212 HIGH RATES OF GENITAL TRACT DYSPLASIA IN LONG-TERM SURVIVORS OF ALLOGENEIC STEM CELL TRANPLANTATION AND ASSOCIATED RISK FACTORS
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Background: High rates of cervical dysplasia in women after allogeneic stem cell transplantation (allo-HSCT) have been reported, but risk factors are not well defined.

Objective: To determine rates and risk factors for genital tract dysplasia in post-transplant women.

Methods: In a prospective long-term study after allo-HSCT, gynecologic and medical history, and cervical cytology (Pap) were obtained with follow-up colposcopy and biopsy for abnormal results. Prior genital tract dysplasia history, time to abnormal Pap/dysplasia, chronic graft-versus-host disease (cGVHD), and prolonged immunosuppressive therapy (IST) were assessed for their association with genital tract dysplasia post-transplant. Chi-squared tests were used for categoric variables, and logistic regression was used for multivariate analysis.

Results: All patients received allogeneic transplantation from HLA-matched sibling donors with fully myeloablative total body irradiation based conditioning regimens in 55 subjects. The graft source was marrow in 6 women and ex vivo T lymphocyte depleted peripheral blood stem cells in 54. Of 60 women enrolled, 51 had complete gyn assessments. Of these 51, 18 (35.3%) had cGVHD requiring IST for >3 years. Seven (13.7%) women had a history of genital dysplasia prior to allo-HSCT. Of 23 (45.1%) women with abnormal Pap, 15 (29.4%) had biopsy-proven genital dysplasia: 9 cervical, 2 vaginal and 4 vulvar with other lesions. Chronic GVHD (p = 1.0), prolonged IST for >3 years (p = 1.0), genital GVHD (p = 1.0) and genital GVHD treated by steroids (p = 0.35) were not associated with post transplant dysplasia but pretransplant dysplasia was an important risk factor (p = 0.018) on univariate analyses and subsequently confirmed by multivariate analysis (Odds ratio 10.3; p = 0.013).

Conclusion: Women who have undergone allo-HSCT have a high rate of genital tract dysplasia, especially those with a prior history, suggesting HPV disease is not newly acquired. While the accelerated course may be related to immunologic dysfunction our data showed no relationship to chronic GVHD or to prolonged immunosuppression. Cervical cytology testing (Pap) is the screening method for cervical dysplasia in women, but its utility has not been studied in women after Allogeneic Stem Cell Transplantation (SCT) in the context of genetic chronic graft-versus-host disease (genetics). Cervical cytology screening in women after allo-HSCT may be an important aspect of post transplant care. Our data supports the use of routine post-transplant HPV vaccination in susceptible women after allogeneic stem cell transplantation.

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213 IMMUNE RESPONSES CONTRIBUTE TO DEPRESSION, FATIGUE, AND PAIN IN BLOOD AND MARROW TRANSPLANT RECIPIENTS
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Depression, fatigue, and pain are prevalent and distressing quality of life concerns for individuals recovering from blood and marrow transplantation (BMT). Recent research in other cancer populations suggests inflammatory cytokines can activate central nervous system pathways, evoking adverse behavioral responses including depressed mood, fatigue, and pain. We hypothesized that immune responses also contribute to these symptoms among BMT recipients. Allogeneic (n = 24) and autologous (n = 68) transplant recipients completed well-validated measures of depressive symptoms, fatigue, and pain. To determine rates and 30, 100, and 200 days post-transplant, Circulating proinflammatory (IL-6, TNFα) and regulatory (IL-10) cytokines were measured by ELISA in peripheral blood plasma at the same points. Subject-level fixed effects and mixed effects linear regression models were employed to examine relationships between cytokine levels and quality of life assessments. Results indicated that depression and fatigue were most severe 30 days post-transplant, with allogeneic recipients showing markedly slower improvement than autologous recipients at later assessments. Pain was more stable across time. Autologous and allogeneic transplant recipients had comparable cytokine levels prior to transplant, but allogeneic recipients had significantly higher concentrations post-transplant (p values < .05), which remained high through Day 200. Among individual patients, changes in IL-6 levels across the assessment points were associated with corresponding changes in depression (r = 2.0, p = .048), fatigue (r = 2.7, p = .008), and pain (r = 2.0, p = .048), after covarying for effects of time since transplant. Similarly, participants with elevated IL-6 levels reported more severe depression (z = 2.9, p = .004), fatigue (z = 2.9, p = .004), and pain (z = 3.0, p = .003) compared to participants with low normal IL-6 levels. All models adjusted for graft type and recipient’s age. Similar relationships were seen for TNFα. Results provide evidence for a novel biobehavioral pathway by which inflammatory processes associated with conditioning therapy, infection, and/or graft-versus-host disease can contribute to depression, fatigue, and pain. Findings may assist health care providers in identifying patients most at risk for this constellation of symptoms and suggest novel targets for therapeutic interventions to improve quality of life for individuals recovering from BMT.

214 CERVICAL CYTOLOGY SCREENING IN LONG-TERM SURVIVORS OF ALLOGENEIC STEM CELL TRANPLANTATION WITH GENITAL GRAFT VERSUS HOST DISEASE
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Background: Cervical cytology testing (Pap) is the screening method for cervical dysplasia in women, but its utility has not been studied in women after Allogeneic Stem Cell Transplantation (SCT) in the context of genetic chronic graft-versus-host disease (genetics). Objective: To examine the clinical findings noted with mildly abnormal Pap reports in women post SCT. Methods: As part of a prospective long-term study after SCT, gynecologic and medical history, assessment for genital eGVHD, and Pap were performed. If atypical cells of uncertain significance (ASCUS) were reported on Pap, high risk (HR) HPV testing was done. Those with ASCUS+HRHPV underwent colposcopy and biopsy. Patients with moderate or severe genital eGVHD were treated with vulvar steroids and followed by gynecology. Chi-square tests and Kaplan-Meier survival curves were used for univariable and Cox models for multivariable analyses.

Results: All patients received allogeneic transplantation from HLA-matched sibling donors with fully myeloablative total body irradiation based conditioning regimens in 55 subjects. The graft source was marrow in 6 women and ex vivo T lymphocyte depleted peripheral blood stem cells in 54. Of 60 women enrolled, 51 had complete gyn assessments. Of these 51, 11 (21.6%) had genital eGVHD, with 6 (11.8%) requiring vulvar steroids. Of 10 women with ASCUS, 7 were ASCUS–HRHPV. Of the other three, two had biopsy-proven dysplasia. While both genital eGVHD (p = 0.1) and use of vulvar steroids (p = 0.07) were weakly associated with a decreased time to ASCUS Pap in univariable analysis, neither was associated with biopsy-proven dysplasia or time to dysplasia. In multivariable analysis examining the impact of age, pretransplant dysplasia, eGVHD, genital GVHD and vulvar steroids, only vulvar steroids (HR 0.2, p < 0.01) and pretransplant dysplasia (HR 0.26, p < 0.05) were significantly associated with the time to abnormal Pap. Conclusion: ASCUS Cervical cytology in women with genital eGVHD requiring vulvar steroids after SCT may represent cytoclogic changes of genital eGVHD or portend reactivation of HPV disease. Cytology screening is an important aspect of post transplant gynecology care.

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