3-2022

Final Counts of Monoclonal Gammopathy of Renal Significance (MGRS) after Bone Marrow Biopsies (BMB) and Follow-up

Brandon Metcalf
Beaumont Health

James Zhiyan Huang
Beaumont Health

Wei Li
Beaumont Health

Hassan Kanaan
Beaumont Health

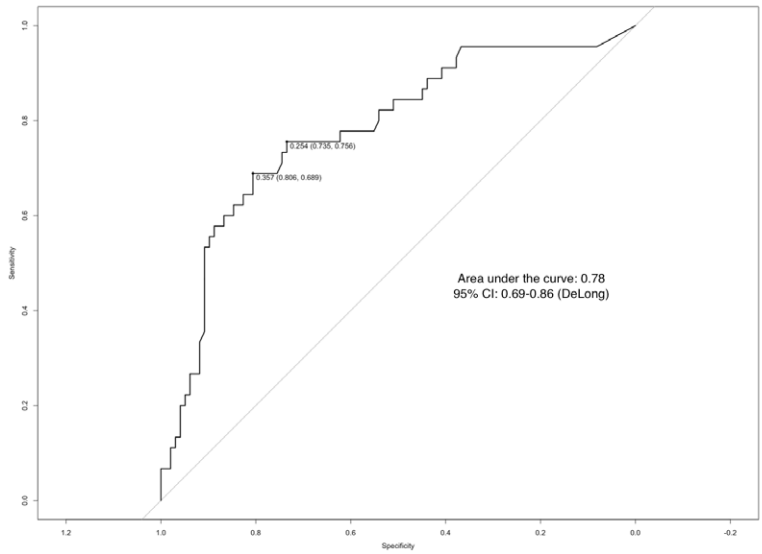
Ping Zhang
Beaumont Health

Recommended Citation

Metcalf B, Huang JZ, Li W, Kanaan H, Zhang P. Final counts of monoclonal gammopathy of renal significance (MGRS) after bone marrow biopsies (BMB) and follow-up. Lab Invest. 2022 Mar;102(Suppl):990-991. doi: 10.1038/s41374-022-00758-y.

Results: Area under the curve was 0.78 with 95% confidence interval of 0.69-0.86. Two distinct thresholds that optimized specificity and sensitivity were 0.36 (Youden method) and 0.25 (closest top left method); both are plotted on ROC curve in Figure 1. For the Youden method, the specificity was calculated as 81% and sensitivity as 69%. Negative predictive value was 85% and positive predictive value was 62%. The 19 false positives showed FL in biopsy, including only one FL grade 3A, 14 FL grade 1-2, and 4 FL that could not be graded.

Figure 1 - 915



Conclusions: Statistical analysis of FSC in transformed FL cases demonstrated that a threshold of 36% large cells optimizes identification of the transformed subset while minimizing false positives per Youden J statistic. However, despite threshold optimization, multiple false positives still occurred when relying only on the FSC parameters by FACS. Therefore, correlation with intact tissue morphology is critical to prevent overcalling transformation.

916 Final Counts of Monoclonal Gammopathy of Renal Significance (MGRS) after Bone Marrow Biopsies (BMB) and Follow-up

Brandon Metcalf[1], James Zhiyan Huang[2], Wei Li[2], Hassan Kanaan[3], Ping Zhang[4]
[1]Oakland University William Beaumont School of Medicine, Rochester, MI, [2]William Beaumont Hospital, Royal Oak, MI, [3]Beaumont Health, Royal Oak, MI, [4]William Beaumont Hospital, Birmingham, MI

Disclosures: Brandon Metcalf: None; James Zhiyan Huang: None; Wei Li: None; Hassan Kanaan: None; Ping Zhang: None

Background: MGRS is a relatively new concept for patients with renal paraprotein deposition (RPD) (except monoclonal cast nephropathy) with no bone marrow confirmed diagnosis of malignancy or premalignancy (< 10% monoclonal plasma cells). This concept has been used as a reason for a nephrology consult for a bone marrow biopsy (BMB), therefore it is important to evaluate the outcome of MGRS tentatively diagnosed via renal biopsy and confirmed by BMB. This study's purpose was to identify what percentage of various subtypes of MGRS tentatively diagnosed via renal biopsy can be confirmed as MGRS by BMB and follow-up.

Design: In total, 124 renal biopsies with variants of RPD were identified at our center out of 3811 renal biopsies (3.3% of overall cases) over past 10 years. Biopsy cases with known Myeloma, B Cell Lymphoma or Monoclonal Cast Nephropathy were separated as a heavy burden group. The remaining biopsies with RPD were considered as tentative MGRS diagnoses. Their BMB and clinical indices were followed up to determine the percent that resulted in a confirmed MGRS diagnosis.

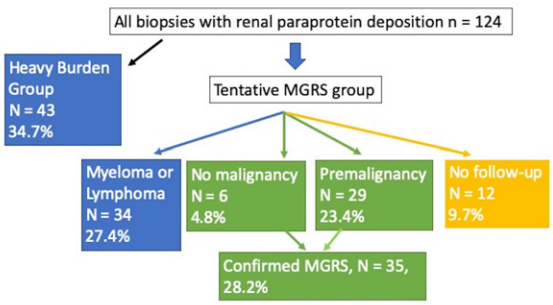
Results: Among the 124 renal paraprotein deposition cases, 43 cases (34.7%) were categorized to the heavy burden group (Figure). The remaining 81 cases with other variants of RPD were further divided into four categories based on the follow-up. Myeloma or Lymphoma were found in 34 cases (27.4%). Twelve outside consultation cases (10%) did not show follow-up biopsies as we were unable to obtain record access. BMB's diagnosed as nonmalignant (6 cases, 4.8%) or premalignant (29 cases, 23.4%)

were confirmed to be MGRS for a total of 35 cases (28.2%). Among the different categories of tentative MGRS, Monoclonal Light/Heavy Chain Deposition Diseases (L/HCDD) had the highest positivity rate for myeloma on the subsequent BMB (Table). Proliferative Glomerulonephritis with Monoclonal Immunoglobulin Deposition (PGNMID) had a high rate of nonmalignant or pre-malignant diagnosis by BMB. Monoclonal Amyloidosis had some nonmalignant and pre-malignant diagnoses after BMB although myeloma was associated with this renal entity (Table).

Different categories of RPD	Malignant	Nonmalignant	Premalignant	Confirmed MGRS
L/H CDD n = 19	15 (78.9%)	0	4 (21.1%)	4 (21.1%)
Amyloidosis n = 28	15 (53.6%)	1 (3.5%)	13 (42.9%)	14 (46.4%)
PGNMID n = 9	1 (11.1%)	4 (44.4%)	4 (44.4%)	8 (88.8%)
Proximal Tubulopathy n = 6	2 (33.3%)	1 (16.7%)	3 (50.0%)	4 (66.7%)
Cryoglobulin GN[1] n = 4	1 (25.0%)	0	3 (75.0%)	3 (75.0%)
Immunotactoid GN[1] n = 1	0	0	1 (100.0%)	1 (100.0%)
Fibrillary GN[1] n = 1	0	0	1 (100.0%)	1 (100.0%)

[1] GN: glomerulonephropathy

Figure 1 - 916



Conclusions: The data indicate that BMB is crucial for confirming a diagnosis of MGRS. The study also provides pathologists and clinicians with general expectations regarding the possible BMB outcome for the many variants of MGRS identified tentatively via renal biopsy.

917 The Evaluation of Blast Subsets Increases the Diagnostic Specificity for Myelodysplastic Syndrome by Flow Cytometry

Howard Meyerson[1], Manish Kumar[2]
[1]University Hospital Case Medical Center, Cleveland, OH, [2]Case Western Reserve University/University Hospitals Cleveland Medical Center, Cleveland, OH

Disclosures: Howard Meyerson: None; Manish Kumar: None

Background: We and others have used flow cytometric (FCM) parameters to predict for MDS. We have found CD177+ neutrophils in addition to the Ogata parameters (B cell progenitors percentage, blast percentage, low side scatter and CD45 blast expression) as sensitive and specific for MDS compared to age-matched cytopenic controls. However, false positive FCM analyses occur in roughly 10-15% of low-grade MDS cases mainly due to low B cell progenitor percentage in many cytopenic controls. We therefore examined whether blast subset parameters in addition to the B cell progenitor percentage could be utilized to enhance the specificity of FCM detection of MDS.

Design: 29 MDS cases (17 without excess blasts) and 27 cytopenic controls (negative by NGS, karyotype and morphology) were evaluated. Blast subsets were determined similar to that used by Shameli et. al (PMID 33369070). A total of 100,000 events were collected and CD34 cells were gated. CD34 subsets were enumerated based on 6 color analysis using a tube stained with CD71, CD371, CD38, CD34, CD19 and CD45. Percentage of CD34+ cells that were CD371+CD38+ (GM-like), CD71+CD371- (erythroid-like), CD71-CD38dim/negative (stem-like), CD19+ (B cell progenitor) and other (none of the above) were determined. Cut-offs were based on control samples and applied to the MDS cases. The percentage of cases showing 0, 1 or 2 or more abnormalities were tallied.