza A (H1N1, swine-origin influenza A; S-OIV), is an acute, highly contagious viral respiratory tract infection. It was first identified in Mexico in March 2009. Cases of infection spread rapidly, to the point where the world health organisation (WHO) raised its alert status regarding H1N1 to phase 6 (pandemic phase). The WHO in August 2010 declared that the spread of H1N1 infection had entered the post pandemic period but that localised outbreaks were likely to occur. In the winter of 2010/2011 there was a further spike in the number of H1N1 cases detected in Ireland. The clinical course of H1N1 infection is variable. It is frequently a mild illness which is managed in the primary care setting but can be a more severe infection which can lead to severe respiratory compromise and death. The radiographic findings in patients with H1N1 infection are similarly variable. Many patients have normal radiographs. In those with abnormal studies, the findings differ both in the distribution and pattern of disease. This study aimed to investigate the radiographic findings in a population of patients investigated in an Irish hospital during the second wave of H1N1 infection.

Methods
Cases of H1N1 influenza diagnosed between 3 December 2010 and 26th January 2011 were indentified from an institutional database maintained in the department of clinical microbiology. H1N1 positivity was determined using a PCR for H1N1 RNA conducted in the National Virus Reference Laboratory. The radiological records of patients detected using this method were searched using a picture archiving and communication system (PACS) (Siemens) and a radiology information system (RIS) (Keogh). Patients who had at least one chest radiograph as part of their investigation were included in the study group. Chest radiographs were performed using computed radiography equipment. Radiographs were retrospectively reviewed by a single consultant radiologist using a PACS system. The radiographs were classified into normal or abnormal. Within the abnormal category, the pattern of disease was classified as either airspace, interstitial or nodular. The location of disease was classified as being predominantly upper or lower zone and predominantly perihilar or peripheral. The number of lung field zones involved by disease was counted (up to a maximum of 6). The radiograph was also examined for the presence of lobar or non-lobar atelectasis, an effusion or lymphadenopathy.

Results
Between 3rd December 2010 and 26th January 2011, 37 patients who tested positive for H1N1 had chest radiographs performed in our institution. 30 (81.1%) were adults and 7 (18.9%) were children. 17 (46%) were male and 20 (54%) were female. The mean subject age was 36, with an age range of 6 month to 83 years. 20 (59%) chest radiographs were abnormal and 17 (41%) were normal. Regarding pattern of disease in subjects with abnormal radiographs, 16 (80%) had airspace disease, 2 (10%) had interstitial disease and 2 (10%) had mixed airspace and interstitial disease. Overall 2 (5.4%) patients had a pleural effusion and 4 (10.8%) had radiographically identifiable mediastinal adenopathy. Of the abnormal cases, 13 (65%) had lower zone predominant disease, 4 (20%) had upper zone predominant disease and 3 (15%) had mixed distribution. 11 (55%) had peripheral disease, 5 (25%) had a perihilar pattern of disease while 4 (20%) had a mixed pattern of both peripheral and perihilar disease.

The mean number of zones involved was 2 (range 0 zones to 6 zones). 13 (35.1%) involved either 1 or 2 zones while 3 (8.1%) involved all 6 zones. A series of radiographs was available for 9 patients. 6 of these showed a radiographic deterioration from the initial study. In those that deteriorated, there was a mean of 7 days to the worst radiograph. Of these cases, 3 (50%) demonstrated an increase in the number of zones affected, while in the other half there was...
worsening on the degree of disease in the originally existing zones. Overall there was an increase in the number of zones by a mean of 1.8. All of those who deteriorated in terms of the number of zones demonstrated a progression of diffuse disease involving all 6 zones. 2 cases were followed to radiographic resolution, while the remainder were followed clinically. In the 7 paediatric patients, 4 (57%) had a perihilar distribution of disease, 2 (28%) had peripherally based disease with 1(14%) having a mixed distribution. The average number of zones involved was 1.4. No effusion was seen in a child. 2 (29%) demonstrated evidence of adenopathy.

Figure 1: Chest radiograph of a 70 year old male diagnosed with H1N1. Airspace involvement is seen bilaterally but predominantly in the right upper and mid-zone where confluent disease is seen.

Discussion

Influenza is a viral infection which classically causes seasonal outbreaks of an acute respiratory illness. It is an RNA virus which is a member of the orthomyxovirus family. Subtypes A, B and C exist, but infection is most commonly caused by influenza A or B. Influenza A, in particular has a propensity to mutate, thus creating several different varieties of influenza A. These sub-classifications depend on the particular combination of hemagglutinin (HA) and neuraminidase (NA) subtypes within the virus. Novel influenza A is termed H1N1, if spread by respiratory droplet, and the most common symptoms are fever, cough, sore throat and dyspnoea. The incubation period is between 1 and 7 days, and patients are deemed infectious from 1 day prior to symptom onset to 7 days after symptom onset.

Epidemiological studies of H1N1 suggested that the age demographics of those affected would be significantly different than those affected by seasonal influenza (which typically affects the very young and old). In their initial series of patients from Mexico, Perez-Padilla et al found that 90% of patients were less than 52 years old affected will be middle aged or young adults, and the majority will have a benign clinical course, those that are most severely affected tend to be the very young, very old, or those with pre-morbid conditions.

Most patients with suspected or confirmed H1N1 infection are likely to be initially seen and investigated in a primary care setting, and then transferred for management if necessary. The chest radiograph is an important initial investigation in the work up of these patients. We aimed, to assess the chest radiography findings in a group of Irish patients with confirmed H1N1 referred from both primary care practices and those seen in an acute hospital setting. The results of our study demonstrate that the Irish population of patients infected with H1N1 have broadly similar radiographic appearances to other, international, patient populations. Other authors have shown that between 45%-77% of patients will have a normal initial chest radiograph (41% in our population). The trend for lung infiltrates to be predominantly peripherally based, although slightly lower in our study, also conforms to worldwide experience. 65% of patients had this pattern of disease compared to between 71%- 85% in previously published reports.

Furthermore, the predominance of an airspace pattern of disease in our study group also tallies with prior experience. Our findings suggest that development of clinically significant pleural effusion is not a common association with H1N1 infection. In total 2 (5.4%) of our patients showed radiographic evidence of an effusion. Neither of these was large enough to warrant drainage. It must be stressed that the sensitivity of plain radiography is somewhat limited in this regard and that small effusions could be missed (the likely-hood of such an effusion being clinically significant in this setting is small however). Of 6 patients in whom follow-up radiographs were available, there was an average of 7 days to the development of the worst study. This figure masks a subset of 2 patients who had a rapidly deteriorating radiological picture, worsening over 1 and 2 days respectively, highlighting that there is a small group of patients in whom H1N1 infection can be swiftly progressive, with both aggressive clinical and radiological features. Both of these patients were managed in an intensive care unit with a clinical adult respiratory distress syndrome picture, and radiographic evidence of diffuse bilateral airspace disease. Another patient developed a similar pattern of disease but over a longer period of time (10 days).

The 7 children included in our study formed a small subset. Of note, all the children investigated had an abnormal radiograph. They had a much higher proportion of perihilar predominant disease than the adult group, 22 (57%) of children demonstrating this pattern compared with 5 (25%) of adults. Adenopathy was almost twice as common in children as in adults (29% versus 15%). None of the children had the rapidly progressive radiological course described above. Two patients were referred from a primary care setting. The remainder were admitted acutely via the accident and emergency department. Both patients from a primary care setting had abnormal radiographs. Both radiographs exhibited predominantly airspace disease. One patient was admitted to the ICU for a duration of six days. Follow-up radiograph of this patient three weeks after presentation demonstrated complete resolution. The significance of normal chest radiography in the setting of suspected H1N1 infection needs close clinical correlation. It has been noted that those infected with H1N1 may display significant hypoxia even in the setting of a normal radiograph. This chest radiograph should not be falsely reassuring. Conversely the combination of a normal radiograph and a clinically stable patient could help support a decision to manage a patient in the community.

In conclusion, the majority of patients with confirmed H1N1 infection sent for chest radiography will have an abnormal finding. However, the radiological picture, worsening over 1 and 2 days respectively, highlighting that there is a small group of patients in whom H1N1 infection can be swiftly progressive, with both aggressive clinical and radiological features. Both of these patients were managed in an intensive care unit with a clinical adult respiratory distress syndrome picture, and radiographic evidence of diffuse bilateral airspace disease. Another patient developed a similar pattern of disease but over a longer period of time (10 days). Thus a normal radiograph should not be falsely reassuring. Conversely the combination of a normal radiograph and a clinically stable patient could help support a decision to manage a patient in the community.

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