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Perspectives

Human infection caused by avian influenza A (H10N5) virus

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On January 27, 2024, the National Health Commission of the People's Republic of China reported a confirmed case of human infection with a combination of avian influenza A (H10N5) virus and seasonal influenza A (H3N2) virus in Anhui Province.¹ Avian influenza infections are mostly caused by influenza viruses that normally circulate in various types of wild and domestic birds, but they rarely infect humans and other animal species. In surveillance conducted between January 2013 and June 2022, 17 (8.8%) out of 194 World Health Organization (WHO) Member States reported 2000 human avian influenza virus (AIV) infections involving 10 virus subtypes. Among these, H7N9 (1568/2000, 78.40%) and H5N1 (254/2000, 12.70%) viruses accounted for the majority of human infections,² but there was no reported case of human H10N5 infection before. Given the proximity of Taiwan to China and the potential health, economic, and food security risks posed by the outbreak of avian influenza infection, addressing the management of this H10N5 infection has become a critical issue.

Case history

The first case of H10N5 infection occurred in a female farmer aged over 60, with underlying comorbidities, who experienced symptoms of cough, sore throat, and fever starting on November 30, 2023. Initial, she sought medical attention at a local hospital on December 2. Subsequently, on December 7, she was transferred to a medical institution in the neighboring Zhejiang Province and unfortunately succumbed to the infection on December 16.

Microbiological investigation

The patient did not receive influenza vaccine and was initially diagnosed with influenza A virus infection. Further investigations by Zhejiang Province health officials, involving nucleic acid testing, viral culture, and gene sequencing conducted by local healthcare facilities, led to the isolation of both seasonal influenza A (H3N2) subtype and avian influenza A (H10N5) subtype viruses from the patient's samples on January 22, 2024. Finally, the Chinese Center for Disease Control and Prevention (CDC) conducted confirmatory testing on January 26, 2024, verifying the laboratory results obtained from Zhejiang Province.

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Surveillance investigation

The patient had a history of exposure to live poultry, specifically through the purchase of a duck on November 26, 2023, but did not report any contact with pigs or other mammals. Subsequent testing of duck meat stored in the fridge revealed that seven samples tested positive for H10N5, and two samples were positive for N5 (with no result for haemagglutinin). Environmental samples collected from her home all tested negative for the virus.

Medical observation and surveillance efforts targeting close contacts in both Zhejiang and Anhui provinces did not reveal any additional suspected cases. Furthermore, retrospective case finding activities conducted during the same period did not identify any other cases related to the H10N5 infection. As a result, the Chinese healthcare authority stated that the case was an “incidental” cross-species transmission from poultry to humans and that there was a low risk of the virus infecting people.

Avian influenza infections are caused by influenza viruses which normally circulate in several types of wild and domestic birds but can also infect humans and other animal species. Infections in humans are usually sporadic and mostly due to direct contact with infected animals or contaminated environments. The primary risk factor for human infection appears to be exposure to either infected live or dead poultry or contaminated environments, such as live bird markets. Current zoonotic influenza viruses have not demonstrated sustained person-to-person transmission.

Epidemiology

H10 subtype AIVs have been isolated from domestic poultry, wild waterfowl worldwide,³ and have occasionally infected mammalian hosts. In 1949, the first H10 subtype AIV, specifically H10N7, was isolated from chickens in Germany. In 1984, the first reported mammalian infection with H10 occurred in mink in Sweden, where a subtype of the H10N4 virus caused severe pneumonia and death.⁴ Until 2004, the first human infection caused by H10N7 AIV was reported in Egypt.⁵ Thereafter, H10N8 and H10N3 AIV causing human infections have been reported in China.^{6,7} Regarding H10N5, it has been isolated from swine in Hubei, China in 2008 and then Wang et al. reported the first case of inter-species transmission of an H10N5 AIV to domestic pigs under natural conditions.⁸ Until now, the first case of H10N5 infection in a human was confirmed in China.¹ Given the limited data available, additional research is necessary to ascertain the epidemiology of H10N5 viruses among animal populations. This information is crucial for guiding surveillance efforts and implementing preventive measures.⁹ Surveillance becomes particularly important to monitor the spread of the virus, especially in bird populations. This is pertinent given the sporadic nature of human infections with other H10Nx subtypes, such as H10N3.

Pathogenicity

While previous studies suggested that H10N5 exhibited low pathogenicity, Jia et al. reported conflict findings. According to their research,¹⁰ H10N5 AIV has the potential to cause

significant body weight loss and fatalities in mice. Additionally, the virus was found to replicate in mouse brain tissue, indicating a potential for enhanced pathogenicity after passage in mammals. Despite H10N5 being considered low pathogenicity AIV, causing mild morbidity in poultry, the virus may mutate and become high pathogenicity AIV, leading to severe disease and mortality. In humans, AIV infections can initially manifest as mild symptoms such as high fever, cough, sore throat, and muscle aches. However, the disease may rapidly progress to severe pneumonia, acute respiratory distress syndrome, and even altered mental status or seizures, particularly in cases involving high pathogenic AIV or immunocompromised hosts. These findings underscore the importance of continuous surveillance and biosecurity assessments for H10N5 viruses, highlighting the necessity to monitor and evaluate the potential risks they may pose to human health.

Diagnosis

Rapid detection is crucial for the prevention and control of avian influenza viruses (AIVs).^{11,12} While methods for detecting the H5, H7, and H9 subtypes of AIVs have been developed and applied to surveillance and clinical care,¹³ rapid assays for the detection and surveillance of H10 subtype AIVs are limited. A new reverse-transcription loop-mediated isothermal amplification (RT-LAMP) assay, developed by Luo et al., may serve as a valuable diagnostic tool. This assay can specifically amplify H10 subtype AIVs without cross-reactivity with other AIV subtypes or avian pathogens.¹⁴

Treatment and prevention

Currently, US Centers for Disease Control and Prevention recommend the prescription of antiviral agents as soon as possible for individuals who get AIV infection.¹⁵ This is because the effectiveness of antiviral treatment is maximized when initiated at the onset of symptoms. Early administration of antiviral medications is crucial for managing AIV infections and mitigating the severity of the illness. Lastly, the best way to prevent AIV is to effective vaccination and avoid sources of exposure whenever possible.¹⁶

Recommendation

To management the arrival of H10N5 AIV human infection, the Chinese government and WHO proposed several recommendations. China authority has taken the several measures, including (1) conducting risk assessment, (2) strengthening syndromic surveillance in local healthcare facilities, (3) undertaking epidemiological investigation, close contact tracing, and monitoring, (4) conducting retrospective screening, case finding, environmental sampling and testing, (5) expanding surveillance and testing among live poultry and the environment in farms and slaughterhouses in the city (Xuancheng Prefecture, Anhui Province), and (6) implementing culling and hazard management of the ducks which tested positive for H10N5 in a traceback investigation and has carried out disinfection of affected areas. Additionally, WHO advised that (1) the

public should avoid high-risk environments, such as live animal markets or farms, (2) avoid contact with live poultry or surfaces that might be contaminated by birds or poultry droppings and (3) hand hygiene with frequent handwashing or using alcohol-based hand sanitizer. However, WHO does not recommend any specific measures for travelers, including any travel and/or trade restrictions toward China based on the currently available information.¹

Conclusions

As there is only one reported case of human infection with H10N5 AIV in China, the epidemiology of this strain remains largely unknown. The limited information available from the single case emphasizes the need for continued vigilance and research to better understand the potential risks and characteristics of H10N5 AIV in human populations. Monitoring for any shifts in the virus's behavior, transmissibility, or impact on human health is essential for developing effective prevention and control strategies. Ongoing and comprehensive global surveillance is crucial to detect any virological, epidemiological, and clinical changes associated with circulating AIV strains. This ongoing vigilance is particularly important given the unpredictable nature of influenza viruses and their potential to undergo genetic changes that may impact their behavior in human populations. By maintaining a robust surveillance system, health authorities can promptly identify and respond to emerging threats, potentially preventing the spread of AIV and minimizing the associated public health risks.

CRedit authorship contribution statement

Chih-Cheng Lai: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.
Po-Ren Hsueh: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

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