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Project: Other Malignancies in Chronic Lymphocytic Leukaemia - A retrospective analysis

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Introduction:

Chronic Lymphocytic Leukaemia (CLL) is a haematological malignancy typically affecting patients from the 7th decade of life. Although incurable, the disease course is largely indolent and life expectancy is greater than 10 years in early stages. At this age, skin cancer incidence is relatively high. Squamous cell tumours in particular can be removed by the immune system before they become malignant however, the malignant B-cells in these leukaemic patients suppress the immune system leaving the patient immunocompromised. A link to higher skin cancer incidence in this group has been explored in three previous studies but details regarding the skin cancer features themselves and population comparisons have been poor. Additionally, the higher levels of UV radiation exposure in New Zealand present another challenge for haematologists when interpreting this data.

Aim:

1. To determine if the true risk of skin cancer is greater here than currently recognised.
2. To explore the relationship between skin cancer frequency and overall survival
3. To investigate any potential relationship between skin cancers and progression of CLL (Binet stage B/C)

Method:

A retrospective analysis was conducted involving all patients referred to the Canterbury District Health Board (DHB) haematology department with B-Cell Chronic Lymphocytic Leukaemia between January 1998 to January 2015. Patients with other forms of CLL were excluded. Disease information was accessed from both clinical and electronic records and malignancy data was obtained from the CDHB Anatomical Pathology database. This study defined 'skin cancers' as invasive carcinomas with metastatic potential only (i.e carcinoma in situ and basal cell carcinomas were not included). Analysis was performed using SPSS 2 and models were generated with Prism.

Results:

375 patients were included in the study with an average follow up time of 6.5 years. The median age was 67. The study found that 153 patients (40.8%) developed at least one second malignancy with 58 patients developing a total of 182 invasive skin cancers. 8.5% of patients developed metastases. 'Younger patients' (below median age) developing more than 2 skin cancers had significantly poorer Kaplan-Meier survival curves (76 ± 5.6 months vs 176 ± 9.7 months; $p=0.019$) but no significant effect was seen in older patients. Patients with more advanced stage CLL (Binet B/C) developed skin cancers significantly earlier than those with stage A (40 ± 12.4 months vs 72 ± 8.3; $p=0.027$).

Results are reported as time from diagnosis to event in months. The large sample size and long follow up time mean this study is representative of the typical disease course in New Zealand. The decision to exclude non-metastatic skin cancers means survival risks are not diluted by the more common basal cell carcinoma, as in other studies.

By obtaining comprehensive histology records the analysis of skin cancer features can be done in greater depth than any prior study. This study is not without limitations. In New Zealand suspicious skin lesions are often removed by general practitioners without being processed by histopathology. As these cases could not be included, it is almost certain that the true rates are even greater than what have been presented. Awareness of the risk of skin cancer for CLL patients has increased over the past decade thus surveillance bias should be kept in mind when comparing to the general population. Firstly, the rate of second malignancies was unexpectedly high – even for the CLL subgroup. Compared to general population data from Tan et al. CLL patients develop 9 times as many malignancies which is vastly greater than the 2 – 3 times risk reported by other CLL studies. Furthermore the metastases occur over twice as often in this group suggesting their skin cancers may be more aggressive but further research is needed.

Cancers at younger ages are known to have poor prognoses however, the age used (67) is not particularly young for skin cancer and identifies a significant point in cancer surveillance of younger patients however, the age of this 'young' group cannot be established from this study alone. Further work would assist both national and local screening protocols. The observation that patients with advanced CLL (Binet B/C) have a higher incidence of skin cancer incidence is expected as these progressive states result in greater immune compromised however, until now there has been no New Zealand specific data available. In addition to the information presented, information from this study is also being used to explore the features of CLL invasive skin cancers compared to the general population, expand on the recently published link between CD38 and overall survival as well as updating information on CLL outcomes in New Zealand to assist haematologists both in New Zealand and further abroad.

Conclusion:

It is hoped that practitioners are prompted by these findings to conduct thorough, regular surveillance of CLL patients for skin cancers however, this should not be limited to Binet B/C or younger patients. The absolute number of malignancies appearing in this population are surprisingly high and a general surveillance plan could have substantial benefits for both the patient and the healthcare system.