LUNG DISORDERS IN PATIENTS WITH SWINE-ORIGIN INFLUENZA A (H1N1) VIRAL INFECTION: THORACIC FINDINGS

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<th>Lung disorders in patients with Swine-origin influenza A (H1N1) viral infection: thoracic findings</th>
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Objective

The goal of this study was to present the main computed tomography findings identified in patients with pneumonia caused by infection with influenza A (H1N1).
Introduction

Pneumonia is one of the most common complications of H1N1 influenza and results in the majority of fatal outcomes in the world. The spectrum of the pandemic influenza A (H1N1) virus infection ranges between non-febrile mild upper respiratory tract disease to severe and even fatal pneumonia. Infections with the swine-origin influenza A (H1N1) virus emerged in Mexico in April 2009, and spread rapidly around the world. For the majority of patients with this infection, chest radiograph provides adequate imaging information. However, computed tomography (CT), particularly high-resolution CT (HRCT), is an important tool when the clinical suspicion of pneumonia is high, and the radiographic findings are normal or questionable (Figure 1). CT is also helpful in assessing complications, and providing evidence of mixed pulmonary infections in patients that are not responding to appropriate therapy.
Introduction

Fig. 1. 32-year-old male patient with H1N1 pneumonia.

(A) Chest radiography shows normal lungs.

(B) CT performed on the same day shows mild ground-glass opacities in both lungs that predominates in the lower lobes.
Clinical and laboratory findings

The most common clinical findings for influenza A (H1N1) virus infection are fever, cough, dyspnea, myalgia, and headache. Most cases are mild and self-limited; however, a small percentage of individuals have a severe course that may result in respiratory failure and death. Some publications also have shown that the levels of serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), and lactate dehydrogenase (LDH) were significantly higher in clinically more severe patients, and a combination of clinical and HRCT indicators would be useful in predicting the clinical outcome of pandemic H1N1 pneumonia.

Secondary bacterial pneumonia usually presents a pattern consistent with bronchopneumonia, and the most common bacteria found in the autopsy included *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Staphylococcus aureus*, *Streptococcus mitis*, *Haemophilus influenzae*, and *Acinetobacter baumannii*. 
Pathological findings

Histologically, the influenza virus proliferates on the surface of respiratory mucosa and is characterized by destruction and desquamation of the pseudocolumnar and columnar epithelia.

The most frequent findings include classic exudative diffuse alveolar damage (DAD) with alveolar and interstitial edema, alveolar fibrinous exudate with hyaline membranes and reactive pneumocytes; severe necrotizing bronchiolitis characterized by extensive necrosis of the bronchiolar wall and dense neutrophilic infiltrate within the bronchiolar lumen; and exudative DAD with an intense hemorrhagic component. In the latter stages, fibrosing and organizing DAD may be seen.
CT parenchymal findings

The predominant CT findings are ground-glass opacities (GGO) (Figure 2 and 3), areas of consolidation, or a mixed pattern of GGO and areas of consolidation.

Fig. 2. 60-year-old female patient with dyspnea and cough. HRCT obtained 4 days after the onset of the symptoms showing bilateral and peripheral ground-glass opacities.
CT parenchymal findings

Fig. 3. 59-year-old female with H1N1 pneumonia. HRCT obtained 7 days after the onset of symptoms showing bilateral and peripheral ground-glass opacities.
CT parenchymal findings

The abnormalities are frequently bilateral, and may have a peripheral subpleural (Figure 3), peribronchovascular (Figures 4 and 5), lobular (Figure 6) or a random distribution.

Fig. 3. 29-year-old male patient with H1N1 pneumonia. CT shows bilateral and predominant peripheral focal ground-glass opacities in both lungs.
CT parenchymal findings

Fig. 4. 31-year-old female patient with H1N1 pneumonia. Consolidations with a peribronchovascular distribution are seen in the right lung base. The left lung is normal.
CT parenchymal findings

Fig. 5. 44-year-old male patient with H1N1 pneumonia. CT scans at the carina level (A) and the main bronchi level (B) show bilateral round consolidations with a peribronchovascular distribution. Also seen is a small bilateral pleural effusion (arrowheads).
**CT parenchymal findings**

Fig. 6. 35-year-old female patient with H1N1 pneumonia. CT axial scan (A), coronal reformatted image (B), and sagittal reformatted image (C) show bilateral patchy areas of ground-glass opacities predominating in the upper lobes in a lobular pattern (black arrows).
CT parenchymal findings

Parenchymal abnormalities may also be diffuse without zonal predominance or, more rarely, unilateral (Figure 7).

Fig. 7. 34-year-old male patient with H1N1 pneumonia. Extensive ground-glass opacities is seen in the left upper lobe with air bronchograms.
Patients with widespread consolidations have a more severe clinical course (Figure 8 and 9). Although none of these patterns is specific of the condition, the main patterns of disease that would be most suggestive of H1N1 are scattered lung consolidations and/or GGO in a peribronchovascular or subpleural distribution.

**Fig. 8.** 25-year-old female patient with H1N1 pneumonia. (A) CT shows bilateral consolidations predominantly involving the upper lung regions. (B) Coronal reconstruction demonstrates that the consolidations are diffuse but predominate in the upper lung portions. Also seen is a bilateral pleural effusion (arrowheads).
CT parenchymal findings

Fig. 9. 34-year old female patient with severe H1N1 pneumonia. HRCT obtained 8 days after the onset of symptoms showing consolidation and ground-glass opacities predominantly involving the peripheral regions (A). In (B), a coronal reconstruction better demonstrates the distribution of pulmonary lesions.
CT parenchymal findings

Although the presence of areas of consolidation with lobar distribution is somewhat different from the typical viral pneumonia pattern, and may be consistent with secondary bacterial pneumonia, this aspect may be seen in patients with influenza A (H1N1) without secondary bacterial infection (Figure 10). In these cases, a differential diagnosis should be based on clinical and laboratory findings.
CT parenchymal findings

Fig. 10. 4-year-old female immunocompetent patient with H1N1 pneumonia. CT shows consolidation with air bronchograms and ground-glass opacities in the middle lobe.
Scattered interlobular septal thickening associated with GGO has been reported in some cases (Figure 11); and a crazy-paving pattern has been reported in patients with more severe disease progression (Figure 12).

**Fig. 11.** 62-year-old male patient with H1N1 pneumonia. (A) Axial CT slice of the right lung shows smooth septal thickening in the middle lobe (arrowheads). (B) Axial CT slice of the lower lobes shows a crazy-paving pattern (arrows) in the middle lobe, consolidations in the right lower lobe and GGO on the left side.
CT parenchymal findings

Fig. 12. 25-year-old male patient with H1N1 pneumonia. CT slice at the level of the upper lobes demonstrates patchy areas of ground-glass opacities with smooth septal thickening (crazy-paving pattern). Note also bilateral posterior upper lobes consolidations.
CT parenchymal findings

Another uncommon parenchymal finding is the halo sign, which is GGO surrounding a consolidation, nodule, or mass (Figure 13).

Fig. 13. 64-year-old female immunocompetent patient with H1N1 pneumonia. CT at the level of the lower lobes shows a round mass in the right lower lobe with a discrete ground-glass halo (halo sign).
CT parenchymal findings

Although most reports do not describe findings of small airway disease that are commonly associated with viral pulmonary infection, Elicker et al. reported that CT features associated with either large or small airways, such as thickening/dilatation, centrilobular nodules (Figure 14 and 15), and tree-in-bud opacities were frequent in their series of immunocompromised patients.

Fig. 14 62-year-old male immunocompetent patient with H1N1 pneumonia. CT with coronal (A) and sagittal (B) reconstructions shows multiple small centrilobular lung nodules, mainly in the middle and right lower lobe, with areas of confluence and branching structures (tree-in-bud pattern), consistent with peripheral airway disease.
Figure 15: 52-year-old male with cough and dyspnea for 2 weeks. (A)- Minimum intensity projection (MinIP) with coronal reconstruction shows scattered areas of ground-glass opacities and consolidation. (B) - Axial images show a peripheral consolidation and (C) confluent centrilobular nodules in the right lower lobe.
CT parenchymal findings

Little information is available in the literature regarding CT aspects during the recovery period of H1N1 infection. Often, multifocal areas of consolidation develop during follow-up. In this situation, the differential diagnosis with secondary bacterial infection is very difficult. However, in most of the cases the pulmonary opacities secondary to H1N1 infection regress during convalescence. Even in these cases with benign evolution, the consolidations may occasionally progress to linear opacities (parenchymal bands), that probably represent organizing pneumonia (Figures 16 and 17), or the patient develop air trapping (Figure 18), which was clinically and radiologically suggestive of bronchiolitis.
CT parenchymal findings

Fig. 16. 30-year-old female patient with H1N1 pneumonia. CT performed one month after the onset of symptoms demonstrates bilateral linear opacities (parenchymal bands) in the lower lobes.

Fig. 17. 42-year-old female patient with H1N1 pneumonia. CT performed two weeks after the onset of symptoms shows consolidations and perilobular thickening in both lower lobes consistent with organizing pneumonia.
CT parenchymal findings

Fig. 18. 38-year-old female patient with H1N1 pneumonia. CT slices on end-inspiration HRCT performed two months after the onset of symptoms show very subtle mosaic attenuation pattern in the left lower lobe. (B) A full expiration scan at the same level highlights the irregular area of air trapping in the left lower lobe.
CT parenchymal findings

After the first week, the organizing phase of DAD predominates and is characterized by organizing fibroblastic tissue and fibrosis. Here is a difference between patients with evidence of fibrosis at thin-section CT and those without in terms of rate of mechanical ventilation therapy, cumulative prednisolone-equivalent dose, maximum levels of AST, LDH, CK, and peak radiographic opacification during treatment, which suggests that fibrosis is more likely to develop in patients with more severe disease (Figure 19).
Figure 19: A 69-year-old woman diagnosed with novel influenza A pneumonia.

Follow-up inspiration thin-section CT images obtained 4 months after the onset of clinical symptoms shows scattered areas of pulmonary fibrosis, with architectural distortion, parenchymal bands and a mosaic pattern.
Pulmonary emboli were identified on contrast-enhanced CT of H1N1-infected patients. Parenchymal damage may predispose to the formation of cysts, which may rupture causing extra-alveolar air collection. Free air may dissect and rupture through the visceral pleura, causing pneumothorax, or may track centrally into the hila and mediastinum, causing pneumomediastinum (Figure 20). Small unilateral or bilateral pleural effusion has been reported. However, in most studies, chest CT with soft-tissue windows displayed several notable negative findings, including the absence of lymphadenopathy, and pleural or pericardial effusions.

Fig. 20. 30-year-old female patient with H1N1 pneumonia. Axial CT images (lung window setting) show bilateral patchy areas of consolidation and ground-glass opacities. Pneumomediastinum, small pneumothorax (arrow), and subcutaneous emphysema are also seen.
References


References

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