中文題目:肺炎支原體造成罕見的急性呼吸窘迫綜合症並具有遺傳性

英文題目:Mycoplasma pneumoniae: A rare cause of acute respiratory distress syndrome with a genetic contribution

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Introduction

Community-acquired pneumonia (CAP) remains a frequent cause of morbidity and mortality worldwide. The incidence of CAP is 24.8/1000 adults in the US. The common pathogens of CAP are streptococcus pneumoniae, Haemophilus influenzae, Staphylococcus aureus, Mycoplasma pneumoniae, group A streptococci, Legionella species, Chlamydophila, and Moraxella catarrhalis.[1]

Acute respiratory distress syndrome (ARDS) is an acute diffuse, inflammatory lung injury, associated with increased pulmonary vascular permeability with a relatively common syndrome with a high mortality. In a recent international study involving 29,144 patients, ARDS accounts for 10% of intensive unit admission and 23% of mechanically ventilated patients.[2] ARDS is widely considered to be “diffuse alveolar damage” cause by direct lung injury (eg, pneumonia, aspiration), or indirect lung injury(eg, sepsis, nonthoracic trauma, pancreatitis).[3] Pneumonia and sepsis are the leading causes of ARDS.

Mycoplasma pneumoniae is a frequent pathogen of CAP and it is often self-limited. Mycoplasma pneumoniae-related ARDS is scarce.[4] We expected a genomic variant to induce ARDS rather than sorely pneumonia. Therefore, we performed whole exome sequencing (WES) on our patient and which showed LRRC16A variant. We report a case of Mycoplasma pneumoniae coinfected with Chlamydia pneumonia in an immune-competent with variant of LRRC16A young woman causing ARDS.

Case report

A 31-year-old female without a systemic disease presented at our emergency department after 10 days of productive cough and fever. Her daughter had been diagnosed with pneumonia 2 weeks earlier. The patient was febrile (38.5°C) and had bilateral rhonchi in the lower lungs, a white blood cell (WBC) count of 15,400 × 10^3 /μL, and a platelet (PLT) count of 90 × 10 3 /μL. On day 1, she was treated with

piperacillin and clarithromycin for bacterial pneumonia; however, progressive dyspnoea was observed on day 2. When she was transferred to the intensive care unit for intubation, her arterial partial pressure to the fraction of inspired oxygen was 198 mmHg, and chest X-rays revealed rapid progression of a bilateral patchy opacity in the lower lungs (Figure 1). An atypical pneumonia-related acute respiratory distress syndrome (ARDS) was suspected. On day 3, the antibiotic treatment was changed to levofloxacin (500 mg per day) to prevent clarithromycin resistance. Follow-up blood examination revealed WBC and PLT counts of 8,400 and 230 × 10^3 /μL, respectively. Assays for atypical pneumonia pathogens revealed a positive cold agglutinin titre (1:64) and high Mycoplasma IgM titre (75.01 Bethesda units/mL). Real-time polymerase chain reaction assays for influenza viruses in nasopharyngeal aspirates were negative. Extubation was performed on day 7, and she was discharged on day 12.

Because of the rarity of M. pneumoniae/C. pneumoniae induced ARDS. We discussed with our patient to examine her gene sequence and she signed the permit. We performed whole exome sequencing (WES) of our patient but no variants classified at pathogenic or likely pathogenic levels (according to American College of Medical Genetics and Genomics guidelines) for the interpretation of sequence variants were identified. Then, we consulted with our gene laboratorian and extrapolated all the variants identified in the patient's sample and filtered them by ARDS-related genes. All but six variants were classified at benign level. The remaining six variants were classified at variants of unknown significance (VUS) levels and were found within LRRC16A, GGH, SFTPB, TGFBR3, THBS1, and TLR1 genes, respectively. The VUS variant within LRRC16A gene is an intronic variant, rs1226748546. A total of five variants (rs1226748546, rs1034051, rs10456324, rs1012899, rs913455) were found in the LRRC16A gene in this patient's sample. However, besides rs1226748546 being at VUS level, the others were classified as benign.

Discussion

We report an immune-competent young woman with LRRC16A variant who has Mycoplasma pneumoniae associated with ARDS.

Selected genes that have been associated with ARDS risk since 2000. Genes are listed by their Human Genome Organization gene nomenclature committee–approved

symbols and are exhibited at yearly publication. We discussed with our gene laboratorian and extrapolated all the variants identified in our patient and filtered them by ARSD-related genes as mentioned in Reilly et al.,[5] such as surfactant protein B (SFTPB), angiotensin-converting enzyme (ACE), nuclear factor erythroid-derived 2-like 2 (NFE2L2), serine protease inhibitor (serpin) protein (SERPINE1) have replicated their ARDS association.[5] And we found the VUS variant within LRRC16A gene is an intronic variant, rs1226748546.

Platelets (PLT) are shown to be important contribution in pulmonary-origin ARDS among critically ill patients through endothelial damage. LRRC16A encodes capping protein ARP2/3 and myosin-I linker (CARMIL), essential in actin-based cellular processes. And actin-based cellular processes are important for megakaryocyte maturation. The intronic SNP rs7766874 has been proposed to be in linkage disequilibrium with latent functional variants that alter the activity of CARMIL and result in abnormal megakaryocyte maturation and altered platelet formation.[6] The intronic SNP rs1226748546 of our patient may also similar effect. However, further studies are needed.

This case illustrates the polymorphism in the presentation of M. pneumoniae infection and result in ARDS, even in an immunocompetent patient. We believed LRRC16A play a critical role in the pathogenesis of ARDS. We also emphasize the importance of adequate treatment of the underlying disease of ARDS such as pneumonia and discourage the use of steroid.

References

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