Renal Allograft Rejection
(Part 1)
By
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Renal Allograft Rejection

PART - I

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Objectives

• Banff Grading System
• Acute Cellular rejection [Pathology, Diagnosis, Management]
• Chronic T-Cell mediated rejection
• Antibody Mediated Rejection:
  ✓ Impact
  ✓ Mechanism and Pathogenesis
  ✓ DSA
  ✓ Pathology
  ✓ Prevention
The Banff 2017 Meeting Report

American Journal of Transplantation

Banff lesion grading system

Acute lesions:
- Inflammation (i),
- Tubulitis (t),
- Intimal arteritis (v),
- Glomerulitis (g),
- Peritubular capillaritis (ptc score),
- Total inflammation (ti),
- Inflammation in area of interstitial fibrosis and tubular atrophy: i-IFTA score

0: < 10%
1: < 25%
2: 25 – 50%
3: > 50%

Quantitative criteria for C4d score

- **C4d0** No staining of PTCs (0%)
- **C4d1** Minimal C4d staining (>0 but <10% of PTCs)
- **C4d2** Focal C4d staining (10–50% of PTCs)
- **C4d3** Diffuse C4d staining (>50% of PTCs)

Chronic Lesions:

- Quantitative criteria for double contour: cg score [cg0, cg1a, cg1b, cg2, cg3]
- Quantitative criteria for mesangial matrix expansion: mm score
- Quantitative criteria for arteriolar hyalinosis: ah score
- Alternative quantitative criteria for hyaline arteriolar thickening: aah score
- Quantitative criteria for vascular fibrous intimal thickening: cv score
- Quantitative criteria for interstitial fibrosis: ci score
- Quantitative criteria for tubular atrophy: ct score

0: No
1: < 25%
2: 25 – 50%
3: > 50%

cg1a No GBM double contours by light microscopy but GBM double contours (incomplete or circumferential) in at least 3 glomerular capillaries by EM, with associated endothelial swelling and/or subendothelial electron-lucent widening

 ci0 Interstitial fibrosis in up to 5% of cortical area
Acute T cell-mediated (cellular) rejection
• Acute TCMR occurs most commonly **within the 1st year** after transplantation

• TCMR **rarely occurs after 5 years** posttransplant

• Associated with a **reduction in long-term allograft survival**
• Acute TCMR is caused by T cells that react to donor histocompatibility antigens present within tubules, interstitium, vessels, and glomeruli of the allograft

• However, natural killer (NK) cells, macrophages, and other cells may also contribute

• The degree of allograft dysfunction may correlate better with the degree of monocyte compared with T cell infiltration
The Banff classification of Acute TCMR

**Borderline:**

Mild interstitial inflammation (<25 % of nonsclerotic cortical parenchyma; i0 or i1) + any tubulitis (t1, t2, or t3)

OR Significant interstitial inflammation (>25 % of nonsclerotic cortical parenchyma; i2 or i3) + foci of mild tubulitis (t1)

**Type IA:** Significant interstitial inflammation (>25 % of nonsclerotic cortical parenchyma; i2 or i3) and foci of moderate tubulitis (t2) involving 1 or more tubules, not including tubules that are severely atrophic

**Type IB:** Significant interstitial inflammation (>25 % of nonsclerotic cortical parenchyma; i2 or i3) and foci of severe tubulitis (t3) involving 1 or more tubules, not including tubules that are severely atrophic
The Banff classification of Acute TCMR

- **Type IIA:** Mild-to-moderate intimal arteritis *(v1)* with or without interstitial inflammation and/or tubulitis

- **Type IIB:** Severe intimal arteritis comprising >25% of the luminal area *(v2)* with or without interstitial inflammation and/or tubulitis

- **Type III:** Transmural arteritis and/or arterial fibrinoid change and necrosis of medial smooth muscle cells with accompanying lymphocytic inflammation *(v3)* with or without interstitial inflammation and/or tubulitis
• The diagnosis of acute TCMR requires a histologic score of at least $t_2$ and $i_2$. **Any scores below this (eg, $i_1+t_2$ or $i_2+t_1$) are considered to be borderline rejection.**

• The significance of the presence of **intimal arteritis alone** (eg, $v_1$) is controversial but still allows for the diagnosis of TCMR.
Chronic Active TCMR

**Grade IA:**
Interstitial inflammation involving >25% of the total cortex (ti score 2 or 3) and >25% of the sclerotic cortical parenchyma (i-IFTA score 2 or 3) with moderate tubulitis (t2) involving 1 or more tubules,
Not including severely atrophic tubules.
Other known causes of i-IFTA should be ruled out

**Grade IB**
Interstitial inflammation involving >25% of the total cortex (ti score 2 or 3) and >25% of the sclerotic cortical parenchyma (i-IFTA score 2 or 3) with severe tubulitis (t3) involving 1 or more tubules,
Not including severely atrophic tubules.
Other known causes of i-IFTA should be ruled out

**Grade II:**
Chronic allograft arteriopathy (arterial intimal fibrosis with mononuclear cell inflammation in fibrosis and formation of neointima)
(A) Mild tubulitis in borderline acute T cell-mediated rejection. The arrow is pointing to a rare lymphocyte within the tubular epithelium (400x).

(B) Moderate tubulitis in a case of Banff IA acute T cell-mediated rejection. Thick arrows point to lymphocytes within the tubular epithelium (H&E, 400x).

(C) Severe tubulitis is seen in this example of Banff IB acute T cell-mediated. As the degree of cellular rejection increases, increased numbers of lymphocytes are seen within the tubular epithelium (short arrows). rejection (PAS, 400x).

(D) Vascular rejection: endothelialitis (attachment of lymphocytes to the vascular wall). Banff IIA rejection, mild endothelialitis (H&E, 400x).

(E) Banff IIB acute T cell-mediated rejection, severe endothelialitis (dashed arrow, H&E, 400x).
Treatment of Acute T Cell-Mediated Rejection of the Renal Allograft
Significance of revised criteria for chronic active T cell-mediated rejection in the 2017 Banff classification: Surveillance by 1-year protocol biopsies for kidney transplantation

Kaneyasu Nakagawa¹, Akihiro Tsuchimoto¹, Kenji Ueki¹, Yuta Matsukuma¹, Yasuhiro Okabe², Kosuke Masutani³, Kohei Unagami¹, Yoichi Kakuta⁴, Masayoshi Okumi⁵, Masafumi Nakamura², Toshiaki Nakano¹, Kazunari Tanabe³, Takanari Kitazono¹, and Japan Academic Consortium of Kidney Transplantation Investigators
Figure 5

Survival at the composite graft endpoint

Table 4. Determinants of chronic active T cell-mediated rejection in the 1-year protocol biopsy

<table>
<thead>
<tr>
<th></th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Age (per 1-year increase)</td>
<td>1.01</td>
<td>0.98–1.04</td>
</tr>
<tr>
<td>Male (vs. female)</td>
<td>1.47</td>
<td>0.69–3.13</td>
</tr>
<tr>
<td>Diabetic nephropathy</td>
<td>1.42</td>
<td>0.64–3.22</td>
</tr>
<tr>
<td>ABO incompatible</td>
<td>1.26</td>
<td>0.58–2.75</td>
</tr>
<tr>
<td>Living donor (vs. deceased)</td>
<td>0.47</td>
<td>0.17–1.33</td>
</tr>
<tr>
<td>Preemptive KT</td>
<td>0.34</td>
<td>0.079–1.47</td>
</tr>
<tr>
<td>Dialysis vintage over 5 years</td>
<td>1.92</td>
<td>0.94–3.95</td>
</tr>
<tr>
<td>Donor age (per 1-year increase)</td>
<td>1.01</td>
<td>0.98–1.05</td>
</tr>
<tr>
<td>Male donor (vs. female)</td>
<td>0.69</td>
<td>0.32–1.51</td>
</tr>
<tr>
<td>HLA mismatches (per one increase)</td>
<td>1.53</td>
<td>1.06–1.67</td>
</tr>
<tr>
<td>Preformed DSA</td>
<td>0.56</td>
<td>0.16–1.88</td>
</tr>
<tr>
<td>Preoperative plasma exchange</td>
<td>0.83</td>
<td>0.39–1.73</td>
</tr>
<tr>
<td>Preoperative rituximab use</td>
<td>0.85</td>
<td>0.41–1.75</td>
</tr>
<tr>
<td>Cyclosporine (vs. tacrolimus)</td>
<td>4.59</td>
<td>1.53–13.8</td>
</tr>
<tr>
<td>Delayed graft function</td>
<td>1.83</td>
<td>0.51–6.56</td>
</tr>
<tr>
<td>Acute rejection within 1 year</td>
<td>11.2</td>
<td>5.18–24.1</td>
</tr>
<tr>
<td>BKPyVAN within 1 year</td>
<td>38.3</td>
<td>7.38–199.0</td>
</tr>
</tbody>
</table>

ajt_16093_f5.tif
Treatment for CA-TCMR

- **NO agreed policy** about the treatment for CA-TCMR.
- Extensive heterogeneity of treatment after the 1-year PB
- Difficult to determine an effective treatment for CA-TCMR.
- **More aggressive or innovative immunosuppression**
- A **prospective interventional study** on the treatment of CA-TCMR is required
Antibody Mediated Rejection (AMR)
Antibody Mediated Rejection

Major cause of graft dysfunction and leads to graft failure

**Diagnosis:**

Both pathological and clinical criteria are required (Banff 2017)
## Evolution of AMR diagnosis and definitions

<table>
<thead>
<tr>
<th>Year</th>
<th>Milestone</th>
</tr>
</thead>
<tbody>
<tr>
<td>1964</td>
<td>Immediate rejection of a kidney in the presence of preformed antibodies described</td>
</tr>
<tr>
<td>1970</td>
<td>Kidney recipients with de novo DSA developed obliteratorative vascular lesions &amp; poor outcomes</td>
</tr>
<tr>
<td>1990</td>
<td>AMR defined as a triad of 1) graft dysfunction, 2) neutrophils in peritubular capillaries, and 3) antibody against class I HLA without classical T-cell-mediated rejection</td>
</tr>
<tr>
<td>1993</td>
<td>C4d in PTC confirmed the role of DSA in rejection</td>
</tr>
<tr>
<td>1997</td>
<td>Banff meeting defined diagnostic categories for renal allograft biopsies:</td>
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<tr>
<td></td>
<td>Antibody-mediated rejection defined as rejection demonstrated to be due, at least in part, to anti-donor antibody and can be</td>
</tr>
<tr>
<td></td>
<td>immediate (hyperacute) or delayed (accelerated acute)</td>
</tr>
<tr>
<td>2001</td>
<td>Chronic Rejection, defined as progressive loss of renal function with hypertension and proteinuria more than 3 months after transplantation, was shown to be often associated with C4d, which could distinguish antibody-mediated AMR from nonspecific chronic allograft nephropathy (CAN)</td>
</tr>
<tr>
<td></td>
<td>Banff: C4d staining in peritubular capillaries became <em>sine qua non</em> of AMR, defined as due to documented anti-donor antibody</td>
</tr>
<tr>
<td></td>
<td>(<em>suspicious for</em> if antibody not demonstrated)</td>
</tr>
<tr>
<td>2005</td>
<td>Banff replaced CAN with chronic active AMR</td>
</tr>
<tr>
<td>2007</td>
<td>Banff developed PTC inflammation grading, C4d scoring, and interpretation of C4d deposition without morphological evidence of active rejection</td>
</tr>
<tr>
<td>2013</td>
<td>Banff made the first AMR revision since the 2001 meeting (published 2003). The absolute requirement for C4d replaced by microvascular inflammation or validated gene expression</td>
</tr>
<tr>
<td>2017</td>
<td>Banff accepts C4d and molecular classifiers as surrogate markers for DSA</td>
</tr>
</tbody>
</table>
Impact of Rejection
Graft survival (%)

- No rejection
- T cell-mediated rejection
- Antibody-mediated rejection

Log rank p < 0.0001

Number at risk

- No rejection: 1777, 1600, 1408, 1152, 933, 673, 473
- T cell-mediated rejection: 192, 182, 163, 134, 101, 71, 37
- Antibody-mediated rejection: 110, 100, 78, 61, 40, 26, 12

Graft Survival based on Histological Findings at Last Indication Biopsy

Mechanisms and Pathogenesis
Antibody-Mediated Rejection (ABMR)

**Type 1 ABMR:**
- Results from persistence and/or a rebound of preexisting donor-specific antibodies in sensitized patients
- Occurs early post-transplantation

**Type 2 ABMR:** associated with
- *De novo* donor-specific antibodies
- More interstitial fibrosis/tubular atrophy and more frequent cell-mediated rejection
- Occurs late (usually over one year post-transplantation)

**Hess et al, Kidney Int. 2017 Mar;91(3):729-737**
Allograft rejection caused by antibodies directed against

Donor-specific HLA molecules
- class I
- and
- class II

Blood group
- ABO
- iso-agglutinins
Antibody Mediated Rejection

Non-HLA tissue specific antigens

Vimentin
Collagen IV

Endothelial cell antibodies (AECA)

The target of AECA is:
- Angiotensin type 1 receptor (AT1R).
- Major-histocompatibility complex (MHC) class I-related chains A and B (MICA and MICB)
Mechanism of AMR

Defining the phenotype of antibody-mediated rejection in kidney transplantation: Advances in diagnosis of antibody injury

Neetika Garg a,*, Milagros D. Samaniego b, Dana Clark b, Arjang Djamali a

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b Department of Medicine, Nephrology Division, University of Michigan, Ann Arbor, MI 48109, United States

Transplantation Reviews 31 (2017) 257–267
Mechanism of AMR
DSA
# Comparison of Class 1 vs Class 2 DSA

<table>
<thead>
<tr>
<th>Table 1. Comparison of the dominant characteristics of classes 1 and 2 donor-specific antibodies (6–10,25–30)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HLA</strong></td>
</tr>
<tr>
<td>Antigens</td>
</tr>
<tr>
<td>Epitopes location</td>
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<tr>
<td>Expression</td>
</tr>
<tr>
<td><strong>Preformed donor-specific antibodies</strong></td>
</tr>
<tr>
<td>Important</td>
</tr>
<tr>
<td>Positive crossmatch</td>
</tr>
<tr>
<td>Transplant decision</td>
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<tr>
<td><strong>De novo donor-specific antibodies</strong></td>
</tr>
<tr>
<td>Detection</td>
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<tr>
<td>IgG subclasses</td>
</tr>
<tr>
<td>Complement binding</td>
</tr>
<tr>
<td>Frequency</td>
</tr>
<tr>
<td><strong>Antibody-mediated rejection</strong></td>
</tr>
<tr>
<td>Phenotypes</td>
</tr>
<tr>
<td>Presentation</td>
</tr>
<tr>
<td>Graft dysfunction</td>
</tr>
<tr>
<td>C4d deposit</td>
</tr>
<tr>
<td>Treatment</td>
</tr>
<tr>
<td>Graft loss</td>
</tr>
<tr>
<td><strong>Class 1 Donor-Specific Antibodies</strong></td>
</tr>
<tr>
<td>A, B, and C</td>
</tr>
<tr>
<td>α-chain</td>
</tr>
<tr>
<td>All nucleated cells</td>
</tr>
<tr>
<td>Very</td>
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<tr>
<td>T cells</td>
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<tr>
<td>No transplant</td>
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<tr>
<td>Sooner</td>
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<tr>
<td>IgG1, IgG3</td>
</tr>
<tr>
<td>Strong</td>
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<tr>
<td>Fewer</td>
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<tr>
<td>Acute</td>
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<tr>
<td>Early</td>
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<tr>
<td>Rapidly</td>
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<tr>
<td>Positive</td>
</tr>
<tr>
<td>More responsive</td>
</tr>
<tr>
<td>Early</td>
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<tr>
<td><strong>Class 2 Donor-Specific Antibodies</strong></td>
</tr>
<tr>
<td>DR, DQ, and DP</td>
</tr>
<tr>
<td>α- and β-chains</td>
</tr>
<tr>
<td>Antigen-presenting cells</td>
</tr>
<tr>
<td>Less</td>
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<tr>
<td>B cells</td>
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<tr>
<td>Permissible</td>
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<tr>
<td>Later</td>
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<tr>
<td>IgG2, IgG4</td>
</tr>
<tr>
<td>Weak/no</td>
</tr>
<tr>
<td>Common, especially DQ</td>
</tr>
<tr>
<td>Chronic, subclinical</td>
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<tr>
<td>Later</td>
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<tr>
<td>Slowly</td>
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<tr>
<td>Negative</td>
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<tr>
<td>Less responsive</td>
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<tr>
<td>Later</td>
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</tbody>
</table>
Detection of Anti HLA Antibodies

- **Cross match: CDC crossmatch.** AAMR may occur with –ve CXM. It detect only c fixing antibodies
- **Mixed Lymphocytic culture.**
- **Panel reactive antibodies**
- **Solid Phase antibody testing for:**
  - **HLA class I/II antibodies**, (complement/non complement fixing)
  - **Non HLA directed antibodies [MHC class I-related chain A (MICA)]**(Eliminating the need for viable cells)
Detection of Anti HLA Antibodies

**Types of Solid Phase antibody testing**

**ELISA**-based system. (microplate) detect non fixing complement Abs

**Color-coded bead-based fluorometric assays (beads):**
Detected by flowcytometry (Flow panel reactive Abs beads) or **Luminex** (using pool of HLA I and II Ag coated micro particles) (mean fluorescence intensity (MFI))

More sensitive.

Less susceptible to drug interference.
The C1q assay was designed to distinguish complement fixing from non-complement-fixing antibodies and does not require complement activation other than the binding of C1q to the antibody.

Proteomics approaches using protein extracts from different sources, including cell lysates and protein microarrays are being used for antibody screening and identification of specificities.
Table 1: Comparison of antibody testing methods

<table>
<thead>
<tr>
<th>Antibody test methods</th>
<th>CDC cross match</th>
<th>Flow cross match</th>
<th>Solid phase single antigen assay</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diagram of protocols</strong></td>
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<tr>
<td>B/T cell</td>
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<td></td>
<td></td>
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<tr>
<td>+ recipient serum</td>
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<td></td>
<td></td>
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<tr>
<td>B/T cell</td>
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<td></td>
<td></td>
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<tr>
<td>+ complement</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B/T cell</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Cell death</td>
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</tbody>
</table>

- Usage of test: Usually pre-transplant
- Antigen source: Native antigens on donor lymphocytes
- Antibody detected: Cytotoxic, complement fixing IgG and IgM, donor specific
- Antibody specificity determined: No
- Quantitation: Scale 1-8 binary
- Sensitivity: Low
- Repeatability: Low
- Requirement for live cells: Yes
- HLA, human leukocyte antigen; CDC, complement dependent cytotoxicity.

Both pre- and post-transplant
- Purified single antigens on beads
- Donor specific IgG
- IgG anti-HLA antibodies in general
- Yes (HLA)
- Semi-quantitative
- High
- Semi-quantitative
- High
- Yes
- No
Development of De Novo DSA Is Associated With Allograft Loss

Graft survival of patients with de novo DSA versus those without

\[ P < .0001 \]

DSA in ABMR: Pre-existing vs De novo

Log rank $P < .0001$

Pre-existing DSA
De novo DSA

Aubert et al. JACN. 2017.
Graft Survival by Clinical Phenotype and DSA Ss

- No dnDSA No Dysfunction (n=388)
- No dnDSA Dysfunction (n=56)
- Subclinical dnDSA (n=45)
- Clinical dnDSA (n=19)

p<0.0001

Wiebe et al. Am J Transplant. 2015
Types of AMR:

Preformed Or De Novo
### Mansoura Luminex Experience: (153 patients)

**Value of Donor-specific Antibody Detection in First-Graft Renal Transplant Recipients with a Negative Complement-dependent Cytotoxic Crossmatch**

*Khaled Mohamed Mahmoud, Amani Mostafa Ismail, Hussein Attia Sheashaa, Osama Ashry Gheith, Mohamed Mohamed Kamal, Mohamed Ahmed Ghoneim*

<table>
<thead>
<tr>
<th></th>
<th>No antibodies (n 104)</th>
<th>Donor non-specific AB (n 33)</th>
<th>Donor specific AB (n 16)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AMR (n,%)</strong></td>
<td>5 (3.4)</td>
<td>2 (6)</td>
<td><strong>5 (31)</strong></td>
</tr>
</tbody>
</table>

Experimental and Clinical Transplantation 2009; 2: 124–128
De Novo DSA:

The detrimental impact of persistent vs an isolated occurrence of de novo donor-specific antibodies on intermediate-term renal transplant outcomes

Jennifer M. Loucks-DeVos\textsuperscript{1} | Todd N. Eagar\textsuperscript{2} | A. Osama Gaber\textsuperscript{3} | Samir J. Patel\textsuperscript{4} | Larry D. Teeter\textsuperscript{5} | Edward A. Graviss\textsuperscript{6} | Richard J. Knight\textsuperscript{3}
C3d Binding:

AMR and Graft Survival

265 previously identified as having de novo DSA

Transpl Int. 2018 Apr;31(4):424-435
IGG3 Anti-HLA-DSA

Pediatric Transplantation. 2018;e13219., Accepted: 13 April 2018
Angiotensin II type 1 Receptor Antibodies

Association of angiotensin II type 1 receptor antibodies with graft histology, function and survival in paediatric renal transplant recipients

Alexander Fichinger1, Genser Sökel1, Claudia Schröder1, Britta Hübner1, Susanne Kögler1, Rüdiger Waldherr1, Jens H. Westhoff1, Anita Sander1, Danka Dragan1, and Berndhard Frishholz

1Department of Paediatrics, University Children’s Hospital, Heidelberg, Germany; 2Department of Transplantation Immunology, Institute of Immunology, University of Heidelberg, Heidelberg, Germany; and 3Department of Experimental Therapy, Institute of Clinical Pathology, Heidelberg, Germany.

Original Article

Anti Endothelial Cell Antibodies

Microarray studies indicated that endothelial gene expression in kidney transplant biopsies with DSA detects ABMR and predicts poor graft survival

↑Endothelial Gene Expression in kidneys Transcripts:

vWF, caveolin-1, E-selectin, CD31, CD34
Phenotypes of ABMR

- Clinico-pathological
  - Hyperacute
  - Acute
  - Subclinical
  - Chronic

- Antibody types
  - Antigen targets
  - Timing
  - Isotypes/Subclasses
  - Complement binding

- Molecular tools
  - Kidney
  - Blood
  - Urine

Transplantation Reviews 31 (2017) 257–267
Diagnostic Criteria for Acute AMR

• Characteristic histologic features including:
  1) Glomerulitis/capillaritis
  2) Margination of neutrophils in the PTC
  3) Fibrin thrombi
  4) Interstitial hemorrhage
  5) Severe or necrotizing vasculitis

• Diffuse, linear C4d staining in the PTC
• Identification of DSA
Active ABMR; all 3 criteria must be met for diagnosis

1. **Histologic evidence of acute tissue injury, including 1 or more of the following:**
   - Microvascular inflammation (g > 0 and/or ptc > 0), in the absence of recurrent or de novo glomerulonephritis, although in the presence of acute TCMR, borderline infiltrate, or infection, ptc ≥ 1 alone is not sufficient and g must be ≥ 1
   - Intimal or transmural arteritis (v > 0)
   - Acute thrombotic microangiopathy, in the absence of any other cause
   - Acute tubular injury, in the absence of any other apparent cause

2. **Evidence of current/recent antibody interaction with vascular endothelium,** including 1 or more of the following:
   - Linear C4d staining in peritubular capillaries (C4d2 or C4d3 by IF on frozen sections, or C4d > 0 by IHC on paraffin sections)
   - At least moderate microvascular inflammation (g + ptc ≥ 2) in the absence of recurrent or de novo glomerulonephritis, although in the presence of acute TCMR, borderline infiltrate, or infection, ptc ≥ 2 alone is not sufficient and g must be ≥ 1
   - Increased expression of gene transcripts/classifiers in the biopsy tissue strongly associated with ABMR, if thoroughly validated

3. **Serologic evidence:**
   Donor-specific Antibodies (DSA to HLA or other antigens).

   C4d staining or expression of validated transcripts/classifiers as noted above in criterion 2 may substitute for DSA; however thorough DSA testing, including testing for non-HLA antibodies if HLA antibody testing is negative, is strongly advised whenever criteria 1 and 2 are met.
Diagnostic Misinterpretation

Banff Survey on Antibody Mediated Rejection Clinical Practices in Kidney Transplantation: Diagnostic Misinterpretation has Potential Therapeutic Implications

Schinstock, Carrie A¹; Sapir-Pichhadze, Ruth²; Naesens, Maarten³; Batal, Ibrahim⁴; Bagnasco, Serena⁵; Bow, Laurine⁶; Campbell, Patricia⁷; Clahsen-van Groningen, Marian C.⁸; Cooper, Matthew⁹; Cozzi, Emanuele¹⁰; Dadhania, Darshana¹¹; Diekmann, Fritz¹²; Budde, Klemens¹³; Lower, Fritz¹⁴; Orandi, Babak J.¹⁵; Rowshani, Ajda T¹⁶; Cornell, Lynn¹⁷; Kraus, Edward¹⁸

Am J Transplant. 2018, Accepted  Jun 23
Prevention
The ideal regimen for the prevention of ABMR in sensitized patients remains unknown.

Strategies to Prevent AMR

Why Donor Exchange?

**Traditional Paired Exchange**

Two Pair Exchange

![Diagram of traditional paired exchange]

![Diagram of three pair exchange]

Review article:

Kidney paired donation program, a national solution against commercial transplantation?

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ABMR: Preventive strategies

- Anti-HLA DSA screening
- Preventing non-compliance
- Surveillance protocol biopsies
Development of De Novo DSA:

Impact of Adherence

Automated Reminders and Physician Notification to Promote Immunosuppression Adherence Among Kidney Transplant Recipients: A Randomized Trial

wireless pill bottle openings

Am J Kidney Dis. 2017;69(3):400-409
A Randomized Trial of a Multicomponent Intervention to Promote Medication Adherence: The Teen Adherence in Kidney Transplant Effectiveness of Intervention Trial (TAKE-IT)

Conclusions: The multicomponent TAKE-IT intervention resulted in significantly better medication adherence than the control condition. Better medication adherence may result in improved graft outcomes, but this will need to be demonstrated in larger studies.
Value of Protocol biopsy

Changing Kidney Allograft Histology Early Posttransplant: Prognostic Implications of 1-Year Protocol Biopsies
THANK YOU !!