

Diagnostic utility of the Lymphoid Screening Tube for Ogata score calculation in MDS investigation



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OBJECTIVES

The diagnosis of myelodysplastic syndrome (MDS) is not always straightforward in the absence of objective markers such as ringed sideroblasts, an excess of blasts or clonal cytogenetic abnormalities. Moreover, the lack of specificity of dysplasia makes the differentiation with other causes of peripheral cytopenia difficult. The WHO 2016 classification of MDS recognizes multiparameter flow cytometry (MFC) as an

adjuvant tool for MDS diagnosis. An easily applicable MFC protocol based on CD34 and CD45 is proposed by Ogata *et al.* Furthermore, in the diagnostic workup of patients with peripheral cytopenia, MFC by means of a Lymphoid Screening Tube (LST) is recommended by the EuroFlow™ consortium. The aim of this study was to investigate whether the LST, supplemented with CD34, can be used to calculate the Ogata score.

METHODS

Samples

All bone marrow samples (n=108) received between January 2016 and December 2016 for investigation of peripheral blood cytopenia were analyzed:

- MDS (n=32)
- non-MDS (n=76)

Table 1. Ogata score calculation.

| FC parameter | Cut-off | Score |
|--|------------|-------|
| 1. Myeloblasts in all CD45+ cells (%) | ≥2 | 1 |
| 2. Lymphoblasts in all CD34+ cells (%) | ≤5 | 1 |
| 3. Lymphocytes ÷ myeloblasts MFI of CD45 ratio | ≤4 or ≥7.5 | 1 |
| 4. Granulocytes ÷ lymphocytes SSC ratio | ≤6 | 1 |

Methods

The Ogata score is considered positive, and thus suggestive of MDS, if a value of 2 or more is observed. Results of the Ogata score were compared with the clinical diagnosis according to the WHO criteria, based on extensive history taking, cytomorphology and cytogenetics, but not on flowcytometric data.

The Ogata score was calculated with an LST based on the tube designed by the EuroFlow™ consortium, but with addition of CD34 and without TCRγδ.

Table 2. LST - EuroFlow™ vs. AZ Sint-Jan.

| Fluorochrome | EuroFlow™ | AZ Sint-Jan |
|--------------|-----------|-------------|
| HV450 | CD20 | CD20 |
| HV450 | CD4 | CD4 |
| HV500 | CD45 | CD45 |
| FITC | CD8 | CD8 |
| FITC | Lambda | Lambda |
| PE | Kappa | Kappa |
| PE | CD56 | CD56 |
| PerCP-Cy5.5 | CD5 | CD5 |
| PerCP-Cy5.5 | - | CD34 |
| PE-Cy7 | TCRγ/δ | - |
| PE-Cy7 | CD19 | CD19 |
| APC | CD3 | CD3 |
| APC-H7 | CD38 | CD38 |

RESULTS

Table 3. Patient characteristics and microscopic evaluation of dysplasia.

| | Number (M/F) | Mean age (range) | Abnormal karyotype | Microscopic dysplasia evaluation | | |
|-------------------|--------------|------------------|--------------------|----------------------------------|----------------|--------|
| | | | | significant | in-significant | absent |
| MDS (n=32) | | | | 26 | 6 | 0 |
| Low-grade (n=22) | | | | 16 | 6 | 0 |
| SLD | 4 (4/0) | 70 (65-79) | 3 (75%) | 1 | 3 | 0 |
| MLD | 13 (9/4) | 72 (46-88) | 5 (38%) | 10 | 3 | 0 |
| RS-SLD | 1 (1/0) | 67 | 0 | 1 | 0 | 0 |
| RS-MLD | 1 (0/1) | 78 | 0 | 1 | 0 | 0 |
| 5q- | 3 (1/2) | 79 (73-83) | 3 (100%) | 3 | 0 | 0 |
| High-grade (n=10) | | | | 10 | 0 | 0 |
| EB-1 | 4 (1/3) | 71 (49-85) | 2 (50%) | 4 | 0 | 0 |
| EB-2 | 6 (3/3) | 68 (57-78) | 2 (40%) | 6 | 0 | 0 |
| Non-MDS (n=76) | | | | 5 | 13 | 58 |

Insignificant (=doubtful) morphological dysplasia was found in 19 cases, impeding diagnostic interpretation. In this group

- a true positive Ogata score was found in 4/6 MDS cases
- a true negative score was found in 13/13 non-MDS cases

Table 4. Results Ogata score.

| | Ogata score | | | | | Positive score | Sensitivity | Specificity |
|-------------------|-------------|---|---|---|---|----------------|-------------|-------------|
| | - | 0 | 1 | 2 | 3 | | | |
| MDS (n=32) | | | | | | 20/32 | 63% | NA |
| Low-grade (n=22) | | | | | | 12/22 | 55% | NA |
| SLD | 0 | 2 | 2 | 0 | 0 | 2/4 | 50% | NA |
| MLD | 5 | 1 | 4 | 3 | 0 | 7/13 | 54% | NA |
| RS-SLD | 0 | 0 | 1 | 0 | 0 | 1/1 | 100% | NA |
| RS-MLD | 1 | 0 | 0 | 0 | 0 | 0/1 | 0% | NA |
| 5q- | 1 | 0 | 1 | 1 | 0 | 2/3 | 67% | NA |
| High-grade (n=10) | | | | | | 8/10 | 80% | NA |
| EB-1 | 0 | 1 | 1 | 2 | 0 | 3/4 | 75% | NA |
| EB-2 | 0 | 1 | 1 | 2 | 2 | 5/6 | 83% | NA |
| Non-MDS (n=76) | | | | | | 6/76 | NA | 92% |

Sensitivity

- MDS: 63%
- low-grade MDS: 55%
- high-grade MDS: 80%

Specificity

- non-MDS: 92%

CONCLUSION

Besides screening for clonal lymphocytes, plasma cells and blasts, an LST supplemented with CD34 allows the

calculation of the Ogata score as an adjuvant tool in the diagnostic workup of cytopenic patients suspected of MDS.