

Risk of Melanoma among Survivors of Hematologic Malignancies

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Editorial

According to Surveillance, Epidemiology, and End Results (SEER) reports, 71,850 new cases of Non-Hodgkin's Lymphoma (NHL) and 54,270 cases of leukemia were estimated in 2015, corresponding to 7.6 % of all newly-diagnosed malignancies [1]. In the past few years, with the development of new therapies, median 5-year overall survival rates for patients with hematologic malignancies have reached 50% to 85%, depending on the subtype, with higher percentages seen in more indolent conditions, including Follicular Lymphoma (FL), Chronic Lymphocytic Leukemia (CLL) and Hodgkin's Lymphoma (HL). As a result, a rapidly growing population of cancer survivors is expected and concerns about long-term treatment-related toxicities and incidence of Second Malignant Neoplasms (SMNs) have gained even greater importance [1].

A meta-analysis including a total of 10 studies investigating the incidence of solid SMNs, encompassing 115916 NHL survivors treated between 1961 and 2004 suggested a 1.32-fold increased risk for solid tumors [2]. Similarly, Schaapveld et al. reported a standardized incidence ratio of 4.6 (95% confidence interval 4.3 to 4.9) among 3905 patients treated for HL in comparison to the general population in the Netherlands and a sustained risk for second cancers even 40 years after treatment [3]. Another study based on SEER registries between 1992 and 2006 identified lung cancer and cutaneous melanoma as malignancies with an increased risk in CLL and FL survivors [4]. In line with previous findings, a recent publication of a Canadian group reported an increased cancer death rate in solid-organ transplant recipients compared to the expected in general population suggesting that immunosuppressed environment may contribute to the development of those neoplasms [5]. The factors underlying the increased risk of second malignancies among survivors of hematologic neoplasms are complex. Most authors suggest that differing immunologic alterations, genetic susceptibility, specific treatments (especially with alkylating agents) and environmental factors, such as tobacco use and infections may be involved [4].

In a recently-published and extremely relevant contribution, Lam et al. [6] evaluated the risk of second cutaneous melanoma among NHL survivors. Among the 44870 NHL 1-year survivors, diagnosed at the age of 66 to 83 from 1992 to 2009, two hundred and two second melanomas were identified, with a median interval from the NHL of 3 years. The cumulative incidence of melanoma was higher for those who had CLL than for non-CLL (1.37% v 0.78%). Survivors of CLL who were diagnosed with T-cell-activating autoimmune conditions before or after the diagnosis of the NHL had more than a two-fold increased risk of developing cutaneous melanoma. Another rising concern in this population was the 1.90-fold increased risk in those treated with fludarabine-containing chemotherapy [4,6]. Also, patients

treated for HL in the Schaapveld et al. cohort study had a risk of second melanoma 2.8 times as high as that observed in the general population [3].

Taking these results into consideration, melanoma screening becomes a topic of great concern in survivors of hematologic malignancies. At this time, no randomized trials have established the efficacy of screening for melanoma. The United States Preventive Services Task Force (USPSTF) found insufficient evidence to recommend for or against routine screening. Conversely, The American Cancer Society recommends skin examination as part of the broader cancer-related checkup for people over 20 years of age. In this controversial scenario, the SCREEN Project carried out in Northern Germany in 2003-2004 implied that an annually population screening would lower the mortality from melanoma in citizens with 20 years or older [7-9]. Based on this data, Germany started a nationwide screening program in 2008. From the age of 35 years onwards, every individual was entitled to full-body visual inspection of the skin at two-year intervals. Unfortunately, recently data up to the year of 2013 concluded that there had not been any downward trend in melanoma mortality since the introduction of the screening project [10]. Hopefully, the incorporation of new techniques such as dermoscopy, confocal microscopy and total body photography will potentially increase the accuracy of screening methods.

In the absence of definitive data, experts advocate that individuals at higher risk for melanoma (white men ≥ 50 years, history of significant sunburn, multiple moles, history suggesting a familial melanoma syndrome or with multiple atypical nevi) should be counseled about skin self-examination, use of regular sunscreen and have a periodic full body skin examination performed by a properly trained clinician/ dermatologist. In addition to detection of early melanoma, such measures could potentially translate into a reduction of cause-specific mortality. Based on the data that subgroups of hematologic malignancies, such as CLL and lymphoma survivors are at increased risk for cutaneous melanoma, these specific populations should be included in the high-risk group and currently available recommendations should be extended to these patients. Moreover, efforts to better characterize the long-term risks in patients treated for acute leukemia and recipients of autologous or allogeneic bone marrow transplant are of utmost importance.

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