Routine Use Of A Multiplex Serological Assay In The Management of Prosthetic joint Infection

A-L. ROUX1,4, F. EL Sayed1,4, A. Bicard-See1,4, T. Bauer1,4, B. Combœuri1ex, C. Nick3, G. Giordano4, E. Bonnet2, J-L. Herrmann1,4, J-L. Gaillard1,4, M. Rottman1,4
1Hôpital Ambroise Paré (AP-HP), Boulogne-Billancourt; 2Hôpital Joseph Ducoule, Toulouse3; 3Hôpital Raymond Poincaré (AP-HP), Garches, 4UMR 1173, INSERM, UFR Simone Veil, Université de Versailles Saint-Quentin-en-Yvelines; France.

BACKGROUND
The diagnosis of prosthetic joint infections (PJI) is a critical challenge for orthopedic surgeons and infectious disease specialists. The diagnosis of PJI is often delayed because non-invasive assays lack sensitivity and specificity.

Bill Inoplex™ is a CE-IVD marked serological Multiplex Antibody Detection (MAD) assay quantifying antibodies against Staphylococcus aureus, S. epidermidis, S. lugdunensis, Propionibacterium acnes and Streptococcus agalactiae to assist in the diagnosis of chronic and delayed PJI. The Lumines® based assay measures serum IgG against an array of recombinant purified antigens that are informative in the context of PJI.

GOAL
To evaluate the performance of the MAD immunoassay in the routine care of patients suspected of PJI in three French centers. The gold standard was the intraoperative microbiological documentation according to IDSA guidelines.

PATIENTS, MATERIALS AND METHODS
Cases were extracted from the US of the microbiology laboratory of Hôpital Poincaré, France between the dates of Apr 9 2015 and Apr 9 2016. 363 assays were performed on 314 patients. Of those, 80 patients had a revision arthroplasty performed within three weeks with available microbiological documentation and accessible records. Antibiotics were withheld at least 14 days before surgery. Bacteriological documentation was obtained from at least three beadmilled intraoperative tissue and hardwre samples or synovial fluid cultures, with blood culture media enrichment for 14 days.

Bill Inoplex™ MAD assay was performed according to the manufacturer’s instructions on a Lumines® Magpix instrument. For interpretation, patients with ‘Negative’ or ‘Indetermined’ results were not considered infected with the target organism. All staphylococcal species were considered to match the ‘Staphylococcus’ MAD assay due to cross-reactivity.

PJI patients whose index arthroplasties had occurred less than 3 months prior to the MAD assay were categorized as ‘acute’ cases vs ‘delayed/chronic’ cases. Patients with negative culture or with a culture positive for other organisms were considered ‘not infected’ with the target organism.

Patients with an acute infection occurring more than 2 years after surgery were defined as Acute Hematogenous PJI cases

RESULTS

Test principle: Diagnose Staphylococcus, Streptococcus agalactiae and P. acnes PJI

1] Patient generates a humoral response
2] Draw blood
3] Simultaneously quantify IgG binding 16 bacterial proteins
4] Antibody profiling
Result: Prosthetic Joint Infection with Staphylococcus sp
Streptococcus agalactiae Propionibacterium
YES/NO YES/NO YES/NO

Species TP FP FN TN Sen (%) Spe (%) PPV (%) NPV (%)
Staphylococcus-Chronic 20 2 1 36 95,2% 94,7% 90,9% 97,3%
Staphylococcus-Acute 1 2 9 36 10,0% 94,7% 33,3% 80,0%
S. agalactiae 2 7 0 69 100,0% 90,8% 22,2% 100,0%
P. acnes 2 6 3 67 40,0% 91,8% 25,0% 95,7%

Acute Hematogenous infections
Seven cases of AH-PJI were among the 21 acute cases. The assay was negative in five cases. Preoperative aspiration yielded K. pneumoniae in one case with positive a Staphylococcus Bill Inoplex™ result. Definitive documentation evidenced a co-infection with K. pneumoniae and S. capitis. In a case of AH-PJI with S. aureus documentation and P. acnes positive Bill Inoplex™ result, PCR hybridization yielded a diagnosis of P. acnes and S. aureus co-infection. AH-PJI is amenable to debridement and implant retention. However, an underlying chronic infection can be suspected based on the positivity of MAD assay in an acute context. Implant revision could be preferred in these cases.

Conclusion
Bill Inoplex™ is a novel multiplex serological test which allows the rapid and non-invasive documentation of PJI caused by Staphylococcus sp., Streptococcus agalactiae and Propionibacterium acnes.

The routine use of the test yielded very good performance in this retrospective study involving consecutive patients. The performance of the S. agalactiae and P. acnes assays are comparable to published results but the number of cases too limited to draw conclusions.

In acute PJI, the assay is excellent in chronic or delayed cases with a sensitivity and specificity of >95%.

In acute settings the assay is expected to be negative due to the time required to mount a humoral response specific of PJI.

Microbiologically significant isolates chronic acute
Staphylococcus aureus 8 8
Staphylococcus epidermidis 10 3
Staphylococcus lugdunensis 2
Staphylococcus capitis 2
Staphylococcus schleiferi 1
Enterococcus faecalis 2
Streptococcus agalactiae 1
Streptococcus dysgalactiae 1
Dermabacter hominis 1
Corynebacterium striatum 2
Corynebacterium amycolatum 1
Propionibacterium acnes 3 1
Propionibacterium avidum 2
Finegoldia magna 1
Peptostreptococcus harei 1
Citoabacter freundii 1
Citoabacter koseri 1
Margarbella morganii 1
Serratia marcescens 1
Salmonella enterica 1
Enterobacter cloacaee 2 1
Escherichia coli 4 4
Klebsiella pneumoniae 4 2
Pseudomonas aeruginosa 4 2

Implant Location

Timing of Infection

Acute
Chronic
Hematogenous
Infection
Invasive
Microbiology
Implant
Infection
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology
Invasive
Microbiology