AST T3 Webinar on Banff Conference 2013 – Additional Q&A
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1. Not always easy to demonstrate presence of non-HLA antibody and like wise some antibodies (HLA or non) can cause noncomplement mediated injury. Are we saying that while pathologically one cannot make a ABMR Dx without all three, 2 out of 3 may suffice for a clinically Dx in the appropriate setting?
Answer: The recognition that some antibodies can produce injury by mechanism(s) other than complement (e.g., ADCC) was a major reason for the change in ABMR criteria. C4d is no longer specifically required, but evidence of recent antibody interaction with endothelium is - which may be in the form of C4d, moderate to severe microvascular injury (g + ptc $\geq$2), or molecular evidence such as increased ENDAT expression in labs that do such testing. If there is only DSA and mild microvascular injury - (g + ptc) = 1 or TMA (that is, 2 of the 3 criteria), then the lesion is termed "suspicious" for ABMR. Likewise if there is histologic evidence of ABMR with evidence of recent antibody interaction with the endothelium [C4d, (g + ptc $\geq$2), or high ENDAT expression] in the absence of demonstrable DSA, this is likewise termed suspicious for ABMR, with the suggestion that non-HLA DSA be looked for.

2. Did you ever see BK and ABMR?
Answer: I have seen BKV nephropathy with chronic, active ABMR (transplant glomerulopathy, glomerulitis, and DSA) in a small number of highly sensitized patients but never BKV nephropathy with acute ABMR although that doesn't mean it cannot happen. This is probably rare, however, since BKV nephropathy tends to occur at least several months post-transplant while acute ABMR tends to occur earlier except in cases of non-compliance with immunosuppressive meds (and one might assume that patients who are under-immunosuppressed are less likely to develop BKVN).

3. C4d (-) can be do to technique, non-HLA Ab, Ab affinity, avidity, etc, fibrosis. Is tehre a good way to tell them apart?
Answer: There should be fewer problems due to technique and fibrosis now that focal C4d (by IF on frozen sections) and focal or focal, minimal C4d (by IHC on paraffin sections) are considered positive - in the previous version of the classification diffuse C4d was required. With regard to the effects of low affinity antibodies, non-HLA DSA, and non-complement fixing antibodies there is really no way to tell these apart on a biopsy. We have seen cases of acute, active ABMR (most C4d-negative, but a small number with focal C4d) in patients with no anti-HLA DSA but with anti-endothelial antibodies or antibodies to AT1R.

4. Mark, given the early findings of TG by EM, could we recommend EM routinely in all transplant biopsies, regardless of the time port-transplant?
Answer: We do EM routinely at out center on all indication biopsies; we only do protocol biopsies on highly sensitized patients. However, it has been my experience with early biopsies (1st 6 months post-transplant) in low risk patients (negative crossmatch and PRA = 0) that the early findings of TG by EM are extremely rare, and that the combination of early GBM duplication plus endothelial swelling and/or subendothelial electron-lucent widening is never seen. In such cases I now take a small amount of tissue for EM (as we do with all biopsies except implantation biopsies) and always look at the 1-micron sections, however if there is no glomerulitis, peritubular capillarities, or intimal arteritis by light microscopy with negative C4d I defer the EM.

5. Would we able to diagnose Polyoma vrus allograft nephropathy and concurrent acute cellular rejection?
Answer: This is very hard in many cases. The only way to definitively diagnose ACR in the presence of polyoma virus nephropathy (PVN) is if arterial lesions (intimal or transmural arteritis) are present in addition to the PVN. With cases of PVN that also meet Banff criteria for type 1a or 1b ACR, we always do an immunostain for polyoma virus (antibody to SV-40 large T antigen). If there is inflammation and tubulitis in area(s) of the biopsy with no tubular epithelial cells showing nuclear staining for the virus, we then suggest that there may be concurrent PVN and ACR. However if the staining for the virus is widespread or if it involves or is very close to all foci of inflammation and tubulitis, we attribute the inflammation entirely to the PVN, although stating in a comment that concurrent ACR cannot be completely ruled out.