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LETTER TO THE EDITOR

Deciphering the prognostic significance of autoimmune disorders in myelodysplastic syndromes

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Dear Editor,

It is now clear that myelodysplastic syndromes (MDS) are associated with several immune abnormalities [1, 2] beside an increased frequency of autoimmune disorders (AD) [3]. Montoro and colleagues interestingly analysed the prevalence, clinical characteristics, and outcomes of 142 patients with MDS and AD showing that their overall survival (OS) was inferior even in multivariate analysis and this detrimental effect was confined to patients with clinical rather than laboratoristic manifestations [4]. Although these findings are extremely relevant, it is worth mentioning, as shown in Table 1, that the prognostic significance of AD in MDS patients is still debated. In fact, some more studies apparently suggested a potential negative prognostic impact. Among 153 patients, 19 of which developed AD, the survival of subjects with immune abnormalities was significantly worse, as these patients tended to die more frequently of infection or leukemic progression [5]. Among 117 MDS patients in which the commonest AD were rheumatoid arthritis and ulcerative colitis, the leukemic transformation rate was not increased but the median survival time was shorter [6]. A possible negative prognostic impact was suggested by a further study especially in patients with vasculitis and/or cryoglobulins [7]. A following report focusing on 67 MDS patients with AD suggested that certain clinical pictures are associated with worse survival as quite strikingly neutrophilic dermatosis was also associated with a 1.8-fold increase in mortality [8]. On the other hand, some studies did not suggest a correlation between the clinical evolution of MDS and the occurrence of AD. Among 70 patients enrolled in a prospective cohort study of 4-year duration, 13 of which experienced AD, no particular differences were detected concerning bone marrow blast count, international prognostic scoring system (IPSS), favourable cytogenetic abnormalities, leukemic transformation and survival [9]. Similar results were suggested by a following study [10]. Interestingly, 127 patients with MDS or chronic myelomonocytic leukaemia (CMML) with systemic inflammatory and AD were compared with 665 patients without these manifestations. The former were younger, were male, less often had refractory anaemia with ring sideroblasts, more often had a poor karyotype and less frequently belonged to low and intermediate-1 IPSS categories, but no survival difference was demonstrated [11]. The understanding about the actual prognostic implications of AD in MDS patients was very recently revolutionised by an extensive analysis performed on 1408 patients in the context of a joint effort from the Moffitt Cancer Center in Tampa and King's College Hospital in London. Twenty-eight percent of the patients had AD, with hypothyroidism, idiopathic thrombocytopenic purpura, rheumatoid arthritis and psoriasis being the most common subtypes and accounting for 44%, 12%, 10% and 7% of patients respectively. AD were more common in female patients, in those with refractory anaemia or refractory cytopenia with multilineage dysplasia and in subjects less dependent on red blood cell transfusion. Quite strikingly, median OS was 60 months for patients with AD versus 45 months for those without, and by multivariate analysis, AD were a statistically significant independent factor for OS. Moreover, the rate of leukemic progression was 23% in MDS patients with AD versus 30% in those without [12]. Nowadays, we are fully aware that MDS are characterised by a skewed immunological milieu [13] which can be modified by some of the more efficacious therapeutic options [14]. At the same time, we know that around one third of MDS patients can be involved by AD. However, the available findings are quite controversial and we still need to decipher their actual prognostic significance, very likely due to the heterogeneity of the published studies in terms of patient selection, AD classification and available therapeutic approaches at the time of analysis. Prospective studies may help to address this relevant issue in the MDS scenario and potentially to improve our clinical management of a condition which often impairs the quality of life of our patients.

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Table 1 Most relevant registry studies evaluating frequency and impact of autoimmune manifestations in MDS patients

Authors, year of publication	Patients	Patients with autoimmune manifestations	Type of study	Main results	Impact on survival
Montoro Jet al. 2018	142	68 (48%)	Retrospective	Overall survival for patients with autoimmune Disorders were inferior even in multivariate analysis	Negative
Okamoto T et al. 1997	153	19 (12%)	Retrospective	Survival of subjects with immune abnormalities significantly worse due to infections or leukemic progression	Negative
Zhao S et al. 2002	117	19 (16%)	Retrospective	Leukaemic transformation not increased but shorter median survival in subjects with autoimmune disorders	Negative
de Hollanda A et al. 2011	235	46 (20%)	Retrospective	Possible negative prognostic impact especially in patients with vasculitis and/or cryoglobulins	Negative
Lee SJ et al. 2016	201	67 (33%)	Retrospective randomised	Neutrophilic dermatosis associated with a 1.8-fold increase in mortality	Negative
Giannouli S et al. 2004	70	13 (19%)	Prospective	No impact on disease characteristics and survival; in most patients, autoimmune manifestations develop during the course of MDS	Absent
Marisavljević D et al. 2006	284	32 (11%)	Retrospective	Except for female predominance, no correlations between immune abnormalities and disease features or survival	Absent
Mekinian A et al. 2016	788	123 (16%)	Retrospective	Patients with autoimmune diseases were younger, male, less often with refractory anaemia with ring sideroblasts or low and intermediate-1 IPSS and more often with poor karyotype; no survival difference	Absent
Komrokji RS et al. 2016	1408	391 (28%)	Retrospective	By multivariate analysis, autoimmune diseases were a positive independent factor for Overall survival; rate of transformation into AML was decreased in patients with autoimmune disease	Positive

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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