

## Case Report

# Swine flu fibrosis: Regressive or progressive?

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## ABSTRACT

Swine flu influenza had spread the world over in 2009. The main pathology was bilateral pneumonia. Majority of these cases recovered from pneumonia fully. Though in some cases, pulmonary fibrosis was reported as a sequel. However, long-term progression of such pulmonary fibrosis is uncertain. We are hereby reporting two cases of swine flu that showed residual pulmonary fibrosis. The clinical and laboratory parameters were also recorded. In both the cases, radiological shadows and spirometric values did not show deterioration. We conclude that swine flu pulmonary fibrosis is not a progressive condition.

**KEY WORDS:** Interstitial lung disease, pulmonary fibrosis, swine flu

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## INTRODUCTION

During 2009 swine flu pandemic, million people got affected with H1N1. Between April 2009 and April 2010 a large number of deaths were reported. The disease varied from mild influenza-like illness to severe respiratory insufficiency manifesting as acute respiratory distress syndrome (ARDS) requiring ventilatory support.<sup>[1]</sup> Most of these cases recovered without leaving any residual illness in lungs but in few cases, pulmonary fibrosis became evident. A follow-up case study of 65 subjects of swine flu showed the evidence of ground glass opacity and reduced diffusion after 3 months of infection.<sup>[2]</sup> Another study showed that 10% of the swine flu patients had pulmonary fibrosis.<sup>[3]</sup> However, prognosis of such fibrosis is still not clear. In majority of interstitial lung disease (ILD) patients, fibrosis shows a progressive pattern. Until date, we do not have sufficient evidence to show the pattern of progression of post swine flu pulmonary fibrosis. Retrospectively, we are presenting 5 years follow-up data of two patients with postswine flu fibrosis.

## CASE REPORTS

### Case 1

She was 25 years aged female with a short history of a cough and shortness of breath of 2 days duration. She was admitted in the hospital and diagnosed to have swine flu pneumonia in 2010. She showed a positive result of H1N1 on polymerase chain reaction (PCR) testing of throat swab sample. The details of clinical presentation were published in an earlier publication of Lung India.<sup>[4]</sup> She continued to have complaints of breathlessness on exertion. She was put on a maintenance dose of 5 mg prednisolone. Attempts were made to stop prednisolone, but her symptoms deteriorated, therefore, she was continued on this dose for 3 years. Then, she developed fever, cough, and worsening breathlessness. Sputum examination showed acid-fast bacilli. We could not stop steroids, and she was put on a daily regimen of antitubercular treatment. She recovered from her infection, but the problem of breathlessness still persists.

Initial high-resolution computed tomography scan (HRCT) in January 2010 showed bilateral areas of

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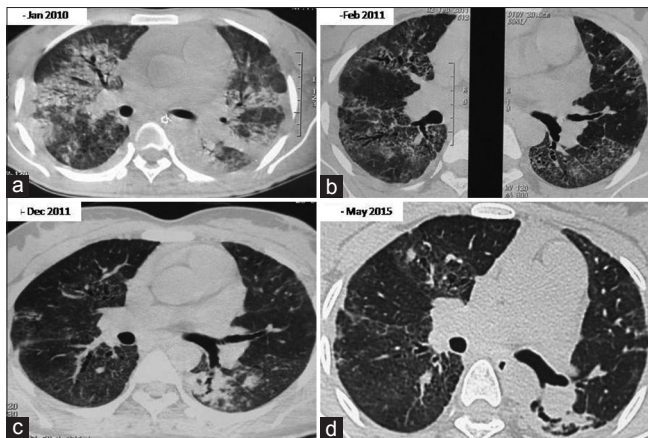
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ground-glass haziness and consolidation with air bronchogram. In subsequent CT scans, there was evidence of interlobular septal thickening, honeycombing, and traction bronchiectasis in areas that initially showed consolidation [Figure 1]. In December 2011, CT scan showed an area of consolidation in the left posterior part. In CT scan of May 2015, this area was also replaced by fibrosed part along with a high-density area. Left lower lobe showed calcification. Serial evaluation of these HRCT scans showed a progressive decrease in the area of reticulation and increase in normal lung parenchyma [Figure 1a-d].

Spirometry showed vital capacity 1.09 L 3 months after discharge from the hospital in 2010. It showed improvement and became 1.25 in 2011. Thereafter, it remained in the range of 1.11–1.5 L [Figure 2]. Six min walk distance increased from 342 m to 468 m.

## Case 2

A 59-year-old male patient presented with fever and bilateral pneumonia. He was admitted and diagnosed with swine flu through H1N1 PCR testing of throat swab sample. With tablet oseltamivir (75 mg orally twice daily for 15 days) and supportive therapy he recovered and got discharged from the hospital on the 8<sup>th</sup> day. However, he continued with a complaint of exertional dyspnea for the next 3 months, and his skiagram chest showed bilateral shadows. He was a nonsmoker and nonalcoholic with no significant medication history. There was no history of significant exposure to visible smoky or dusty environment.



**Figure 1:** HRCT images of Case 1. (a) January 2010 high-resolution computed tomography scan showing areas of ground-glass haziness and consolidation with evidence of air bronchogram. Ryle's tube can be seen *in situ*. (b) February 2011 high-resolution computed tomography scan showing evidence of bilateral involvement of lung. Ground glass haziness in many areas has been replaced by reticulonodular shadows, peripheral honeycombing, and traction bronchiectasis. (c) December 2011 high-resolution computed tomography scan showing an area of consolidation in the left posterior part which was diagnosed as a tubercular patch. Reticulonodular lesions and areas of traction bronchiectasis appear to be resolving. (d) May 2015 HRCT scan showing patches of minimal ground glass haziness and residual fibrosis in the area of consolidation that had significantly diminished in size than the previous scans

Physical examination was normal except for the presence of inspiratory crept heard in left infrascapular area. Chest radiograph showed increased reticular markings in the bilateral lower zone.

HRCT scan performed 6 months later in March 2011 showed bilateral thickened interstitial septal thickening more marked on the right side [Figure 3]. The patient was diagnosed as a case of postviral interstitial fibrosis. The patient was advised chest physiotherapy exercises. Gradually, his exertional dyspnoea improved in the 1-year post swine flu. In due course of time, he became symptom-free.

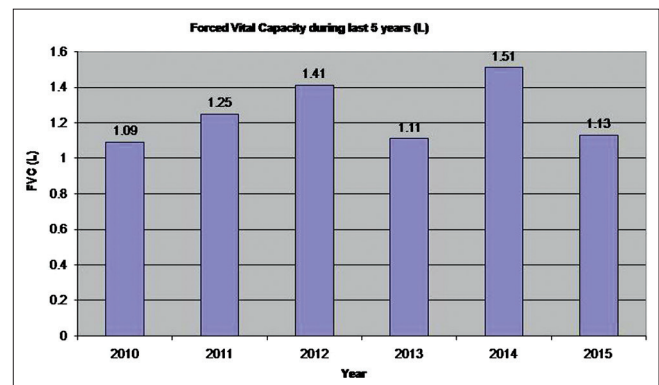
His forced vital capacity, diffusion test, and KCO tests are shown in Figure 4. These indices did not show a significant reduction. A repeat HRCT scan in December 2011 showed reticular shadows in lower zones more marked on the right side. The most recent HRCT scan done in February 2015 showed subtle bilateral reticular shadows with no signs of progression of fibrosis [Figure 3].

## DISCUSSION

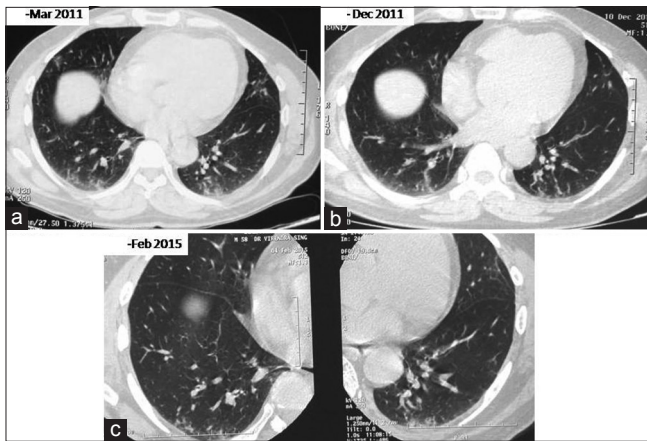
A large number of swine flu patients present with ARDS. The majority of these patients have shown complete recovery. However, in a few cases, pulmonary fibrosis similar to ILD has been reported.<sup>[3]</sup> Since most of diseases included in ILD group mainly the idiopathic interstitial pneumonias (IIPs) usually show progressive pulmonary fibrosis, therefore, it is important to find out the progress of the swine flu-related fibrosis over time.

Our patients continued to have evidence of ILD in the form of ground glass and/or reticular opacities after the subsidence of active disease. On the other hand, serial HRCT scans and pulmonary function tests showed no progression of ILD.

We could find a couple of follow-up studies in patients with swine flu. Toufen *et al.* observed 4 cases of swine flu ARDS for 6 months.<sup>[5]</sup> They found that these patients had a remarkable recovery at 6 months despite having a very



**Figure 2:** Bar diagram showing forced vital capacity in the span of 5 years for case 1

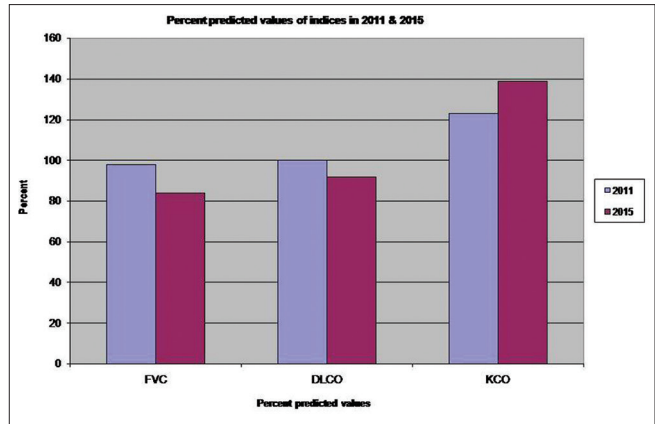


**Figure 3:** HRCT computed tomography images of case 2. (a) March 2011 high-resolution computed tomography showing bilateral peripheral thickened interlobular septa and ground glass haziness (more on the right side). (b) December 2011 - HRCT shows evidence of resolving bilateral ground glass haziness and interstitial thickening. (c) February 2015 - HRCT reveals grossly reduced interstitial thickening when compared to the first scan of March 2011

severe ARDS in the beginning. Another study was done by Li *et al.*, observed the serial HRCT images of 70 patients with swine flu.<sup>[6]</sup> They concluded that initially ground glass opacities appeared on CT. They changed to fibrosis that peaked at 3 weeks of illness and later slowly resolved. Mineo *et al.* followed their 20 patients for over 1 year.<sup>[3]</sup> They reported peripheral fibrosis in 10% of patients. One of the two patients also showed radiological regression of the fibrosis.

It is also postulated that the pathological mechanism underlying fibrosis in H1N1 is different in comparison to ILD. It is probably due to the organizing pneumonia being the underlying process.<sup>[7-11]</sup> Our cases had developed ARDS as a complication of H1N1 infection. ARDS is associated with three phases that include an exudative, proliferative, and fibrotic stage. The latter two stages occur after the initial 7 days of insult and are primarily involved in the repair. The neutrophilic infiltrates subside, and there is an influx of fibroblasts and lying down of collagen in the lung. In many cases, the resolution of neutrophils is not accompanied by fibrosis.<sup>[12]</sup> Larger studies need to be planned to analyze the difference of post swine flu pulmonary fibrosis from residual fibrosis in cases of ARDS due to other causes.

However, we have not come across studies observing the long-term pattern of swine flu associated fibrosis. Our patients were followed-up for 5 years. These patients did not show the progression of the disease both radiologically and on lung function testing. Inference can be drawn that the patients of swine flu may develop an IIP like fibrosis, but that remains static or resolves over a period of time.



**Figure 4:** Bar diagram showing the percent predicted values of spirometric parameters for years 2011 and 2015 for case 2

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### Conflicts of interest

There are no conflicts of interest.

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