401. Predictors of Treatment Failure for Hip and Knee Prosthetic Joint Infections in the Setting of Prosthesis Removal: A Multi-Center Retrospective Cohort
Christopher Kandel, MD; Richard Jenkinson, MD, MSc; Nick Daneman, MD, MSc; David Backstein, MD; Matthew P. Muller, MD, FRCP(C), PhD; Kevin Katz, MD, MSc, FRCP(C); Abhijit Sajja, MBBS; Felipe Garcia Jeldes, MD; 1University of Toronto, Toronto, ON, Canada; 2St. Michael’s Hospital, Toronto, ON, Canada; 3North York General Hospital, Toronto, ON, Canada; 4CHU de Québec – Université Laval, Laval, QC, Canada
Session: 48. Infections of Joints
Thursday, October 3, 2019: 12:15 PM

Background. Prosthetic hip and knee joint infections (PJIs) are challenging to eradicate despite prosthesis removal and long courses of antibiotics. We aimed to describe the risk factors for PJI treatment failure in a multicenter retrospective cohort.

Methods. A retrospective cohort of individuals who underwent prosthetic joint removal for a PJI at one of five hospitals in Toronto, Ontario, Canada from 2010–2014. Individuals eligible for the cohort were obtained by searching operative listings and PJIs were defined according to the criteria of the Musculoskeletal Infection Society. Treatment failure was defined as recurrent PJI, amputation, death or chronic antibiotic suppression. Potential risk factors for treatment failure were abstracted by chart review and assessed using a Cox proportional hazards model.

Results. 533 PJIs were analyzed over a median follow-up duration of 1102 days with 21 surgeries performing more than 5 revision arthroplasties for a PJI. Two-stage procedures were performed in 81% (430/533) and the most common organism was coagulase negative staphylococci (32%). Treatment failure occurred in 28% (150/533) over 1443 patient years and was caused by a different bacterial species in 53% (56/107). On multivariate analysis the characteristics associated with PJI treatment failure included liver disease (adjusted hazard ratio (aHR) 3.12, 95% confidence interval (95% CI) 2.09-4.66), the presence of a sinus tract (aHR 1.53, 94% CI (1.12-2.10), preceding diabetes with progression treatment (aHR 1.68, 95% CI 1.13-2.51), a one-stage procedure (aHR 1.72, 95% CI (1.28-2.32), and infection due to Gram-negative bacilli (aHR 1.35, 95% CI 1.04-1.76).

Conclusion. PJI treatment failure remains high despite prosthesis removal and the patient risk factors identified are non-modifiable. Novel treatment options are urgently needed along with efforts to reduce orthopedic surgical site infections.

Disclosures. All authors: No reported disclosures.

402. Clinical Characteristics and Outcome of Staphylococcus lugdunensis Prosthetic Joint Infections
Komal Massod, MD1; Jean Duggan, MD, FACP, AAHIVS; Roberta Redfern, PhD2; Gregory Georgiadis, MD, and Geetha Suleyman, MD2; 1University of Toledo Medical Center, Toledo, Ohio; 2Promedica Health System, Toledo, Ohio; 3ProMedica Health System, Toledo, Ohio
Session: 48. Infections of Joints
Thursday, October 3, 2019: 12:15 PM

Background. Although Staphylococcus lugdunensis is a coagulase-negative staphylococcus, it shares similar characteristics with S. aureus and is increasingly recognized as the cause of serious infections, including prosthetic joint infections (PJIs). The aim of this study was to determine the clinical characteristics and outcome of S. lugdunensis PJIs.

Methods. This was a retrospective multicenter study conducted from January 2007 to December 2017 involving consecutive adult patients with S. lugdunensis PJIs in northwest Ohio. Clinical and microbiologic characteristics, treatment modalities and outcome were evaluated.

Results. A total of 695 patients were evaluated and 24 (4%) patients met inclusion criteria (Table). All patients were Caucasian and 52% were female with a median age 68.8. Comorbidities included Diabetes Mellitus (34%), CAD (41%), CHF (20%), COPD (20%) and cancer (14%). The most common clinical presentations were pain (28/29, 97%), decreased range of motion (27/29, 93%) and joint swelling (21/29, 72%). Two patients had concomitant bacteremia. Knee was the most commonly affected joint (69%), followed by hip (24%). All isolates, except one, were susceptible to oxacillin. Thirteen (45%) patients had a two-stage revision, nine (31%) debridement without revision, six (21%) no surgical intervention and one (3%) a 1-stage revision. The majority of patients (71%) received 21-26 weeks of antibiotics (abs). Two patients with surgical intervention and one with debridement received no abs. One patient was discharged to hospice without intervention. Relapse was observed in two (15%), patients who had a 2-stage revision, four (44%) who had debridement, 6 (100%) who had no surgical intervention or 1-stage revision. Overall, there was a statistically significant difference in cure rates in patients treatment 2-stage revision compared with other treatment modalities (P = 0.003) regardless of abs treatment regimen, including prolonged IV abs therapy. However, IV abs were superior to oral (P = 0.009).

Conclusion. Appropriate management of S. lugdunensis PJIs includes both aggressive surgical management with a prolonged course of abs with excellent clinical responses. Relapse is high in patients treated without two-stage revision irrespective of route or duration of abs therapy.

Disclosures. All authors: No reported disclosures.

403. Clinical Features and Treatment Outcome of Enterobacter Prosthetic Joint Infections
Dima Youssif, MD; Babak Hoosemand, MD and Ashish Bhardwaj, MD
Session: 48. Infections of Joints
Thursday, October 3, 2019: 12:15 PM

Background. Enterobacter prosthetic joint infections (PJIs) are rare, occurring mainly in elderly people usually with complex medical and surgical history, and their treatment is usually challenging. Aim of this study is to assess the characteristics and outcome of Enterobacter PJIs.

Methods. A retrospective multi-centric cohort was studied at three hospitals from January 2012 to December 2018. Patients with PJIs were identified using ICD codes. Enterobacter PJIs were then identified through reviewing patients’ electronic medical records.

Results. 13 enterobacter PJIs were included. 9 (69%) were polymicrobial. Mean age of the patients was 61.7 years, and mean BMI was 34.6 kg/m2. 8 patients (62%) were females, and 8 patients (62%) were Caucasians. Infected sites were: Hip in 5 patients (38%), knee in 5 patients (38%) and ankle in 3 patients (23%). Patients 9. (69%) had osteoarthritis, 3 patients (23%) had diabetes mellitus, and 1 patient (8%) had connective tissue diseases requiring steroids. Most patients (11 out of 13) (85%) presented within 1 week of symptoms onset. Presenting clinical features were pain in 9 patients (69%), drainage in 10 patients (77%), purulence in 7 patients (54%), and fever in 5 patients (38%). 11 patients (85%) were managed with debridement, antibiotics and implant removal (DAIR), and 2 patients (15%) with antibiotics alone. Antibiotics used while managing were as follows: Ceftizime n = 6, quinolones n = 2, carbapenems n = 4 and aminoglycosides n = 1. Outcome: 4 patients (31%) developed deep surgical site infections (and two of them required implant removal), 5 patients had no events in 12 months of follow-up, 3 patients (23%) had less than 6 months of follow-up, and one patient died in the hospital due to cardiac failure.

Conclusion. In our study, most cases of Enterobacter PJIs were polymicrobial. The success in monomicrobial infections was 75% while overall it was noted to be 38%. DAIR was associated with high readmission rates and deep surgical site infections (36%). 18% cases managed with DAIR required implant removal.

Outcome of Enterobacter PJIs:

| Treatment                  | Number of Patients | 12 months follow up |
|----------------------------|--------------------|---------------------|
| DAIR                       | 1                  | Deep surgical site infection requiring implant removal |
|                            | 1                  | No events           |
| One Stage Revision         | 1                  | No events           |
| Two Stage Revision         | 1                  | No events           |

Disclosures. All authors: No reported disclosures.
Methods. miRNA from serum and RNA from PBMCs were acquired from n = 40 participants in a prospective cohort of Filipino septic patients; n = 15 developed septic shock and n = 17 developed renal failure. RT-qPCR was done to measure the expression of 21 sepsis-associated miRNAs. Differentially expressed miRNAs (DEMs) for each outcome were identified, followed by gene target prediction for each DEM. Gene expression microarrays covering 18,616 genes were also performed to identify differentially expressed genes (DEGs; P < 0.05, log FC> |0.3|) for each outcome. Significant miRNA-gene pairs were selected by evaluating the overlap of the predicted gene targets of the DEMs with the DEGs for each corresponding outcome. Given the gene-silencing mechanism of miRNAs, overlap analysis was performed on only the downregulated DEGs when the specific DEM was upregulated (and vice versa).

Results. Septic participants who developed shock, compared with those who did not, had higher expression of 1 DEM, miR-223-5p, and downregulation of 20 DEGs. NUS1 was the only predicted gene target of miR-223-5p that was also downregulated in septic shock. Participants who developed renal failure, vs. those who did not, had lower expression 6 DEMs and upregulation of 6 DEGs. KPN44 is a gene target of the DEMs, miR-126-5p, and miR-181a-5p, that was also upregulated in renal failure.

Conclusion. Significant miRNA-gene pairs related to worse clinical outcomes in sepsis were identified: miR-223-5p with NUS1 for shock and either miR-126-5p or miR-181-5p with KPN44 for renal failure. While the biological significance of these miRNA-gene pairs still needs to be evaluated, these findings can potentially help future efforts in developing prognostic markers or therapeutic targets for shock and renal failure in sepsis.

Disclosures. All authors: No reported disclosures.

405. Serum Antibody Responses Against Carbapenem-Resistant Klebsiella pneumoniae in Infected Patients
Kasturi Banerjee, PhD1; Michael Molley, BS2; Elizabeth Diago-Navarro, PhD MPH1 and Bettina C. Fries, MD/FIDSA2; Stony Brook University, Stony Brook, New York; Stony Brook University Hospital, Stony Brook, New York

Session: 49. Inflammation and Infectious Diseases
Thursday, October 3, 2019: 12:15 PM

Background. Capsular polyaccharide (CPS) of Carbapenem-resistant K. pneumoniae ST258 (CR-Kp) is a potential vaccine target. CPS of these isolates generally falls within two homology groups named clade 1 and clade 2. We and others have made antibodies (Abs) that act against clade2 CR-Kp but failed to make therapeutic Abs against clade1 CR-Kp. Previous studies had shown that studying patient’s antibody responses could help in identifying suitable candidates for developing immunotherapies. Thus, we sought to identify potential vaccine candidates by investigating the humoral response CPS in CR-Kp-infected patients.

Methods. 24 CR-Kp isolates and corresponding serums were collected from inpatients at Stony Brook Hospital. CPS was isolated and purified by size-exclusion chromatography from CR-Kp strains 31 (clade 2), 36 (clade 1), and 38 (clade-Other). Anti-CPS Abs in patient’s serum were detected by enzyme-linked immunosorbent assay (ELISA) and bulk Abs from positive serum were purified using an affinity column. These Abs were tested for activity against CR-Kp by serum bactericidal and agglutination assays.

Results. 50% of clade2 CR-Kp-infected patients had humoral responses against CPS34, 77% of clade 1-infected patients sera cross-reacted with CPS34, but none of them developed Abs against CPS36. Interestingly, 90% of clade1 and 60% of clade 2-infected patients, respectively, showed Abs binding to CPS38. Thus, we selectively purified Anti-CPS Abs from two clade-Other-infected patients and observed that they were cross-reactive with all three CPSs. Further, these Anti-CPS Abs agglutinated all tested CR-Kp isolates (34, 36, and 38) when compared with control human IgG (P < 0.005). Additionally, these Anti-CPS Abs promoted killing of clade2 bacteria and inhibited the growth of clade 1 bacteria in Ab-mediated serum bactericidal assay. These data elucidate that humoral responses developed in clade-Other individuals may be protective in clade1 CR-Kp-infected patients with therapeutic potential.

Conclusion. With the availability of effective antimicrobials for CR-Kp, approaches like developing novel anti-CPS vaccine could serve as an alternate therapy. Our data suggest that developing immunotherapies targeting CPS38 could potentially provide protection across both clade1 and clade2 bacteria in clinical settings.

Disclosures. All authors: No reported disclosures.

406. Cloning Antibodies Against Kawasaki Disease from Acute Plasmablast Responses
Sarah Baron, BS; Hakimuddin T. Sojar, PhD and Mark D. Hicar, PhD; University at Buffalo, Buffalo, New York

Session: 49. Inflammation and Infectious Diseases
Thursday, October 3, 2019: 12:15 PM

Background. Kawasaki Disease (KD) is a childhood vasculitis, marked by prolonged fever and coronary artery inflammation/anerysm in near one-quarter of those untreated. The cause remains unknown; however, epidemiologic and demographic data support a single preceding infectious agent may lead to KD. Plasmablasts (PBs) are a stage of transitional B-cells that lead to plasma cells, the long-lived antibody-producing cells of the bone marrow. After initial infection, peripherally circulating PB populations are enriched for cells with antibodies against the preceding infection. We have recently published data showing children with KD have similar PB responses to children with infections. We sought to define the antibody characteristics, including clonality, of these PBs during KD.

Methods. We used antibody repertoire next-generation sequencing to characterize memory and PB populations. Additionally, pairing of heavy and light chains was performed with Chromium Single Cell Gene Expression (10x Genomics, Pleasanton, CA) using the Human B cell Single Cell VDJ Enrichment Kit.

Results. From subject 24, antibody sequences using VH4-34 and a 19 amino acid length complementarity determining region 3 showed a massive expansion between days 4 and 6 of fever. Chromium single-cell sequencing produced over 946 heavy and light chain paired sequences. Sequence comparison showed 40% of sequences demonstrated markers of clonal expansion, which represented 100 clonal groups. Seven other KD subjects are being processed and comparative analysis will be presented.

Conclusion. This clonal expansion within plasmablast populations supports that Kawasaki disease is caused by an infection. Antigen targeting of these monoclonal antibodies is currently being explored.