Fungal PJI: Attenuated Host Response and Lower Diagnostic Scores

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INTRODUCTION: Fungal periprosthetic joint infections (PJI) present unique diagnostic challenges compared to bacterial PJI, with distinctive clinical and laboratory profiles. A low prevalence has limited diagnostic research into fungal orthopedic infections. The goal of this study was to determine how the characteristics of fungal PJI differ from bacterial PJI in synovial fluid (SF).

METHODS: A retrospective analysis of SF samples from a single clinical laboratory was conducted. Inclusion criteria were: a modified 2018 ICM score >2, hip or knee aspirate, and isolation of a single organism. These criteria yielded 18,368 culture-positive samples, with 858 fungal and 17,510 non-fungal specimens. A comparative diagnostic analysis followed.

RESULTS:

Common fungal species were *Candida parapsilosis* (37.9%), *albican*s (35.0%), *glabrata* (8.5%), *auris* (2.6%), and *tropicalis* (2.3%). Fungal organisms required longer median incubation (32.4 vs 18.0 hours; p<0.001) than non-fungal organisms.

Fungal samples showed significantly lower median biomarkers: SF-CRP (7.8 vs 21.2mg/L), alpha-defensin (2.2 vs 3.1 S/CO), SF-WBC (6,256 vs 30,743 cells/µl), and SF-PMN% (82.2 vs 94.1%). This attenuated response resulted in reduced biomarker sensitivity: SF-CRP (64.8% vs 85.5%), alpha-defensin (86.7% vs 94.8%), SF-WBC (77.7% vs 95.4%), and SF-PMN% (78.1% vs 97.8%). Consequently, fungal samples showed lower ICM scores, with 5-fold higher fungal representation in ICM inconclusive versus infected samples (25.1% vs 4.1%; p<0.0001).

Candida antigen immunoassay levels were elevated in fungal culture-positive samples (5.2 vs 0.7 S/CO) and had higher positivity (86.1% vs 9.5%) than non-fungal samples. Alpha-defensin and Candida antigen demonstrated equivalent sensitivity for fungal organisms (86.7% vs 86.1%; p=1), both superior to SF-CRP, SF-WBC, and SF-PMN% (all p<0.0001).

DISCUSSION AND CONCLUSION:

Fungal PJI is characterized by longer culture incubation times, muted host inflammatory response, lower ICM scores, and higher representation in ICM inconclusive samples. Current PJI definitions, including 2018 ICM criteria, may underperform for fungal infections. Future diagnostic PJI definitions and tools should include the flexibility of using reduced thresholds or points for PJI when fungal organisms are isolated.