Fungal Periprosthetic Joint Infection Identification via Molecular Diagnostic Techniques

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INTRODUCTION: Fungal periprosthetic joint infections (PJI) are rare but particularly challenging to eradicate. Diagnosis of fungal PJI is difficult, as cultures do not always yield positive results. Recent advancements in molecular diagnostics have led to the integration of antigen testing, polymerase chain reaction (PCR), and next generation DNA sequencing (NGS) for diagnosing fungal PJI. However, the effectiveness of these new diagnostic studies to specifically detect fungal PJI has yet to be evaluated. The purpose of this study is to describe the utilization of these tests in diagnosing fungal PJI.

METHODS: This was a single-surgeon, single-institution retrospective review of all patients treated for fungal PJI. Demographic data, comorbidities, perioperative labs, and surgical variables were obtained from medical records. We identified 17 patients who met the Musculoskeletal Infection Society's criteria for PJI with a minimum of 6-month follow-up from time of explantation. Diagnostic studies of interest included serum inflammatory marker analysis and synovial fluid marker analysis, cultures, antigen testing (CD Diagnostics, Claymont, DE), PCR (MicroGen Diagnostics, Lubbock, TX), and NGS (MicroGen Diagnostics, Lubbock, TX).

RESULTS: There were 13 knees, 3 hips, and 1 shoulder included in the study period (2019-2021). The majority of patients were male (58.8%), ASA class 3 (88.2%), and had undergone 3 or more surgical procedures at the operative joint (82.3%). Polymicrobial infections were most common (52.9%) and the most common fungal species identified was *Candida* (82.3%). Preoperative serum inflammatory markers (ESR and CRP) were elevated in the majority of patients (70.6% and 76.5%, respectively). Complete preoperative synovial fluid analysis was available for 12 patients. All patients had positive alpha-defensin and leukocyte esterase markers, whereas 58.3% had a synovial white blood cell count >3,000 and 83.3% had neutrophils >80%. Preoperative cultures were positive for fungal organisms in 53.8% of patients. Preoperative aspirate studies were positive for fungal organisms in 90.9% of antigen tests, 0% of PCR tests, and 38.5% of NGS tests. Intraoperative cultures were positive for fungal organisms in 58.8% of patients. Of note, there were only 3 patients (17.6%) who were positive for fungal organisms with preoperative cultures, antigen testing, NGS, and intraoperative cultures.

DISCUSSION AND CONCLUSION:

In our study, preoperative cultures identified a fungal organism in just over half of the patients, which is similar to rates reported in the literature. In our series, antigen testing had the most number of positive results for fungal organisms whereas both PCR and NGS had fewer positive tests than preoperative cultures. Given that intraoperative cultures yielded positive tests for fungal organisms in just over half of the patients it is difficult to determine which diagnostic study truly identifies a fungal PJI. In fact, only 3 patients had concordance across cultures, antigen testing, and NGS suggesting that we may be over-diagnosing fungal PJI. As new diagnostic technologies continue to improve, it will be important to evaluate their effectiveness in accurately identifying fungal PJI. This will enable orthopaedic surgeons to confidently tailor their treatment to include antifungals to maximize the chance of fungal PJI eradication.

Molecular diagnostic techniques including antigen testing, PCR, and NGS represent new modes to diagnose fungal PJI. In this single-surgeon, single institution retrospective study, antigen testing identified fungal organisms in 90.9% of patients whereas PCR and NGS tests underperformed compared preoperative cultures. Additional investigation is needed to determine the utility of these new diagnostic technologies for fungal PJI.