Delegates:
Emara, Khaled
Embil, John M

Editor:
O'Neil, Joseph
Aiyer, Amiethab
McDonald, Elizabeth

F- 7 - SYNOVIAL BIOMARKERS DX

F- 7 - Is there a role for measuring synovial biomarkers for diagnosis of infected total ankle arthroplasty?

Response/Recommendations:

Yes, measuring synovial biomarkers may play a role in the diagnosis of infected total ankle arthroplasty. The diagnosis of PJI in the setting of a TAA can be confirmed with cultures, provided that a plausible pathogen is recovered in the context of a compatible clinical picture. In the absence of a positive culture, synovial biomarker analysis may help in establishing the diagnosis.

Strength of the Recommendation: Moderate

Rationale:

Total ankle arthroplasty (TAA) has emerged as a successful procedure, improving both pain and function in patients with end-stage arthritis of the ankle. Infections rates of 0-4.6% have been reported.[1] A specific approach does not yet exist for the diagnosis of periprosthetic joint infection (PJI) in TAA. However, the traditional approach for the diagnosis of PJI in other joints involves joint aspiration and sampling of the synovial fluid for analysis, consisting of synovial white blood cell count and differential, culture of the fluid, as well as serum white blood cell count (WBC), erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels.[2,3]

Elevation of several synovial biomarkers has been identified as an indication of potential PJI, including leukocyte count, percentage of polymorphonuclear cells (PMN%), α defensin, leukocyte esterase, interleukin IL-1a, IL-1, IL-6, IL-8, IL-10, IL-17, granulocyte colony-stimulating factor (G-CSF), vascular endothelial growth factor (VEGF), CRP, neutrophil elastase 2 (ELA-2), lactoferrin, neutrophil gelatinase-associated lipocalin (NGAL), resistin, thrombospondin, and bactericidal/permeability-increasing protein (BPI).[4–6] Among the previously mentioned synovial biomarkers, α-defensin is regarded as the most accurate single test for the diagnosis of PJI, with a sensitivity of 97% and a specificity of 96%.[5] Therefore, the accuracy of PJI α-defensin is closest to the 2013 International Consensus Meeting (ICM) criteria for the diagnosis of PJI.[6] α-defensin also appears to provide the most consistent results, regardless of the causative microorganism or its virulence. Its accuracy even remains unaffected in the setting of antibiotic administration to the patient prior to obtaining the synovial fluid sample.[4,5,7] Interleukin-8 follows α-defensin in terms of performance, while the accuracy of synovial fluid culture has been shown to have a sensitivity of 62% and specificity of 94%.[5]

Synovial fluid leukocyte count (sensitivity of 89% and specificity of 86%) and PMN percentage (sensitivity of 89% and specificity of 86%) both demonstrate accuracy in diagnosing PJI.[5,6] However, they are already part of the 6 minor criteria for diagnosis of PJI according to the ICM 2013 definition of PJI.[6] There is great controversy regarding the cutoff point used for the synovial leukocyte count and PMN percentage, which prevents their use as stand-alone diagnostic tests.[4,5,5,8–12] Leukocyte esterase, with a sensitivity of 77% and specificity of 95%, has the advantage of being inexpensive.[5,13–16] However, there is a level of subjectivity present with the interpretation of the results, in addition to the possibility of the presence of blood in the fluid affecting the results.

The combination of two or more markers to detect PJI has been studied. It has been shown that the combination of synovial fluid α-defensin and CRP provided a sensitivity of 97% and a specificity of 100% in diagnosing PJI.[17] The combined use of synovial CRP and adenosine deaminase (ADA) improves the positive predictive value.[18] A synovial fluid CRP should be included in the synovial fluid analysis and correlated with other lab markers.[17]

Conclusion: The diagnosis of PJI in the setting of a TAA can be confirmed with cultures, provided that a plausible pathogen is recovered in the context of a compatible clinical picture. In the absence of a positive culture, synovial biomarker analysis may help in establishing the diagnosis.

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