Disponible en ligne sur
ScienceDirect
www.sciencedirect.com
Elsevier Masson France
EM|consulte
www.em-consulte.com
Médecine et maladies infectieuses 48 (2018) 141–144
Médecine et maladies infectieuses

Short communication

Intensive care admission for *Coronavirus* OC43 respiratory tract infections

Admissions en réanimation pour infection respiratoire à Coronavirus OC43

D. Vandroux [a,b,*], N. Allou [a], J. Jabot [a], G. Li Pat Yuen [c], E. Brottet [d], B. Roquebert [b,c], O. Martinet [a]

[a] *Service de réanimation polyvalente, hôpital Félix-Guyon, CHU La-Réunion, allée des topazes, CS11021, 97400 Saint-Denis-de-La-Réunion, France*
[b] *CHU La-Réunion, Inserm, CIC 1410, 97410 Saint-Pierre, France*
[c] *Laboratoire de biologie moléculaire, service de microbiologie, hôpital Félix-Guyon, CHU La-Réunion, allée des topazes, CS11021, 97400 Saint-Denis, Reunion*
[d] *Santé publique France, CIRE océan indien, 2, bis avenue Georges-Brassens, CS 61002, 97443 Saint-Denis cedex 9, Reunion*

Received 3 February 2017; received in revised form 24 May 2017; accepted 3 January 2018

Abstract

Background. – *Coronavirus* OC43 infection causes severe pneumonia in patients presenting with comorbidities, but clinical signs alone do not allow for viral identification.

Objectives. – To analyze acute manifestations of *Coronavirus* OC43 infections and outcomes of patients admitted to an intensive care unit (ICU).

Patients and methods. – Retrospective and monocentric study performed during a *Coronavirus* OC43 outbreak. We used multiplex PCR to detect an OC43 outbreak in Reunion Island during the 2016 Southern Hemisphere's winter: seven admissions to the ICU.

Results. – Mean age of patients was 71 [67;76] years, SAPS II was 42 [28;53], pneumonia severity index 159 [139;182] vs 73 [40.5;107] for patients in medical wards, and 43% required mechanical ventilation. Comorbidities were diabetes mellitus (87%), chronic respiratory failure (57%), and chronic renal failure (29%). One patient died from *Haemophilus influenzae* co-infection.

Conclusion. – As for MERS Co-V infections, underlying comorbidities impacted the clinical outcomes of OC43 infections.

Keywords: *Coronavirus* OC43; multiplex PCR

Résumé

Introduction. – L'infection à *Coronavirus* OC43 peut induire des pneumopathies sévères chez les patients présentant des comorbidités lors d'épisodes hivernaux en climat tempéré.

Patients et méthodes. – Analyse rétrospective, monocentrique des cas d'infections à *Coronavirus* OC43 admis en réanimation. L'utilisation d'une PCR multiplex pour les infections respiratoires a permis de détecter une épidémie de bronchopneumopathies à *Coronavirus* OC43 durant l'hiver austral 2016 à La Réunion: sept admissions en réanimation.

Résultats. – Des patients, âgés de 71 [67 ; 76] ans en moyenne, présentaient un indice de gravité simplifié II de 42 [28 ; 53] et une ventilation mécanique était requise pour 43 %. Les comorbidités comprenaient diabète (87 %), insuffisance respiratoire chronique (57 %) et insuffisance rénale chronique (29 %). Un décès est survenu au cours d'une co-infection à *Haemophilus influenzae.*

* Corresponding author. Service de réanimation polyvalente, hôpital Félix-Guyon, CHU La-Réunion, allée des topazes, CS11021, 97400 Saint-Denis-de-La-Réunion, France.
E-mail address: vandroux.david@gmail.com (D. Vandroux).

https://doi.org/10.1016/j.medmal.2018.01.001
0399-077X/

Conclusion. – Comme pour le MERS *Coronavirus*, les comorbidités impactent l'évolution clinique d'une infection et conduisent à des admissions en réanimation.

Mots clés : *Coronavirus* OC43 ; PCR multiplex

1. Background

Human *Coronavirus* infections, including *Coronavirus* OC43, usually result in upper respiratory tract infections such as common cold. However, these viruses are responsible for severe lower respiratory tract illness in patients presenting with comorbidities, and may be associated with the development of neurological diseases such as encephalitis [1]. Coronaviruses are enveloped viruses with a large positive-sense, single-stranded RNA genome and a helical nucleocapsid. The epidemiological surveillance of *Coronavirus* infections is facilitated by real-time polymerase chain reaction (RT-PCR) techniques used for routine diagnosis. In the Northern Hemisphere, *Coronavirus* infections have a seasonal distribution and seem to be uncommon outside the cold season running from December to May [2].

Reunion Island is a Southern Hemisphere French overseas territory with 843,529 inhabitants located in the Indian Ocean between Madagascar and Mauritius islands. The climate is tropical with moderate temperatures and the cold and dry season runs from May to November concomitantly with the influenza season [3]. In 2016, no *Coronavirus* OC43 strain was detected before June in the hospital. As of July, a *Coronavirus* OC43 strain was detected in 26 samples by Fast-Track Diagnostics® respiratory pathogens assay: seven from the sentinel practitioner network and 19 from hospital settings. Seven of these hospital strains were detected in patients admitted to the intensive care unit (ICU). A flowchart describing admissions to the ICU during this period is presented in Fig. 1.

2. Patients and methods

We carried out a retrospective review of the medical records to describe the clinical features of seven patients presenting with *Coronavirus* infection and the impact on the ICU. We collected demographic data, reason for admission, concomitant medical conditions, history of illness, clinical characteristics, results of laboratory investigations, disease assessment score including Simplified Acute Physiology Score II (SAPS II) and pneumonia severity index (PSI) of FINE [4], management, and outcome. SAPS II score is used to assess disease severity and is calculated using the worst 12 physiological indicators during the first 24 hours in the ICU. Continuous variables are presented as median and interquartile range, and categorical variables are reported as number or frequency. As per French law (L.1121-1 paragraph 1 and R1121-2 Public Health Code), neither informed consent nor approval from an ethics committee were necessary for anonymous data extraction from an analysis of patients' medical charts.

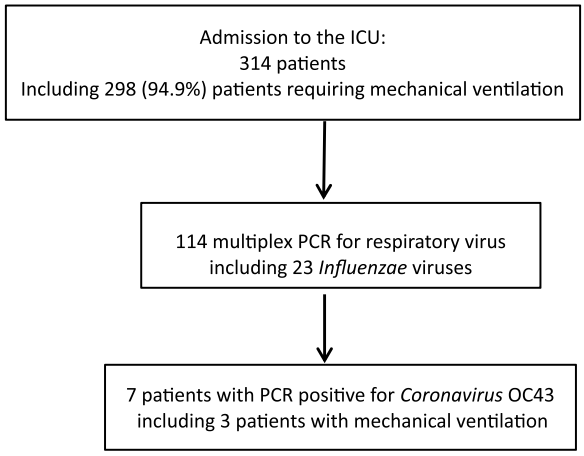

Fig. 1. Flow chart describing ICU admissions in Saint-Denis, Reunion Island, with the proportion of respiratory samples for PCR multiplex and the proportion of mechanical ventilation during the influenza season (June 15, 2016–September 30, 2016).
Flux des patients admis en réanimation polyvalente à Saint-Denis-de-La-Réunion avec la proportion de tests PCR multiplex et de ventilation mécanique pendant la saison grippale d'hiver austral (15 juin 2016–30 septembre 2016).

3. Results

The study population characteristics are provided in Table 1. A comparison between our cohort of patients and patients hospitalized in the medical ward is shown in Table 2. All patients were residents of Reunion Island and none had traveled recently. All patients were admitted for respiratory failure caused by viral pneumonia, but three patients also presented with pulmonary edema and one with septic shock. The median age of patients was 71 [67;76] years. Infections occurred in elderly patients presenting with several comorbidities who were admitted for serious conditions as evidenced by a high SAPS II and PSI scores. Time between onset of clinical signs and ICU admission was short for two patients presenting with chronic disease failure. The other patients presented with influenza-like illness several days before hospitalization. Chest radiographic findings were abnormal for all patients. Biological results revealed that all patients had leukocytosis with lymphopenia. Three patients required mechanical ventilation for 4, 6, and 7 days. No patient needed a respiratory assistance with extracorporeal membrane oxygenation. All patients but one were treated with empirical antibacterial drugs: spiramycin and cefotaxime or piperacillin/tazobactam. One (14%) patient died: a 79-year-old woman presenting with type 2 diabetes, severe chronic obstructive pulmonary disease, and prior exposure to traditional firewood for cooking. She was admitted for acute exacerbation

Table 1
Characteristics of seven patients admitted to the ICU for *Coronavirus* OC43 community-acquired pneumonia.
Caractéristiques de sept patients admis en réanimation pour pneumopathie à Coronavirus *OC43.*

Characteristics	Data ($n = 7$)
Body mass index	29 [26;30]
Medical history	
Diabetes	6 (87)
Chronic respiratory failure	4 (57)
Chronic renal failure	2 (29)
Heart failure	2 (29)
Cirrhosis	1 (14)
Severity assessment scores at admission	
Simplified Acute Physiology Score II	42 [28;53]
Pneumonia Severity Index	159 (139;182)
Leukocytes	12,960 [11,440;13,830]
Lymphocytes	1,320 [940;1,485]
Pro b-type natriuretic peptide	587 [224;700]
Procalcitonin	0.22 [1.16;0.25]
Lactic acid	1.7 [1.3;2.0]
Duration of ICU stay	6 [3.5;7.5]
ICU management	
Mechanical ventilation	3 (43)
Non-invasive ventilation	5 (71)
High-flow nasal cannula oxygen therapy	1 (14)
Renal replacement therapy	2 (29)
Death	1 (14)

ICU: intensive care unit. Data is presented as number (%) or median [interquartile range].

Table 2
Comparison of patients hospitalized in the intensive care unit and in the medical ward during an OC43 *Coronavirus* outbreak.
Comparaison de patients hospitalisés en réanimation et en soins courants durant la période d'infection à Coronavirus *OC43.*

Characteristics	ICU patients $n = 7$	Medical ward patients $n = 12$
Age	71 [67;76]	34 [9;62]
Aged < 12 years (*n*)	0	4
Female sex	3 (43)	7 (58)
Diabetes	6(87)	2 (17)
Chronic renal failure	2 (29)	3 (25)
Duration of hospital stay (days)	14 [9.5;26]	4.5 [3.25;5.75]
Pneumonia severity index[a]	159 [139;182]	73 [40.5;107]

Data is presented as number (%) or median [interquartile range]. ICU: Intensive Care Unit
[a] The Pneumonia Severity Index is only calculated for patients over 18 years of age.

and septic shock. The laboratory detected *Coronavirus* OC43 and *Haemophilus influenzae* in the respiratory specimen. She died despite six days of mechanical ventilation.

4. Discussion

The small number of patients, not necessarily requiring mechanical ventilation, and the duration of stay seem to indicate a low epidemic impact. However, *Coronavirus* epidemics may be contemporaneous with an influenza outbreak.

Clinical aspects of *Coronavirus* infection cannot be recognized in the absence of laboratory investigations as coronaviruses are usually responsible for illness that cannot be distinguished from that caused by many other viruses. A cross reactivity between *Coronavirus* (in particular SARS-CoV and OC43) must be considered when interpreting serological tests for *Coronavirus* [5]. Since the emergence in the 1990s of nucleic acid amplification-based techniques, especially PCR, the diagnosis of several viral agents causing pulmonary infections has greatly improved. The use of a multiplex PCR test for respiratory tract infection allows for a high rate of detection of etiological agents, and enables the detection of *Coronavirus* outbreaks [6]. Antiviral drugs are yet to be developed in the treatment of *Coronavirus* infections, but characterization of such severe infections in patients presenting with comorbidities or in immunocompromised patients could enhance the medical research. These outbreaks mainly occur when the temperature is low. However, *Coronavirus* OC43 outbreaks have been reported in tropical climates: Malaysia [7] and Brazil [8] in 2012-2013. The 2016 Southern Hemisphere's winter in Reunion Island was among the coldest of the last decade [9]. This could have induced a small increase in ICU admissions of elderly and frail patients.

5. Conclusion

OC43 infection cannot be detected on the sole basis of clinical signs. The presence of underlying comorbidities impacted the clinical outcomes of OC43 infections, similar to what is observed in the ongoing MERS-CoV infection in the Middle East.

Contribution of authors

All authors contributed to the interpretation of results, the article revision, and approved the final version of the article.

DV wrote the article. DV and EB conducted the data analysis. JJ, NA, and OM contributed to collecting the data in the intensive care unit. BR and GLPY performed the characterization of viruses.

Disclosure of interest

The authors declare that they have no competing interest.

References

[1] Morfopoulou S, Brown JR, Davies EG, Anderson G, Virasami A. Human *Coronavirus* OC43 associated with fatal encephalitis. N Engl J Med 2016;375:5.
[2] Vabret A, Mourez T, Gouarin S, Petitjean J, Freymuth F. An outbreak of *Coronavirus* OC43 respiratory infection in Normandy, France. Clin Infect Dis 2003;36:985–9.
[3] Filleul L, Brottet E, Gauzere BA, Winer A, Vandroux D, Michault A, et al. Reunion, a sentinel territory for influenza surveillance in Europe. Euro Surveill 2012;17(27) [pii=20212].
[4] Fine MJ, Auble TE, Yealy DM. A prediction rule to identify low-risk patients with community-acquired pneumonia. N Engl J Med 1997;336:243–50.

[5] Patrick DM1, Petric M, Skowronski DM, Guasparini R, Booth TF, Krajden M, et al. An outbreak of human *Coronavirus* OC43 infection and serological cross-reactivity with SARS *Coronavirus*. Can J Infect Dis Med Microbiol 2006;17(6):330–6.

[6] Templeton KE, Scheltinga SA, van den Eeden WC, Graffelman AW, van den Broek PJ, Claas ECJ. Improved diagnosis of the etiology of community-acquired pneumonia with real-time polymerase chain reaction. Clin Infect Dis 2005;41:345–51.

[7] Al-Khannaq MN, Tien Ng K, Oong XY, Pang YK, Takebe Y, Chook JB, et al. Molecular epidemiology and evolionary histories of human *Coronavirus* OC43 and HKU1 among patients with upper respiratory tract infections in Kuala Lumpur, Malaysia. Virol J 2016;13:33.

[8] Trombetta H, Faggion HZ, Leotte J, Nogueira MB, Vidal LR, Raboni SM. Human coronavirus and severe acute respiratory infection in Southern Brazil. Pathog Glob Health 2016;110(3):113–8.

[9] http://www.meteofrance.re/climat/previsions-saisonnieres.