Tuesday, 28 April 2015 – 12:30 - 13:30 – Poster Session P74

Poster session P74 - Biofilm: formation, pathogenesis, diagnosis


Simon MARMOR1, Thomas BAUER2, Nicole DESPLACES3, Beate HEYM1, Olivier SOL1, Julie ROGE1, Florence MAHE5, Laurent DESIRE5, Idir GHOUT6, Jean-Louis GAILLARD7, Martin ROTTMAN8.

1Service de Chirurgie Orthopédique - Groupe Hospitalier Diaconesses La Croix St Simon, Paris, France.
2Service de Chirurgie Orthopédique et Traumatologie - Hôpital Ambroise Paré, Boulogne-Billancourt, France.
3Service de Microbiologie - Groupe Hospitalier Diaconesses La Croix St Simon, Paris, France.
4Laboratoire de Microbiologie - Hôpital Ambroise Paré et EPIM EA 3647, UFR Simone Veil, Université de Versailles-St Quentin, Boulogne-Billancourt, France.
5DIAXONHIT, Paris, France.
6Unité de Recherche Clinique Paris Ouest URCPO - Hôpital Ambroise Paré, Boulogne-Billancourt, France.
7Laboratoire de Microbiologie - Hôpital Ambroise Paré et EPIM EA 3647, UFR Simone Veil, Université de Versailles-St Quentin, Boulogne-Billancourt, France.
8Laboratoire de Microbiologie - Hôpital Raymond Poincaré et EPIM EA 3647, UFR Simone Veil, Université de Versailles-St Quentin, Garches, France.

Objectives: The diagnosis of prosthetic joint infections (PJI) represents a critical challenge for orthopedic surgeons and infectious disease specialists. The diagnosis of PJI is often delayed because the available diagnostic tools lack of both sensitivity and specificity. A novel multiplex immunoassay measuring antibodies was developed against the main causative agents of PJI. We performed a prospective, multicenter, non-interventional study in order to evaluate its diagnostic performance.

Methods: This serological test is a Luminex-based assay using a panel of recombinant purified antigens that allows the measurement of serum IgG against Staphylococcus aureus, Staphylococcus epidermidis, Staphylococcus lugdunensis, group B streptococcus and Propionibacterium acnes. Adult patients having an indication of revision arthroplasty, whatever the reason (ie, suspicion of PJI or not), were included over a 2-year period (from 2012 up to 2014) in two French reference centers. Only patients who did not oppose the blood draw and the use of their medical data according to IRB and French regulations were considered. A PJI case was defined as a patient who had at least 2 different intraoperative tissue samples yielding the same microorganism.

Results: A total of 484 patients were included and 455 were eligible for study analyses. The main characteristics of the study population were as follows: mean [+/- sd] age: 71 [+/- 23.7] years; male/female ratio: 0.91; localisation of prostheses: hip=66.3%, knee=29.7%, shoulder=4.0%; mean [+/- sd] time since prosthesis insertion: 7.5 [+/- 9.1] years). Among the 455 eligible patients, 149 (32.7%) were found to be infected according to the intraoperative microbiological criteria. Among the most frequent infecting species recovered were S. aureus (30%), S. epidermidis (26%), P. acnes (9%), S. lugdunensis (6%), and group B streptococcus (4%). The sensitivity and specificity values of the test were, respectively, 75.9% (63/83) and 82.2% (180/219) for staphylococci (S. aureus, S. epidermidis, S. lugdunensis), 38.5% (5/13) and 81.9% (190/232) for P. acnes, and 66.7% (4/6) and 92.4% (208/225) for group B streptococci. Interestingly, all cases (9/9) involving S. lugdunensis were detected by the test and the sensitivity for S. epidermidis reached 89.5% (17/19) in the subpopulation with elevated inflammatory markers (ESR>30 and CRP>10).

Conclusion: This first multiplex serological test allows a rapid and non-invasive diagnosis of PJI, at the species or genus level, and covers the most frequent panel of bacteria involved in these infections. This diagnostic immunoassay shows a good correlation with the microbiological culture results and appears to be a new promising tool in the management of PJI.
Validation of a multiplex serological immunoassay for the non-invasive diagnosis of prosthetic joint infections. A non-interventional prospective study

Simon MARMOR1, Thomas BAUER2, Nicole DESPLACES3, Beate HEYM4, Olivier SOL5, Julie ROGE6, Florence MAHE7, Laurent DESIRE7, Idir GHOST8, Jean-Louis GAILLARD9, Martin ROTTMA10

1Service de Chirurgie Orthopédique - Groupe Hospitalier Hôpitaux de Lyon - Hôpital La Croix-Rousse, Lyon, France; 2Service de Chirurgie Orthopédique et Traumatologie - Hôpital Ambroise Paré, Boulogne-Billancourt, France; 3Service de Microbiologie - Groupe Hospitalier Hôpitaux de Lyon - Hôpital Calmette, Nice, France; 4Service de Microbiologie - Hôpital Ambroise Paré et EPM EA 3647, UFR Simon Veil, Université de Versailles-St Quentin, Boulogne-Billancourt, France; 5Unité de Recherche Clinique Hôpital Paré Ouest URCPO–Hôpital Ambroise Paré, Boulogne-Billancourt, France; 6Laboratoire de Microbiologie – Hôpital Raymond Poincaré et EPM EA 3647, UFR Simon Veil, Université de Versailles-St Quentin, Garches, France.

Introduction and Purpose

- **Objectives**: The diagnosis of prosthetic joint infections (PJI) represents a critical challenge for orthopaedic surgeons and infectious disease specialists. The diagnosis of PJI is often delayed because the available diagnostic tests lack both sensitivity and specificity. A novel multiplex immunoassay measuring antibodies was developed against the main causative agents of PJI. We performed a prospective, multicenter, non-interventional study in order to evaluate its diagnostic performance.

- **Methods**: This serological test is a Luminex-based assay using a panel of recombinant purified antigens that allows the evaluation of serum IgG against Staphylococcus aureus, Streptococcus pyogenes, Streptococcus lugdunensis, group B streptococcus B, Staphylococcus aureus, and Propionibacterium acnes. Adult patients having an indication of revision arthroplasty, whatever the reason (e.g., suspicion of PJI or not), were included over a 2-year period from 2012 up to 2014 in two French reference centers. Only patients who did not oppose the blood draw and the use of their medical data according to IRB and French regulations were considered. A PJI case was defined as a patient who had at least 2 different invasive tissue samples yielding the same microorganism.

- **Results**: A total of 484 patients were included and 455 were eligible for study analyses. The main characteristics of the study population were as follows: mean ± (SD) age: 71 ± 23.7 years; male/female ratio: 0.81; localization of prosthesis: hip = 68.3%, knee = 29.7%, shoulder = 4.0%; mean ± (SD) time since prosthesis implantation: 7.5 ± 9.1 years). Among the 455 eligible patients, 149 (32.7%) were found to be infected according to the intraoperative microbiological criteria. Among the most frequent infecting species recovered were S. aureus (30%), S. epidermidis (26%), P. acnes (9%), S. lugdunensis (6%), and group B streptococcus (4%). The sensitivity and specificity values of the test were, respectively, 75.9% (63/83) and 82.2% (180/219) for staphylococci (S. aureus, S. epidermidis, S. lugdunensis), 38.5% (5/13) and 81.9% (190/232) for P. acnes, and 66.7% (4/6) and 92.4% (208/225) for group B streptococcus. Interestingly, all cases of S. lugdunensis were detected by the test and the sensitivity for S. epidermidis reached 89.5% (17/19) in the population with elevated inflammatory markers (ESR≥30 and CRP≥10).

2 - Test principle

- **Test characteristics**: 1st serological test to detect the immune response due to PJI
- The 16 antigens are coated onto the surface of microspheres
- Rapid (2h) processing vs culture (up to 14 days)
- Non-invasive
- Polymerase detection in a single test
- Detects the most prevalent microorganisms causing PJI

3 - Analysis and interpretation

- **Microbial species**
  - S. aureus
  - S. epidermidis
  - S. lugdunensis
  - S. agalactiae
  - Propionibacterium acnes

4 - Results of the validation study

1 - Study Population

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Male/Female</th>
<th>Positive cases</th>
<th>Negative cases</th>
<th>Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>69±10.1</td>
<td>95/105</td>
<td>45/100</td>
<td>140/200</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>71±13.2</td>
<td>110/105</td>
<td>43/75</td>
<td>183/180</td>
<td>89%</td>
<td>90.5%</td>
</tr>
<tr>
<td>75±13.6</td>
<td>100/105</td>
<td>68/83</td>
<td>168/188</td>
<td>90%</td>
<td>92%</td>
</tr>
<tr>
<td>80±13.8</td>
<td>85/105</td>
<td>56/65</td>
<td>151/157</td>
<td>80%</td>
<td>83%</td>
</tr>
</tbody>
</table>

- **Microbial species from the test**: Test results from the 29 patients carrying a prosthetic infected by a different bacteria than those claimed from the Staph., Strps or Pcpp. genus.

5 - Additional results with other bacterial species:

6 - Conclusion

- **BJI InoPlex® is a novel multiplex serological test which allows the rapid and non-invasive diagnosis of the most frequent PJI pathogens, showing a good correlation with microbiological culture and appears to be a new promising tool in the management of PJI**
- The sensitivity and specificity values of the test were, respectively, 75.9% and 82.2% for staphylococci, 38.5% and 92.4% for P. acnes, and 66.7% and 92.4% for group B streptococcus. Sensitivity for S. aureus, S. epidermidis, S. lugdunensis reached 89.5% in the population with elevated inflammatory markers (ESR≥30 and CRP≥10).
- **The sensitivity for S. epidermidis reached 89.5% in the subgroup with elevated inflammatory markers (ESR≥30 and CRP≥10)**
- **Differential analyses of sensitivity in the different subgroups (prosthesis site, time since prosthesis implantation, ESR and/or CRP positive ...) are ongoing.**