Coronavirus NL63-induced Adult Respiratory Distress Syndrome

To the Editor:

Coronaviruses are positive RNA-enveloped viruses. The first two human coronaviruses, HCoV-229E and HCoV-OC43, were discovered in the mid-1960s. They are a well-known cause of the common cold (1). The world epidemic of severe acute respiratory syndrome human coronavirus (SARS-HCoV) in 2002–2003 reintroduced the Coronaviridae family. In 2004 and 2005, respectively, two new coronaviruses were discovered: NL63 and HUK1 (2, 3). The Coronaviridae family is further subclassified into two genera: the alpha coronaviruses (HCoV-229E and HCoV-OC43) and beta coronaviruses (HCoV-HUK1, HCoV-OC43, Middle East respiratory syndrome [MERS]-HCoV, and SARS-HCoV). HCoV-NL63 infection causes mostly upper and at times lower respiratory tract infection, community-acquired pneumonia, and also group in children (4). In 2012, another coronavirus-related epidemic occurred, this time in the Middle East, which led to the identification of the MERS-HCoV (5).

A 76-year-old woman was admitted because she had experienced 4 days of low-grade fever, dyspnea, and malaise. She had no discernible comorbidities and took no medications. Ceftriaxone and azithromycin were initiated, but shortly after admission, her respiratory failure worsened, requiring mechanical ventilation. Her PaO2/FiO2 ratio was 70, consistent with severe adult respiratory syndrome (ARDS), which remained her only failing system throughout her entire course. She was turned prone, and inhaled nitric oxide was added.

Chest roentgenogram revealed bilateral pulmonary infiltrates, and echocardiogram showed normal biventricular function. White blood cell count was normal. Blood, urine, and respiratory secretion cultures were all sterile. Serology for HIV was negative. Polymerase chain reaction (PCR) for cytomegalovirus from both blood and bronchoalveolar lavage (BAL) was negative. PCR from oral swab and nasal wash were negative for influenza species, human respiratory syncytial virus, and para-influenza viruses but were positive for coronavirus NL63. PCR from BAL was positive for HCoV-NL63 as well (cell count and differential were not performed). The presence of the virus was confirmed in consecutive samples from the nasal and oral cavities, revealing a persistent increase in viral load (Figure 1). BAL fluid was sterile for bacteria and for Pneumocystis jirovecii. PCRs from BAL fluid for SARS-HCoV and MERS-HCoV were negative. Because of the rarity of coronavirus-induced ARDS, a search for occult malignancy or immune deficiency revealed normal bone marrow biopsy, immunoglobulins, and abdominal ultrasound.

The persistently positive PCR for HCoV-NL63 in both upper and lower respiratory tract secretions, and the increase in viral load, as well as a negative extensive search for an alternative etiology, strongly suggest that HCoV-NL63 was indeed the cause of her fatal illness. After 27 days of nonresolving severe ARDS, she died as a result of hospital-acquired sepsis and multiorgan failure. A postmortem exam was not performed.

In 2010, a case of fatal HCoV-NL63 pulmonary infection during the late-engraftment phase was reported (6). An Australian study reported that 2% of patients presenting to the hospital because of respiratory symptoms tested positive for HCoV-NL63, and 81% of these patients were diagnosed with lower respiratory tract disease; all of them required admission to the hospital, 56% had an abnormal chest roentgenogram, and one immunocompromised patient died, yet none of these patients had ARDS (7).

Acute interstitial pneumonitis (AIP), an idiopathic form of acute lung injury first described by Hamman and Rich in 1935 (8), is a rapidly progressive disease frequently leading to respiratory failure and mechanical ventilation and is associated with very poor...
unidentified is an entity encompassing a wide variety of etiologies that are often been performed. As we previously suggested, it is possible that AIP diagnosed as another case of AIP, had PCR for HCoV-NL63 not evaluation (9). The patient under discussion could have been easily identifiable, some of which may be viral in origin (10). This distinction can be ascertained only when there is no identifiable alternative etiology after a thorough clinical evaluation (9). The patient under discussion could have been easily diagnosed as another case of AIP, had PCR for HCoV-NL63 not been performed. As we previously suggested, it is possible that AIP is an entity encompassing a wide variety of etiologies that are often unidentified, some of which may be viral in origin (10). This understanding, as well as our ever-improving diagnostic abilities in identifying viral pathogens, may have important implications on clinical practice. When clinically appropriate, a thorough search for viral etiology should be a part of the diagnostic workup of these patients, as it may obviate invasive procedures (biopsies) and potentially harmful therapeutic interventions such as broad-spectrum antibiotics, corticosteroids, and cytotoxic agents.

Figure 1. Relative quantification of coronavirus NL-63 by multiplex hydrolysis probes-based real-time polymerase chain reaction. The raw data fromnasopharyngeal washing matter, or bronchoalveolar lavage, or swabs were added to a test tube containing 1.0 ml RPMI solution that was vortexed. Nucleic acid extraction was performed using NuclSense EasyMag (Biomerieux, Marcy l’Etoile, France). Four hundred microliters of aspirate was extracted into 50 μl elution solution. A set of primers and probes was used to detect four coronaviruses (229E, HKU1, OC43, and NL63), along with an internal control set, by multiplex hydrolysis probes-based real-time polymerase chain reaction. The relative expression of coronavirus RNA transcripts for each day tested is conveyed in 45 quantitation cycle values (after correction to the quantitation cycle value of the internal control). Diamonds represent swabs; circles represent nasal wash, and triangles represent bronchoalveolar lavage.

prognosis. The histopathologic appearance in AIP is of diffuse alveolar damage characterized by three phases: acute exudative, organizing proliferative, and fibrotic. It should be emphasized that AIP cannot be distinguished from ARDS on the basis of histology alone (because of the patient’s clinical condition, a lung biopsy was not done). This distinction can be ascertained only when there is no identifiable alternative etiology after a thorough clinical evaluation (9). The patient under discussion could have been easily diagnosed as another case of AIP, had PCR for HCoV-NL63 not been performed. As we previously suggested, it is possible that AIP is an entity encompassing a wide variety of etiologies that are often unidentified, some of which may be viral in origin (10). This understanding, as well as our ever-improving diagnostic abilities in identifying viral pathogens, may have important implications on clinical practice. When clinically appropriate, a thorough search for viral etiology should be a part of the diagnostic workup of these patients, as it may obviate invasive procedures (biopsies) and potentially harmful therapeutic interventions such as broad-spectrum antibiotics, corticosteroids, and cytotoxic agents.

Author disclosures are available with the text of this letter at www.atsjournals.org.

Ori Galante, M.D.
Yonat Shemer Avni, Ph.D.
Lior Fuchs, M.D.
Ofira Azulay Ferster, M.D.
Yaniv Almog, M.D.
Ben Gurion University of the Negev
Beer-Sheva, Israel

References


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FAIM3:PLAC8 Ratio Compared with Existing Biomarkers for Diagnosis of Severe Community-acquired Pneumonia: Comparing Apples to Oranges?

To the Editor:

We read with interest the article by Scicluna and colleagues (1) that describes a novel genomic marker to assist in rapid diagnosis of community-acquired pneumonia (CAP). The authors suggest that FAIM3:PLAC8 ratio performed better than the current ratio of NLR to PLSCR1.