Plasma Cytokine Levels Distinguish Chronic Graft Versus Host Disease (cGVHD) Symptom Profile Groups

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Abstract:

Understanding the biologic milieu associated with differing symptom profiles in allogeneic HSCT survivors with cGVHD has the potential to clarify the pathogenesis of cGVHD activity and tissue damage, and may direct the development of new strategies to ameliorate symptoms and improve quality of life.

Keywords: Plasma Cytokine | Chronic Graft Versus Host Disease | Symptom Profiles

Article:

Background: Understanding the biologic milieu associated with differing symptom profiles in allogeneic HSCT survivors with cGVHD has the potential to clarify the pathogenesis of cGVHD activity and tissue damage, and may direct the development of new strategies to ameliorate symptoms and improve quality of life.

Objective: To determine if differing cGVHD symptom profiles are associated with unique patterns of pro-inflammatory cytokine expression and markers of systemic immune activation.

Methods: Plasma levels of sBAFF, IL-1 β , IL-1 receptor antagonist, IL-6, soluble IL-6 receptor, soluble TNF-receptor II, MCP-1, and MIG were assayed by sandwich ELISA. Lymphocyte subset quantities were measured. Concurrently, the Lee Chronic GVHD Symptom Scale, a self-report measure of cGVHD symptoms, and clinical data were obtained. Data from 79 patients were analyzed using descriptive statistics, latent profile analysis, and multinomial logistic regression.

Results: Three distinct symptom subgroups were identified through latent profile analysis: Group 1 (low on all symptoms), Group 2 (prominent oral, upper GI, and weight loss symptoms); and Group 3 (eye, muscle/joint, fatigue and mood symptoms). Multinomial logistic regression, controlling for age, length of time since transplant, cGVHD severity, intensity of immunosuppression and post-transplant lymphocyte reconstitution, revealed that IL-6, TNF-RII, MCP-1 and sBAFF levels significantly distinguished the three symptom subgroups.

Odds Ratios and 95% Confidence Intervals for the Multinomial Logistic Regression of Symptom Latent Class Membership on Cytokines † Controlling for Age, Time Since Transplant, cGVHD Severity, Intensity of Current Immunosuppression and Absolute Lymphocyte Counts †

	Symptom Profile 1 (low on all symptoms) vs. Symptom Profile 2 (prominent oral/GI symptoms) OR (95% CI)	Symptom Profile 1 (low on all symptoms) vs. Symptom Profile 3 (prominent eye, muscle/joint, fatigue and mood symptoms) OR (95% CI)	Symptom Profile 2 (prominent oral/GI symptoms) vs. Symptom Profile 3 (prominent eye, muscle/joint, fatigue and mood symptoms) OR (95% CI)
IL-1 β	1.59 (0.30-8.45)	0.92 (0.32-2.60)	0.58 (0.10-3.32)
IL-6	0.27 (0.09-0.79)*	1.15 (0.52-2.52)	4.26 (1.32-13.82)*
IL-1 RA	0.69 (0.22-2.14)	0.55 (0.29-1.07)	0.81 (0.26-2.48)
sIL-6R	0.50 (0.12-2.13)	1.78 (0.54-5.90)	3.53 (0.83-15.13)
TNF-RII	0.29 (0.04-2.42)	0.28 (0.08-0.99)*	0.95 (0.12-7.59)
MCP-1	8.70 (1.46-51.66)*	0.40 (0.11-1.40)	0.05 (0.01-0.36)**
MIG	1.33 (0.73-2.44)	1.02 (0.63-1.65)	0.77 (0.42-1.39)
sBAFF	0.40 (0.13-1.30)	1.86 (0.88-3.93)	4.61 (1.39-15.31)**

† values were log normal transformed prior to analysis

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or

*

$p < .01$ or $p < .05$, respectively, multinomial logistic regression.

Higher IL-6 levels significantly differentiated participants in Group 2 from those in Groups 1 and 3. Group 3 had higher TNF-RII compared to Group 1. Those with higher sBAFF levels were significantly more likely to be in Group 2, while those with higher MCP-1 levels were significantly more likely to be in Group 3.

Conclusion: Allogeneic HSCT survivors with differing cGVHD symptom profiles were distinguished by significantly different levels of IL-6, TNF-RII, MCP-1 and sBAFF. These data validate this new symptom grouping system based on the Lee Chronic GVHD Symptom Scale as a measure of cGVHD disease burden. IL-6, TNF-RII, MCP-1 and sBAFF appear to be important biomarkers that reflect specific cGVHD manifestations and merit further study.