BRIEF REVIEW

The diagnostic role of Metagenomic Next-Generation Sequencing in pulmonary infection with accompanying pleural effusion

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Epidemiological studies from North America, Western Europe and East Asia have shown that the incidence of pleurisy (pleuritis) has almost doubled in the 21st century's second decade (compared to the first one) and approaches 6.7-9.9 cases per 100.000 people [1]. The early detection of the responsible pathogens is essential, as it significantly affects the treatment and the patients' prognosis. A delayed diagnosis can lead to pulmonary empyema, which is associated with notably higher morbidity and mortality. The diagnostic value of conventional laboratory methods (microscopic examination, cultivation, Polymerase Chain Reaction-PCR) remains limited, because the pathogens are not detected in 25-60% of cases [1,2]. In addition, conventional specimen cultivation methods are time-consuming and their diagnostic accuracy is limited to fungi and bacteria detection.

Metagenomic Next-Generation Sequencing (mNGS) is an innovative pathogen detection method, which is increasingly used in clinical practice. It detects the responsible pathogens in infected patients' biological samples (blood, bronchoalveolar secretions, tissue, sputum, pleural effusion, cerebrospinal fluid, pus, bone marrow, nasopharyngeal swab) [1,2].

Since 2008, numerous studies from more than 20 countries have revealed the contribution of this technique not only in identifying rare and hard-to-detect new pathogens, but also in the determination of their antibiotic resistance [2,3,4]. mNGS can also detect multiple pathogens simultaneously and document cases of comorbidity, especially in immunocompromised patients [1]. The sensitivity of mNGS is significantly higher than that of cultivation (67.4% vs 23.6%, $p < 0.001$) [2], (79.5% vs 21.3%, $p < 0.001$) [4].Furthermore, related to cultivation, it is less affected by previous exposure to antibiotic therapy [1,4]. Concerning the complicated lower respiratory tract infection, mNGS appears to be superior to the cultivation in detecting the responsible pathogens in blood, bronchoalveolar lavage, sputum and pleural effusion samples [1-5]. Xu et al. emphasize that different strains of streptococcus were the most frequent bacteria detected by mNGS in pleural fluid of

infected patients. Anaerobic bacteria such as Prevotella, Parvimonas and Porphyromonas (accidental infection by inhalation in patients with poor oral hygiene) were also reported. Candida combined with Pneumocystis and CMV were the most common fungi and virus, respectively. Some rare and difficult-to-cultivate pathogens such as Nocardia, Pneumocystis and Mycobacterium tuberculosis were also identified by mNGS [1]. This paper also underlines that the patients whose samples were tested with mNGS had a shorter length of hospital stay compared to those in which conventional cultivation and PCR were used, as the antibiotic treatment was modified in time, according to the results, in the appropriate etiological therapy [1,3,4].

In conclusion, mNGS will likely become a routine method in the diagnosis of infectious diseases in the near future. However, it is crucial that both clinicians and microbiologists not only fully comprehend the advantages of the method, but also correctly interpret its results [3].

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