

Case Report: Severe Imported Influenza Infections Developed during Travel in Reunion Island

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Abstract. We report two cases of severe influenza infection imported by tourist patients from their country of origin and developed during travel. While studies have reported cases of influenza infections acquired during travel, here we examine two cases of severe influenza infection contracted in the country of origin that led to diagnosis and therapeutic problems in the destination country. No international recommendation exists concerning influenza vaccination before travel, and few countries recommend it for all travelers. Our study suggests that travel should be canceled when infectious signs are observed before departure. Influenza is a very common infection that is often benign, but sometimes very severe. The most severe cases include shock, acute respiratory distress syndrome (ARDS), myocarditis, rhabdomyolysis, and multiple organ failure. Management can require exceptional therapies, such as extracorporeal membrane oxygenation. A number of studies have focused on influenza infection in travelers. Cases of influenza acquired during travel have been reported in this literature, but no study has examined cases of influenza imported from the country of origin and developed while abroad. The latter situation may lead to 1) diagnostic problems during the non-epidemic season or in places where diagnostic techniques are lacking and 2) therapeutic difficulties resulting from the unavailability of techniques for the management of severe influenza infection in tourist areas. Here, we report two cases of extremely severe influenza infection imported by tourists from their country of origin and developed during travel.

CASES

These two patients lived in metropolitan France, and had come to Reunion Island for holidays.^{1–5}

Case 1 was a 49-year-old male patient with hypertension, obesity (body mass index of 30 kg/m²), and rheumatoid arthritis treated with long-term corticosteroids. The patient had had contact with a person with influenza-like illness (ILI) 3 days before his trip to Reunion Island in January 2015. On arrival in Reunion Island, he presented ILI-associating fever, myalgia, and cough. He was hospitalized for dyspnea 6 days later. The clinical examination found hypoxemia, atrial fibrillation, and hypotension (which was corrected by fluid expansion). Procalcitonin level was 0.5 µg.L⁻¹ and chest radiography revealed right basal opacity. Antibiotherapy was initiated with amoxicillin and then modified with ceftriaxone and spiramycin because of worsening of respiratory symptoms. Echocardiography was normal, and chest computerized tomography found bilateral diffuse alveolar damage. The patient's clinical condition worsened and required transfer to intensive care unit (ICU) on day 11, tracheal intubation for acute respiratory distress syndrome (ARDS) and noradrenaline on day 12. Severity Acute Physiological Score II (SAPS II) was 37. Finally, the results of explorations, including a bronchoalveolar lavage, found the presence of influenza A (H1N1) pdm09 by polymerase chain reaction (PCR) (multiplex kit FTD FLU[®] [Fast track diagnostics, Luxembourg]), and the patient was treated with oseltamivir. Hemoculture, antigen tests in detection of *Streptococcus pneumoniae* and *Legionella pneumophila* in urine, serodiagnostic for *Chlamydia pneumoniae*, *L. pneumophila*, *Mycoplasma pneumoniae*, *Coxiella burnetii*,

cytomegalovirus, and Epstein–Barr virus were negative. The patient eventually improved: atrial fibrillation was reduced and mechanical ventilation was weaned after 11 days. The patient was discharged from ICU after 15 days and from hospital after 22 days.

Case 2 was a 69-year-old female patient with untreated Horton disease. She had been vaccinated against influenza in metropolitan France in December 2016 and had gone on holiday to Reunion Island 18 days after vaccination. Five days after landing in Reunion Island, she experienced weakness and came to our emergency department. Examination revealed hypotension and a temperature of 35.5°C. Procalcitonin level was 0.05 µg.L⁻¹. Antibiotherapy was initiated with cefotaxime and gentamicin. The next day, the patient was hospitalized in ICU for cardiogenic shock and hypovolemic shock with a SAPS II of 74. Echocardiography revealed left ventricular ejection fraction of 30% and cardiac tamponade. Management initially included epinephrine, norepinephrine, pericardial drainage, massive fluid expansion, and oseltamivir. Peak of the high-sensitivity Troponin T was 397 ng.mL⁻¹. The patient also required venovenous extracorporeal membrane oxygenation (ECMO) for severe ARDS during 4 days. Bacterial and virological tests performed including hemoculture, kit FTD respiratory Pathogens 21[®] (Fast track diagnostics), bacteriology of protected distal bronchial samples, antigen tests in detection of *S. pneumoniae* and *L. pneumophila* in urine, serodiagnostic of human immunodeficiency virus, bacteriology of pericardial effusion were negative except for influenza A (not H1N1) (Kit FTD respiratory Pathogens 21[®] [Fast track diagnostics], and Kit Xpert Flu/RSV XC[®] [Cepheid, Sunnyvale, CA]). The patient eventually improved, and mechanical ventilation was weaned after 9 days. She was discharged from ICU after 12 days with a left ventricular function normalized. She was transferred to a metropolitan hospital with a persistent kidney injury after 21 days.

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DISCUSSION

In this article, we report the first cases of imported severe influenza infection treated during travel.

Reunion Island is located in the Indian Ocean, in the southern hemisphere. The island has 851,000 inhabitants, and it is a tourist area favored especially by travelers from metropolitan France. Despite the 9,300 km distance between Reunion and France, the island is directly connected to Europe via four daily flights to France. The health infrastructure of Reunion meets French standards. Influenza activity on the island generally increases during the austral winter (from May to September), leading to more frequent identification of the influenza virus and to an increase in general practitioner consultations for ILI.⁶ An influenza surveillance system is in operation throughout the year, and all cases of severe influenza are reported. All four (adult and pediatric) ICUs of the island participate in this surveillance system, and every patient with severe acute respiratory failure is swabbed. The strains usually encountered in Reunion Island in 2015 were mostly A (H3N2), and three consecutive strains (B, A [H1N1] pdm09 and A [H3N2]) were identified in 2016.⁷ The strains usually encountered in metropolitan France were mostly A (H3N2) and A (H1N1) pdm09 during the 2014–2015 season, and mostly A (H3N2) in 2016–2017. The French national public health agency regarded these cases as imported cases because of 1) the delay between the date of travel and the onset of symptoms and 2) the fact that the epidemic season had begun in metropolitan France but not in Reunion Island.

In the field of travel medicine, many studies have examined the risks involved in presenting an influenza infection during a stay abroad. Although authors have highlighted the risks associated with acquiring influenza during travel, patients with influenza can often be taken care of after returning to their country of origin, even in cases of severe forms of the disease. Another risk frequently discussed in the literature is that of virus transmission during travel, especially by plane or by cruise ship.^{8–11} In the two cases presented here, patients were likely contagious during the flight (which lasted approximately 12 hours).

Our cases illustrate another risk, i.e., that of developing influenza during travels, possibly in a country where the diagnosis and management of severe influenza infections are impossible. There is a risk of delayed diagnosis (influenza may not be suspected during the non-epidemic season, or PCR may be performed less often), which has been described as a risk factor of death in severe cases.¹² Also, our two patients would probably have died if they had been on a cruise ship or in a country lacking health infrastructure, especially because the very rapid and severe evolution would have prevented medical evacuation to France. Case 2 needed ECMO, a support technique that is clearly not available everywhere.

Our two patients had presented signs that could have alerted to the risk of developing an infection while abroad. The risks of transmitting the virus and developing a severe infection may justify the cancellation or delay of the trip, especially if management of severe infections is impossible in the destination country and/or if the traveler has severe comorbidities. As a recently published review article has shown, no international recommendation exists concerning influenza vaccination before travel, and few countries recommend it for all travelers.⁵

In conclusion, in addition to the risk of acquiring influenza during travel, there is a risk of importing a severe influenza

infection from the country of origin to the destination country. This risk must be explained to travelers before they leave, especially if they plan to travel to countries where management of severe infections may be impossible. In our opinion, the risk of developing severe influenza justifies vaccination before travel; it also justifies canceling a trip when infectious signs are observed before departure.

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