

## POST MORTEM FINDINGS IN FATAL H1N1 INFECTION

Maya Vasaikar<sup>1</sup>, Shivraj Kanthikar<sup>1</sup>, Rajiv Parate<sup>1</sup>, Sisodia SM<sup>2</sup>, Smita Bora<sup>1</sup><sup>1</sup> Department of Pathology, SBH Govt. Medical College, Dhule, Maharashtra, India<sup>2</sup> SBH Govt. Medical College, Dhule, Maharashtra, India

Correspondence to: Maya Vasaikar (skanthikar@gmail.com)

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## ABSTRACT

**Background:** A novel H1N1 influenza virus emerged in April 2009, and rapidly reached pandemic proportion. In India since May 2009 to August 2010, India has reported nearly 37,000 H1N1 cases and 1833 deaths.

**Aims & Objective:** The present study was undertaken to find the cause of death and various histopathological changes which is responsible for high mortality.

**Materials and Methods:** This is a retrospective study of five patients who died due to H1N1. Tissues for histopathological examination were received in Pathology department. All the five patients were confirmed for Novel Influenza A (H1N1) by National Institute of Virology.

**Results:** Four Patients were female in ANC period and a single patient was a young adult. Histopathological examination revealed diffuse alveolar damage (DAD) in both the lungs along with necrotising bronchopneumonia, presence of thrombi in peripheral pulmonary vasculature along with involvement of large vessel was seen in all the cases. Haemophagocytosis was also seen in all the cases.

**Conclusion:** Thus the main cause of death was due to diffuse alveolar damage (DAD). Thus DAD associated with other complication in lungs and Haemophagocytosis in spleen should raise the suspicion of Influenza A (H1N1) virus.

**Key Words:** Influenza A (H1N1); Diffuse Alveolar Damage (DAD); Hemophagocytosis; Post Mortem Findings

## Introduction

The outbreak of Influenza may be either endemic or pandemic. The Pandemic has been associated with H1N1, H2N2 and H3N3. These subtypes harbour novel forms of haemagglutinin molecules.<sup>[1]</sup>

In 2009, The Centre for Disease Control and Prevention (CDC) reported for the first time virus infection with influenza A (H1N1) in two children.<sup>[2]</sup> A few months later the pandemic of H1N1 occurred which was confirmed by WHO on 11 June 2009.<sup>[3]</sup>

Although the world is in Post-pandemic phase. In India and New-Zealand where transmission still remains intense.

In India, new cases are still emerging. It is particularly seen in Maharashtra. Since May 2009 to 2014, India has reported nearly 37,000 H1N1 cases and 1833 deaths.<sup>[4]</sup>

There are many studies which have discussed the morphological, histopathological and cause of death in fatal H1N1 infection. Still more studies are needed to study the pathogenesis, morphological changes in various organs so as to help the clinicians to give appropriate treatment.

## Materials and Methods

This was a retrospective study of five patients who had died due to H1N1 infection. Tissues were sent to Department of Pathology for histopathological examination. Swabs were sent to National Institute of Virology at Pune (Maharashtra) during ante mortem period. All the five cases were positive for H1N1 virus by PCR done by National Institute of Virology. The reports were received after the autopsy was conducted. Lungs, Heart, Liver, Spleen, Kidneys, Uterus and Cerebrum were received. Gross and histopathological examinations were done on all the organs. (Table 1. Clinical histories of the five patients).

Table-1: Clinical histories of the patients

Sr. No.	Patient	Clinical Manifestation	Year
1.	24 yrs. Female ANC 9 months amenorrhea IUD	Breathlessness, High grade fever	2009
2.	22yrs Female ANC 9 months' amenorrhea.	Breathlessness, High grade fever	2009
3.	20 yrs. Male.	Breathlessness, High grade fever	2010
4.	26 yrs. Female ANC 7 month amenorrhea	Breathlessness, High grade fever	2010
5.	24 yrs. Female ANC 9 month amenorrhea.	Breathlessness, High grade fever	2013

## Results

**Gross Autopsy Findings:** All the cases showed

characteristic changes in the lungs. Both lungs were heavy on cut section the lungs were firm, consolidated and congested (Figure 1). Extensive patchy peripheral

haemorrhages were also noted. Rest all the organs were normal in gross appearance except Cerebrum which showed Petechial haemorrhages in two cases.



Figure-1: Gross Pieces of Lungs consolidated, congested

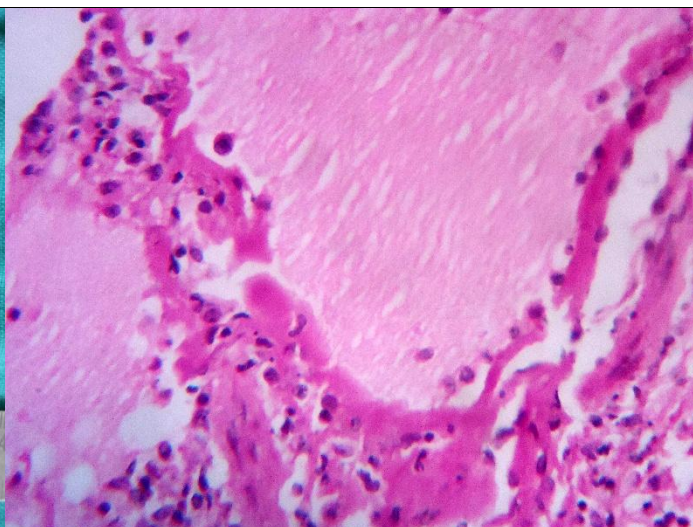


Figure-2: Alveolar walls with Hyaline membrane

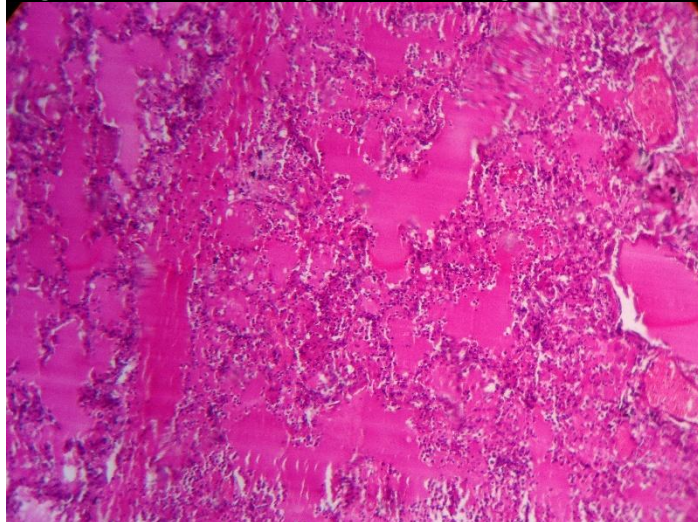


Figure-3: Thickened alveolar Septae

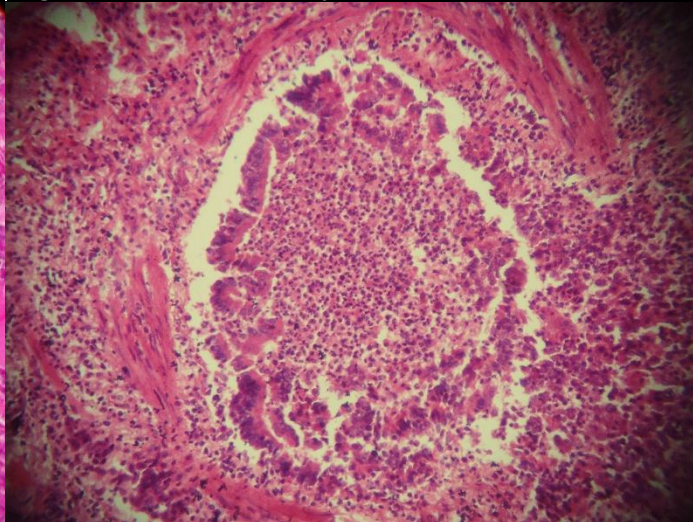


Figure-4: Patchy necrotising Bronchopneumonia and Lobar Pneumonia

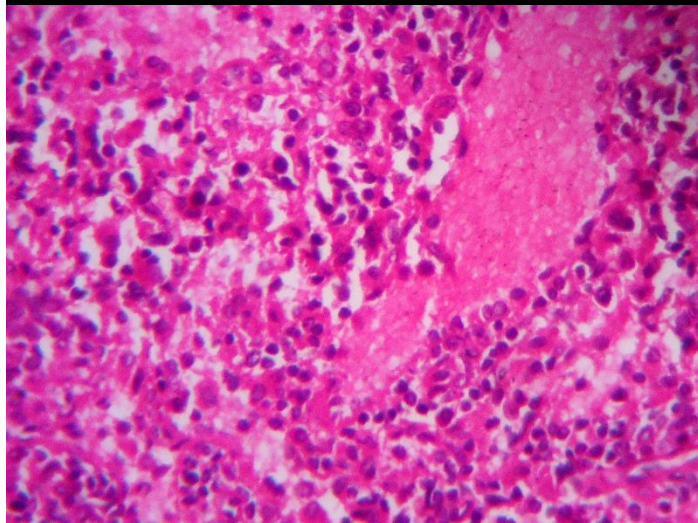


Figure-5: Walls of Bronchi filled with chronic inflammatory cells. (40X High Power)

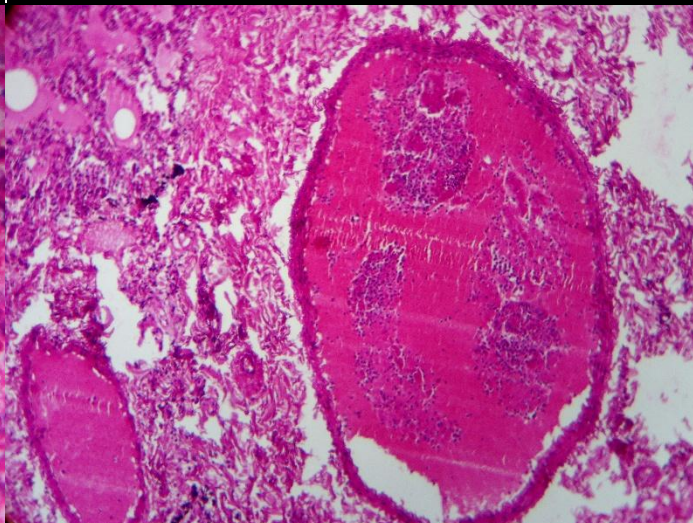


Figure-6: Thrombus in pulmonary vessel

**Microscopic Examination:** Diffuse alveolar damage was present in the lungs of all cases. Alveoli showed pulmonary oedema. The alveolar walls were lined with hyaline membrane in all the cases (Figure 2). Alveolar septae were diffusely thickened with chronic inflammatory cells (Figure 3). Patchy necrotizing Bronchopneumonia and Lobar Pneumonia was present (Figure 4). The wall of the bronchi was infiltrated with chronic inflammatory cells (Figure 5). Thrombus was seen in the large vessels (Figure 6) as well as in the peripheral pulmonary vasculature. Mild to moderate myocarditis in heart was seen in two cases. Prominent haemophagocytosis in spleen was present in all the cases. Cerebrum showed petechial haemorrhage. Liver, Kidneys were normal.

## Discussion

The pandemic (H1N1) 2009 influenza virus differs in its pathogenicity from Seasonal influenza in two key aspects. First majority of population has little or no pre-existing immunity to virus, impact of infection has been in a wider age range. Secondly virus infects lower respiratory tract and can cause rapidly progressive pneumonia. Pregnant woman, obese individual and young children are associated with increased risk in acquiring disease.<sup>[4]</sup> Four of our patients were pregnant female. Thus co-relating with the associated risk factor of influenza A (H1N1) virus.

The most common autopsy findings in our cases were seen in lungs. Both the lungs showed evidence of diffuse alveolar damage. However diffuse alveolar damage is a non-specific manifestation of acute lung injury seen in adult respiratory distress syndrome regardless of aetiology.<sup>[1]</sup>

Pathological changes studied in seasonal influenza virus are similar to pathological changes studied in pandemic influenza. No histopathological features have been identified that distinguish seasonal from pandemic influenza.<sup>[5,6]</sup> However, patchy necrotizing bronchopneumonia, pulmonary thrombo-emboli, bronchitis associated with diffuse alveolar damage should rise suspicious of Novel H1N1 infection.<sup>[7]</sup> Similarly presence of thrombi in peripheral pulmonary vasculature and thrombus of large vessels are unique to Novel H1N1 influenza were seen in all of our cases.<sup>[7]</sup>

Haemophagocytosis was observed in all of our cases indicating strong immune activation, such as viral infection and can be rapidly fatal.<sup>[8]</sup> Mild to moderate myocarditis was seen in two cases. While fulminant myocarditis was observed in 2009 worldwide. It was commonly observed in younger patient and was responsible for death of 1 patient.<sup>[9]</sup> The vascular phenomena that caused haemorrhage and thrombus in all the cases was not associated with decrease in platelet count or disruption of coagulation cascade.<sup>[10]</sup>

## Conclusion

Thus in a peripheral centre like us where the report of PCR was received after the autopsy was conducted, Diffuse alveolar damage, necrotising bronchopneumonia, bronchitis, peripheral pulmonary thrombus as well as thrombus in large vessels without decrease in platelet count should clinch the diagnosis of Influenza A H1N1. Thus post mortem studies is also very helpful to the clinicians to start appropriate treatment early. Hence the need of present study.

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