2009 Pandemic H1N1 Influenza: Previous Infection May Cause Severe And Fatal Cases?

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Abstract

Since 10 August 2010 we are in the post pandemic period of 2009 H1N1 influenza pandemics. However, it does not mean that the 2009 pandemic virus was eradicated, as past pandemics experiences revealed that a pandemic influenza virus will take on the behavior of a seasonal influenza and will continue to circulate.

An intriguing fact is that some severe and fatal cases occurred in previously healthy individuals. One of the possible risk factors in those cases is previous infection with another type of influenza virus. Therefore, this article addressed the issues that are related i.e. the role of innate and specific immune response and possible role of antibody dependent enhancement in H1N1 influenza, and evaluation of vaccination effect.

Introduction

The WHO has declared the pandemic level 5 for Swine origin H1N1 influenza in April 2009 [1], followed by the raise to level 6 in June 2009 [2]; thus, the first influenza pandemic in the 41 years since the pandemic of influenza A (H3N2) in 1968 [1]. Since then, the disease is called 2009 pandemic H1N1 influenza [3].

Further, since 10 August 2010 we are in the post pandemic period, according to the WHO. However, it does not mean that the 2009 pandemic virus was eradicated. Past pandemics experiences revealed that a pandemic influenza virus will take on the behavior of a seasonal influenza and will continue to circulate [4].

According to Morens et al, the 2009 pandemic H1N1 influenza virus is a fourth generation descendant of the 1918 pandemic H1N1 virus, whose “all-eight genes” are still present in human epidemic and swine epizootic H1N1 viruses, and some are present in the 2009 pandemic virus [5]. Therefore, in people that had previous epidemic H1N1 influenza virus infection, the immune system may still recognize the 2009 pandemic virus.

To date, little information is available about the pathogenesis of severe and fatal cases of the new pandemic influenza virus, though various risk factors for severe and fatal cases were reported. However, one third to half of the severe and fatal cases occurred in previously healthy individuals [2]. This fact is intriguing, and further search for risk factors are needed. One of the possible risk factor is previous infection with another type of influenza virus. Therefore, this article addressed the issues that are related i.e. the role of innate and specific immune response, the possible role of antibody dependent enhancement in H1N1 influenza, and evaluation of vaccination effects.

The role of innate immune response

Previous infection may be beneficial, but when it occurred many times they may cause continuous activation of the innate immune system that may trigger aberrant responses and upset the balance in immunity that lead to auto-reactivity [6], and therefore may cause a severe and fatal manifestation.

Most of the 2009 pandemic cases were of moderate severity, with most cases of severe and fatal infections happened in adults between 30 and 50 years, according to the WHO [2], and between 9-52 years (median 45 years) in Mexico [7], the age group that has better immune response and more chance to meet infected people in crowds and work places compared to the younger and older age group. Therefore, we can assume that the age group might have a certain degree of immunity from previous seasonal influenza infection that did not confer a protection against the pandemic influenza virus. Instead, in certain person with impaired immune response, upon repeated infection with other H1N1 virus, the innate immune response cause a boost in immune response that leads to an up regulation of cytokines and chemokines. This up regulation of cytokines and chemokines happened in patients with H5N1 influenza infection, SARS, and H1N1 human influenza virus infection that caused a major influenza pandemic in 1918 to 1919 [8], and therefore might also happen in severe and fatal 2009 pandemic influenza cases.

The role of specific immune response
Previous infection or exposure to seasonal influenza virus is believed to give protective immunity against pandemic influenza [9]. However, a recent study showed that there was no significant protection against the recent pandemic by seasonal vaccine in any age group [10], though another study reported reduction in the number of cases upon vaccination [11]. Further, in an epidemic that happened in 1947, vaccination against seasonal Influenza did not protect against human H1N1 influenza that had intra-sub-type re-assortment. Instead, the cases showed more severe manifestations. Though it was not concluded that the vaccine failure caused more severe disease [12], a possibility still exists that the two events are related, and antibody dependent enhancement phenomenon occurred in the severe diseases.

Antibody dependent enhancement

In dengue fever, when the immune response was primed by previous infection, secondary infection with other serotype may lead to a severe disease, as the antibody from the previous infection might be cross reactive, but instead of neutralizing the virus, the antibody is supposed to cause antibody dependent enhancement by facilitating virus entry into cells, and thus more severe disease [13]. Therefore, this phenomenon might also happen in severe cases of H1N1 influenza.

Evaluation of vaccination effect

One of the strategies to prevent the disease is the development of a vaccine to mitigate the morbidity and mortality [14]. This strategy is in line with the policy of WHO that has made an agreement with influenza vaccine manufacturers to begin the production of the pandemic vaccine as soon as the production of vaccine for seasonal influenza is completed [2]. However, whether unsuccessful vaccination may lead to severe cases is not known. However, if antibody dependent enhancement phenomenon also applies for H1N1 influenza, studies on previous vaccination effects and measurement of the level of antibody against H1N1 influenza virus in severe cases is needed to get more information concerning the pathogenesis of severe form of 2009 pandemic H1N1 influenza.

Conclusion

Studies are needed to know whether previous infection may cause imbalance in immune response that trigger auto reactivity, thus causes severe and fatal cases; and whether previous infection or vaccination with other type of influenza virus may cause severe and fatal cases due to antibody dependent enhancement.

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