Early microbial signatures associated with severe influenza in children

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Résumé

Seasonal influenza is responsible for 3 to 5 million cases of severe illness worldwide, resulting in 250 000 to 500 000 deaths per year. While early identification of patients with high risk of severe influenza is key to patient survival, we still lack accurate virological and host biomarkers to predict outcomes. Previous studies suggest that the respiratory microbiome is changed in influenza-infected patients. However changes in the microbiota have not been associated with disease severity yet because of a lack of clinical metadata.
In this study, we aimed at characterizing the predictive potential of the respiratory microbiome in determining influenza clinical outcome. We used a collection of retrospective respiratory samples from children infected with influenza. Patients' selection criteria were: age $\leq$15 years, first sample collected within 2 days of sample onset, and hospitalization in intensive care unit for acute respiratory distress or neurological complications (group of severe influenza) or discharged patients with mild disease (age- and sex-matched patients with mild influenza). The group of severe influenza included 9 patients with an acute respiratory distress and 16 patients with neurological complications. Average age was 34 months and 15 males were included. After admission, antibiotics were used in 14 cases and antiviral in 17 cases. Seven cases showed a viral co-infection (mainly with RSV or Bocavirus) and 4 developed secondary bacterial pneumonia (Pneumococcus, Haemophilius, Enterobacter).

Metagenomic analysis was performed by sequencing variable regions of the 16S rRNA gene. We analyzed samples collected at the acute phase of infection to define early biomarkers of influenza outcome. In addition, we followed longitudinal microbial responses to infection to identify potential deleterious microbial evolution. We also compared the influenza-infected patients to healthy patients from the human microbiome project.
The development of valid biomarkers predicting mild versus severe influenza outcome has important implication for patient management.

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Mots-Clés: microbiota, influenza, outcomes, pediatrics, biomarkers, metagenomics