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Clinical features and molecular epidemiology of coronavirus-HKU1–associated community-acquired pneumonia

Key Messages

1. Coronavirus (CoV)-HKU1 accounts for 2.4% of community-acquired pneumonia.
2. Clinical features alone cannot differentiate this entity from other community-acquired pneumonia.
3. Further studies are needed to understand the significance of CoV-HKU1 in upper respiratory tract infection and its potential to cause outbreaks of acute viral respiratory illnesses.

Introduction

No microbiological cause can be identified in a large proportion of patients with respiratory tract infections. Recently, we discovered a novel group 2 coronavirus—coronavirus HKU1 (CoV-HKU1)—from a patient with pneumonia.[1] We examined the prevalence of CoV-HKU1 in nasopharyngeal aspirate (NPA) samples from patients with community-acquired pneumonia during a 12-month period.

Aims and objectives

This study aimed to (1) define the clinical features of CoV-HKU1 infection, (2) understand the epidemiology of CoV-HKU1–associated pneumonia, (3) determine the molecular epidemiology and genotypes of the virus, and (4) assess the usefulness of diagnostic tests in identifying such infections.

Methods

Prospectively collected NPAs from patients with community-acquired pneumonia were sent to the clinical microbiology laboratories of four hospitals in Hong Kong during a 12-month period. Community-acquired pneumonia was defined as symptoms and signs consistent with an acute lower respiratory tract infection, together with new radiographic findings that develop before or within 48 hours of presentation. Once CoV-HKU1 was detected in NPAs, hospital records, laboratory results, and chest radiographs of the corresponding patients were analysed.

Possible risk factors associated with CoV-HKU1–associated pneumonia were determined using two age- and sex-matched controls per patient with CoV-HKU1–associated pneumonia that were randomly selected from patients with community-acquired pneumonia whose NPAs were negative for CoV-HKU1. Each set of controls was within 5 years in age (older or younger) and was admitted within 15 days before or after admission of the corresponding patient with CoV-HKU1–associated pneumonia. The hospital records, laboratory results, and chest radiographs of the controls were analysed.

Viral RNA was extracted from NPAs using the QIAamp Viral RNA Mini Kit (Qiagen GmbH, Hilden, Germany).

RT-PCR of the pol gene of CoV-HKU1 was performed using CoV-HKU1–specific primers followed by DNA sequencing. A 453-bp fragment of the pol gene of CoV-HKU1 was amplified by RT-PCR using CoV-HKU1-specific primers (LPW1926 [5'-AAAGGATGTTGACAACCCTGTT-3'] and LPW1927 [5'-ATCATCATACTAAAATGCTTACA-3']) designed by multiple alignment of the nucleotide sequences of the pol genes of CoV-HKU1. Both strands of the PCR products were sequenced twice by use of an ABI Prism 3700 DNA Analyzer (Applied Biosystems, Foster City [CA], US), using the two PCR primers. The sequences of the PCR products were compared with the sequences of the pol genes of CoV-HKU1 and those of other coronaviruses in the GenBank

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database.

The ELISA-based immunoglobulin (Ig) G and IgM antibody tests were performed in accordance with our protocol. Each sample was tested in duplicate, and the mean absorbance for each serum sample was calculated.

The complete pol, S, and N genes of CoV-HKU1 from NPAs from nine of the 10 patients (from whom adequate amounts of RNA were available) were amplified and sequenced using the strategy described in our previous study. The nucleotide and deduced amino acid sequences of the pol, S, and N genes were compared with those of CoV-HKU1 and other group 2 coronaviruses. Phylogenetic tree construction was performed using the PileUp method with GrowTree (Accelrys Inc, San Diego [CA], US). Patient characteristics were compared between those with CoV-HKU1–associated pneumonia and those with non–CoV-HKU1–associated pneumonia, and between those who died of and those who survived CoV-HKU1–associated pneumonia. Fisher's exact test was used for categorical variables, and the Mann-Whitney U test was used for continuous variables. A P value of <0.05 was regarded as statistically significant.

Results

The NPAs from 10 (2.4%) of 418 patients with community-acquired pneumonia were positive for CoV-HKU1. All 10 cases occurred in winter and spring; nine of them were adults; and four had underlying diseases of the respiratory tract. In the six patients from whom serum samples were available, all had a four-fold change in IgG titre and/or presence of IgM against CoV-HKU1. The two patients who died had significantly lower haemoglobin levels, monocyte counts, albumin levels, and oxygen saturation levels on admission and had more extensive involvement visible on chest radiographs. Sequence analysis of the pol, S, and N genes revealed two genotypes of CoV-HKU1.

Discussion

Similar to HCoV-229E, HCoV-OC43, and HCoV-NL63, CoV-HKU1 was a human coronavirus that was endemic in humans. Similar to other human coronavirus infections, cases of CoV-HKU1–associated pneumonia occurred during winter and spring. Most patients with CoV-HKU1–associated pneumonia were old (80% were >65 years old) and had major underlying diseases, especially of the respiratory and cardiovascular systems.

Compared with SARS-CoV pneumonia, CoV-HKU1–associated pneumonia was a monophasic disease, and most patients had relatively mild symptoms localised to the respiratory tract and were therefore hospitalised only briefly. Although dyspnoea was present in 25% of patients with this pneumonia at presentation (compared to 20% in patients with SARS-CoV pneumonia), they often recovered quickly in contrast to those with SARS-CoV pneumonia who tended to deteriorate after 7-10 days.

Despite a relatively mild disease course in most patients, CoV-HKU1–associated pneumonia may be fatal in patients with low haemoglobin concentrations, monocyte counts, serum albumin levels, and oxygen saturation levels on admission and more extensive involvement on chest radiographs.

Conclusion

CoV-HKU1 is a cause of acute community-acquired pneumonia with winter seasonality. More studies should be conducted on this emerging cause of acute viral respiratory illness.

Acknowledgements

Reference

1. Woo PC, Lau SK, Chu CM, et al. Characterization and complete genome sequence of a novel coronavirus, coronavirus HKU1, from patients with pneumonia. J Virol 2005;79:884-95.