Acknowledgements

The authors would like to acknowledge the clinicians who have contributed patient samples for the diagnoses discussed in the present study.

Transparency Declaration

The authors have no known conflicting interests within this work.

References


Kinetics of nasopharyngeal shedding of novel H1N1 (swine-like) influenza A virus in an immunocompetent adult under oseltamivir therapy

C. Charlier1, V. Enouf2, F. Lanternier1, M. Grandadam3, K. Amazzough1, S. Blanche4, M. Lecuit5, O. Lortholary1,* and S. van der Werf2,6

1) Université Paris Descartes, Service de Maladies Infectieuses et Tropicales, Centre d’Infectiologie Necker-Pasteur, Hôpital Necker-Enfants Malades, Assistance Publique-Hôpitaux de Paris, 2) National Influenza Centre (Northern France), Unité de Génétique Moléculaire des Virus à ARN, Institut Pasteur, URA3015 CNRS, Université Paris-Diderot, 3) Unité des Interactions Moléculaires Flavivirus-Hôtes, Institut Pasteur and 4) Université Paris Descartes, Unité Hémato-logie Immunologie, Hôpital Necker-Enfants Malades, Assistance Publique-Hôpitaux de Paris, Paris, France

Abstract

We describe a patient with confirmed novel H1N1 (swine-like) influenza A virus who had daily nasal swabs tested during oseltamivir therapy. Nasal shedding remained positive for 2 days and became negative on day 3. This report presents the first available data on the kinetics of shedding of this novel virus under antiviral therapy.

Keywords: Kinetics, nasal shedding, oseltamivir, PCR, swine-related influenza

Original Submission: 25 May 2009; Revised Submission: 3 July 2009; Accepted: 9 July 2009
Editor: D. Raoult
Article published online: 22 July 2009

10.1111/j.1469-0691.2009.03007.x

Corresponding author and reprint requests: O. Lortholary, Université Paris Descartes, Service de Maladies Infectieuses et Tropicales, Centre d’Infectiologie Necker-Pasteur, Hôpital Necker-Enfants Malades, Assistance Publique-Hôpitaux de Paris, 149 rue de Sévres, 75015 Paris, France
E-mail: olivier.lortholary@nck.aphp.fr
*These authors contributed equally to this work.
Testing of nasal swab specimens is a validated diagnostic method for influenza which is used with success for the diagnosis of the novel H1N1 (swine-like) influenza A virus [1,2]. However, a follow-up study of nasal shedding of this novel virus under antiviral therapy is not available so far. We describe here a patient with confirmed novel H1N1 (swine-like) influenza A who benefited from daily swab examination under oseltamivir therapy. The kinetics of nasal viral eradication and its impact on medical management are presented and discussed.

**Case report**

A 37-year-old male French Caucasian patient was hospitalized at the Centre d’Infectiologie Necker- Pasteur, Paris, for mild fever (38°C), dyspnoea, cough and myalgia following a trip to Yucatan, Mexico. He had no significant past history, or any tobacco, alcohol or drug exposure, and did not receive any medication. Symptoms developed 2 days after he returned from an 11-day trip to Cancun and Tulum, Mexico, with his wife and two sons. The trip included a visit to a Mayan village, where they had close contact with poultry. The patient spent 3 h waiting for a connecting flight at Mexico International airport on his way back to Paris, France. He did not recall any direct contact with swine or patients with influenza. Physical examination revealed a pyrexia, a normal respiratory rate, and a mild conjunctival hyperaemia. Blood oxygen saturation was 96%. Headache and myalgia were noted, as well as mild shortness of breath at rest, but no digestive or neurological disturbance. Lung examination findings were normal. A chest radiograph showed no abnormalities. Laboratory test results were unremarkable. A nasopharyngeal swab allowed the detection of influenza A virus using RT-PCR targeting the M gene, albeit at a low virus load. Seasonal H1N1 and H3N2 influenza strains were not detected. The H1N1 (swine-like) influenza A virus was detected upon random amplification of the RNA using the phi29 polymerase [3] and subsequent determination of the sequences of the M gene by pyrosequencing as previously described [4], but using the primers MR (biotin-ATAGAAACAAGGTAGTTTTTACTC) and M2F (CAGATGCAGCGATTCAAGTG) for amplification and M2F for sequencing. The nucleotide sequence (nucleotides 759–784) was identical to that of A/California/4/2009(H1N1) (swine-like) [2], and was shown to encode the S31N change known to confer resistance to adamantanes.

Antiviral treatment with oseltamivir (75 mg/day) was started on admission 48 h after the onset of symptoms. The evolution was favourable, with complete disappearance of symptoms within 2 days. Nasal swab samples were obtained daily. Interestingly, they remained positive for 2 days, with comparable viral loads, and became negative on the third day of treatment. The patient was then discharged, having fully recovered from H1N1 (swine-like) influenza A. No other case of influenza was detected among familial contacts.

This patient with a virologically confirmed diagnosis of imported swine-like influenza presented with mild clinical symptoms in the absence of comorbidity, a clinical picture corresponding to one reported in the USA [2]. He benefited from antiviral therapy within 48 h after the onset of symptoms, as recommended (http://www.cdc.gov/h1n1flu/recommendations.htm). Recently published data have documented the susceptibility of available swine influenza isolates to neuraminidase inhibitors [2], but, to our knowledge, we are the first to report an evaluation of the kinetics of nasal shedding of the H1N1 (swine-like) influenza A virus under oseltamivir treatment. Nasal viral shedding became negative 3 days after initiation of appropriate and early antiviral therapy. This duration appears to be similar to that reported for cases of human seasonal H3N2 influenza A or influenza B, with 73% of patients whose nasal samples became negative by day 3, and 1–5% of patients whose samples were still positive at day 5 [5]. In a recent meta-analysis of the efficacy of registered antivirals against seasonal influenza, viral nasal titres were significantly reduced by oseltamivir, which also improved the status of patients with symptomatic influenza and prevented lower respiratory tract complications [6].

Thus, treatment should also contribute to reducing transmission. However, delayed viral clearance with shedding of more than 10 days has been reported among immunocompromised patients, including lymphopenic patients and patients who have undergone bone marrow transplantation [7,8]. Prolonged shedding of an H1N1 influenza A virus may also suggest resistance to neuraminidase inhibitors, as it has been reported in up to 15% of cases during seasonal influenza [9].

This preliminary report regarding an immunocompetent adult does not suggest that nasal viral shedding during swine-like influenza occurring in humans differs from what is currently reported during seasonal H1N1 influenza A, meaning that isolation procedures can be stopped as early as at the end of oseltamivir therapy, provided that respiratory symptoms have disappeared. Larger studies are needed to confirm these data and to assess the potential acquisition of resistance to neuraminidase inhibitors of this recently emerged swine-like influenza virus, at least in patients with persistent clinical symptoms.