Next-Generation Sequencing as a Valuable Tool for Determination of Causative Microbial Agents in Bone and Soft-Tissue Infection

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Purpose: Bone and soft-tissue infections (BSTI) pose a serious and often debilitating threat to patient health. Although the gold standard for determination remains culture-based, it is not without fault. Cultures struggle with polymicrobial infections, overlook difficult-to-grow microbes, and cannot incubate organisms killed by antibiotics. Further, fungal and acid-fast bacilli (AFB) cultures have extensive turn-around times (TAT), worsening patient outcomes. We sought to improve the identification of BSTIs by supplementing the use of culture with a DNA-based approach in the form of next-generation sequencing (NGS).

Methods: We performed a review of prospectively collected data of 26 patients at a tertiary referral center presenting with previously confirmed or suspected BSTIs requiring surgical incision and drainage (I&D) or biopsy from May 2023 to August 2024. Patients received cultures from our institution and NGS from a third party.

Results: Group I included negative NGS results/positive cultures (5 of 26, 19.2%); Group II, positive NGS results/negative cultures (6 of 26, 23.1%); Group III, negative NGS results/negative cultures (7 of 26, 26.9%); and Group IV, positive NGS results/positive cultures (8 of 26, 30.8%). Within Group IV, 5 of 8 (62.5%) had partial agreement, 2 of 8 (25.0%) had full agreement, and 1 of 8 (12.5%) had no agreement. Mean and median TATs in days: aerobic ($\bar{x}$= 4.8; $\tilde{x}$ = 5), anaerobic ($\bar{x}$= 9.28; $\tilde{x}$ = 7), fungal ($\bar{x}$= 29.9; $\tilde{x}$ = 30), AFB ($\bar{x}$= 54.5; $\tilde{x}$ = 57), NGS collected-to-reported ($\bar{x}$= 6.96; $\tilde{x}$ = 6), and NGS received-to-reported ($\bar{x}$= 4.52; $\tilde{x}$ = 5). NGS was 42.5% cheaper than cultures.

Conclusion: We recommend NGS as a timely, affordable, and informative tool for concurrent use alongside culture-based detection in suspected or confirmed BSTIs requiring surgical intervention. NGS may improve patient outcomes by bypassing fungal and AFB wait times; by providing a determination when cultures are negative, such as after antibiotic use; and by highlighting the identity of rare or difficult-to-culture organisms in polymicrobial infections, the identity of which may be important in latent and recurring infections.