Sp73 - Role of Next-Generation Sequencing in the identification of pathogen in spinal infection

Shanmuganathan Rajasekaran, Kota Watanabe, Karthik Ramachandran, Gnanaprakash Gurusamy

Response/Recommendation: Next Generation Sequencing serves as a valuable adjunct in enhancing the diagnostic process of spinal infections, especially in culture negative patients. Although NGS cannot replace conventional microbial culture in current clinical practice, its integration with conventional methods offers a comprehensive approach to diagnosing and treating spinal infections.

Level of Evidence: Moderate

Delegate Vote:

Rationale:

Conclusive evidence of spinal infection is predicated upon the successful isolation of pathogens via conventional microbiological culturing techniques. Nonetheless, the efficacy of these cultures is compromised by their low yield, the extended duration required for pathogen identification, and the possible influence of preceding antibiotic treatments [1]

Compared to traditional laboratory testing methods, Next Generation Sequencing (NGS) has demonstrated superior detection rates, increased sensitivity, and a shorter detection time. Its ability to detect mixed infections is particularly noteworthy. Additionally, NGS demonstrated a high level of agreement with clinical diagnoses [1]. A study by Zhang et al. showed that lower white blood cell count, percentage of neutrophilic granulocytes, C-reactive protein and a relatively higher rate of prior antimicrobial treatment history have no effect on the NGS results. The results showed that NGS has a high positive rate for pathogen identification when compared to histopathology and culture results (sensitivity of 75.0% and a specificity of 84.5%) [2] The positive rate of NGS results from samples was significantly higher for those obtained by debridement than by needle biopsy, and the rate for pus and soft tissue was significantly higher than that for vertebral bone tissue [3].

A study by Gao et al. successfully identified the common pathogen of spinal infection in the Chinese population using NGS. The study results in 145 patients highlighted that Staphylococcus is the most prevalent pathogen in iatrogenic spinal infections, whereas Mycobacterium species were the most common in native spinal infections [4].

In a retrospective study by Xu et al., the clinical data of 108 patients with suspected spinal infection was used to comprehensively explore the diagnostic value of NGS technology. The results indicated a higher sensitivity and specificity of the NGS than the conventional microbiological test in the overall identification of bacteria, mycobacteria, and fungi, suggesting a better diagnostic accuracy of NGS in spinal infection. Moreover, the patients treated by NGS-guided antimicrobial therapy had a good outcome. The study highlighted that NGS helped in the identification of novel pathogens, including non-tubercular mycobacteria, because of its ability to identify the pathogen at the species level [5].

In another study by Zhang et al., NGS had a higher detection rate of 78.89% when compared to the microbial culture technique (44.74%), with a sensitivity of 84.2% and specificity of 100% [6,7].

A study by Lv et al. highlighted that NGS exhibited a higher diagnostic value in pus than in tissue, with higher sensitivity and specificity; conversely, the sensitivity and specificity of bacterial culture were higher for tissue than for pus. These results indicate that the bacteria in pus are more likely to be dead, and the nucleic acid sequences of dead bacteria still play an irreplaceable role in NGS. Contrarily, the relatively rich blood supply in infected lesion tissues facilitates bacterial growth, leading to a higher proportion of viable bacteria and a higher diagnostic value in bacterial culture [8].

Role of NGS in spinal TB:

Studies have shown that NGS is a powerful diagnostic tool in the detection of spinal TB infection as well. In a prospective multicentric study by Li et al., pathogens were detected in 82 out of 100 patients, among which 37 had TB and the remaining 45 had other bacterial infections. The results showed that NGS had similar sensitivity to Xpert and T-SPOT TB and better sensitivity than MGIT 960 culture and histopathology. In patients with non-TB spinal infections, the sensitivity of NGS was higher than bacterial culture and histopathology [9,10].
A similar study by Wang et al. showed that the sensitivity of NGS to identify the tubercular infection increased to 80% when compared to the bacterial culture of 11.1%. Whereas among non-tubercular infections, the sensitivity was 72.7% when compared to culture sensitivity of 36.4% with a relatively shorter time duration of 2.16 days. Moreover, the study reported that NGS was positive in > 70% of culture-negative patients [11].
Recent study by Chen et al proved that NGS outperforms traditional microbiological culture in pathogen detection, especially for rare and critical pathogens. Treatment protocols combining NGS, microbiological cultures, and pathological examinations are effective and provide valuable clinical insights for treating spinal infections [12].

Drawbacks :

NGS indiscriminately detects all nucleic acid molecules in specimens, including pathogenic bacteria, colonised bacteria, and exogenous nucleic acid molecules previously integrated into the human body, pathogens need to be distinguished from other bacteria. At the same time, the possibility of contamination, including contamination from specimens, reagents, and operating procedures, exists Therefore, it is necessary to balance the relationship between the sequencing cost, sequencing depth, and sequencing time of NGS from the aspects of sample processing, detection process, and bioinformatics analysis [9-11]

Conclusion:

NGS has emerged as a promising diagnostic tool for suspected spinal infections. As a novel diagnostic tool widely used in the field of infectious diseases, NGS has been proven to be a powerful molecular technique over conventional microbiological tests in spinal infections.
Metagenomic sequencing (mNGS), as an emerging non-culture-based technology with high sensitivity and specificity, fast detection and less affected by pre-sampling antibiotics,22,23 has shown higher sensitivity than traditional culture-based methods in the detection of pathogens

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