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Treating Myelodysplastic Syndrome Improves an Accompanying Autoimmune Disease Along with a Reduction in Regulatory T-Cells

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Myelodysplastic syndrome; autoimmune disease; regulatory T-cells

Approximately 10–20% of myelodysplastic syndromes (MDS) are associated with an autoimmune disease (AID) (1) and recent data suggest T-cell abnormalities are involved in both diseases' pathology (2,3). We therefore asked whether treating the MDS will influence the AID.

A 44-year old man developed a maculopapular rash and arthritic pain in the small joints of his hands. Workup revealed systemic lupus erythematosus (SLE) based on positive antinuclear antibodies (ANA), anti-double-stranded DNA antibodies, arthritis and a skin biopsy. The patient's blood counts were within normal limits at the time. He was started on prednisone and hydroxychloroquine. After a few weeks he started to feel short of breath and was found to be anemic and leukopenic. Hydroxychloroquine was discontinued without improvement of his blood counts. Anemia workup was negative and bone marrow evaluation revealed MDS with marked partial collagen fibrosis, 5% blasts, an average cellularity of 40% and a normal male karyotype. Concomitantly, the patient developed new neurological symptoms consisting of depression, tremors and eventually stroke-like syndrome. Due to his positive family history and positive genetic testing he was diagnosed with Huntington disease. He was followed periodically for two years and remained transfusion independent. His rash and arthritic complaints were stable. A repeat bone

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Authors' Contributions

OAU followed the case and reviewed the literature, JF assisted in the literature review, PKW oversaw the flow cytometry analysis, JA assisted in the autoimmune diagnosis of this patient and MW oversaw the conduct of the study, contributed to the care of the patient and to the manuscript preparation and all authors approved final version.

Conflict of Interest

The authors have no conflict of interest to report.

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marrow evaluation on 04/10/2008 revealed persistent MDS with 12.5% blasts, 65% cellularity and normal karyotype. Therefore, the patient was started on 5-azacitidine and completed eight cycles between June 2008 and May 2009. Treatment was discontinued due to progression of the Huntington disease when he achieved complete hematologic response and the bone marrow revealed <5% blasts. At the same time he had resolution of the rash and the arthritic findings. Following 5-azacitidine discontinuation, the patient had a flare of his rash and arthritis. Resuming 5-azacitidine treatment resulted in disappearance of the rash and improvement of his arthritis within a month. In addition, ANA became negative and a repeat skin biopsy did not demonstrate the previously noted SLE changes. The patient recently completed seven additional courses of 5-azacitidine. Of note, his prednisone dose remained the same throughout his care and therefore cannot be attributed to the improvement in his SLE.

We studied CD4+FOXP3+ regulatory T-cells by flow cytometry as previously described by us (4). The first sample was drawn before starting 5-azacitidine (August 2006) and the second was drawn in December 2009, after completing nine 5-azacitidine cycles. Both samples were cryopreserved and then thawed immediately prior to the analyses described herein. The patient signed informed consent for these tests. The patient had a significant decrease in his CD4+FOXP3+ T-cells from 13.4% to 3.3% following nine courses of 5-azacitidine (Figure 1).

Regulatory T-cells are usually involved in maintaining immune tolerance. Their expansion in malignant diseases results in suppression of host antitumor responses. Kordasti et al (2) found a significant correlation between the percentage of regulatory T-cells in MDS patients and their disease; high risk patients with >5% blasts and high International Prognostic Scoring System scores had higher CD4 regulatory T-cells. On the other hand, quantification of regulatory T-cells in active SLE patients varies. Some observed a higher proportion of functional regulatory T-cells in patients with Sjogren's syndrome (5), SLE (6,7) and in the synovial fluid of rheumatoid arthritis patients (8) while others (9,10) found that patients with active SLE had significantly lower frequencies of regulatory T-cell. Those differences could be related to different patients' populations and study methods.

In our patient the decrease in regulatory T-cells can be explained by the improvement in his MDS following 5-azacitidine treatment with a concomitant clinical improvement of his SLE. To the best of our knowledge, this is the first case of concomitant MDS and AID, where MDS treatment resulted in resolution of AID along with a decrease in regulatory T-cells.

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Figure 1.

A, gating strategy for FOXP3; CD3+CD4+viable lymphocytes were defined by excluding dead cells using fixable live/dead violet (LDViolet) and a lymphocyte region based on forward and side scatter after backgating on CD3+ cells;

B, FOXP3 versus CD127 (left histograms) and CD25 versus CD127 (right histograms) were used to define the number of regulatory T-cells shown here as blue dots in both data sets. Percentages represent CD3+CD4+CD25+FOXP3+ of CD3+.