

Dialogue: what can we learn about the relationship between systemic lupus erythematosus and haematological malignancies from linking disease registries?

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In systemic lupus erythematosus (SLE), there appears to be specific differences in the cancer susceptibility compared with the general population. While the overall cancer incidence rate in patients with SLE is increased about 14%,¹ the standardised incidence ratio of a given cancer is largely dependent on the cancer type. Prominent increases are noted in haematological malignancies (HM),²⁻³ as well as lung, thyroid and vulvar cancer.¹⁻⁴ While HM overall are increased threefold, the risk of non-Hodgkin's lymphoma is increased fourfold, with a predominance of the diffuse large B cell subtype (DLBCL);¹ non-lymphoma HM, including leukaemia, are increased almost twofold and Hodgkin's lymphoma and multiple myeloma trend towards an approximately twofold increase.¹ Several hypotheses are advanced to explain this heightened risk, including dysregulated lymphocyte proliferation, which may promote oncogene translocation, favouring lymphoma development;⁵ the predominance of DLBCL among the non-Hodgkin's lymphomas arising in SLE supports this rationale as they arise from activated lymphocytes, the lineage responsible for most of the inflammation in SLE. Consistent with the potential role of dysregulated lymphocyte proliferation, it was postulated that increased SLE disease activity may mediate lymphoma development, but our research has not supported such a link.⁶ Other explanations include an increased expression of cytokines such as APRIL, interleukin-10 or interferon,⁷⁻⁹ altered ability to clear Epstein-Barr virus,¹⁰ the co-existence of secondary Sjogren's and immunosuppressive therapies, although our research reveals that most lymphoma cases were never exposed to these medications.⁶

In contrast to HM, the incidence of certain hormone-sensitive cancers is found to be consistently lower among patients with SLE including a reduced risk of breast, ovarian, endometrial and prostate cancers.¹ Hormonal changes, genetics, as well as drugs used in SLE such as non-steroidal anti-inflammatory drugs among others are postulated as potential reasons for this decreased risk.¹¹

This retrospective study examines the relationship between HM and SLE by linking disease registries at one institution. Individuals with both diagnoses were divided into those with SLE first followed by HM at least 1 year later and those with HM before or concurrent with the diagnosis of SLE.¹² The majority of the patients were in the after SLE group (29/45), and of the 16 in the before or concurrent SLE and HM group, 9/16 had HM more than 2 years prior to SLE and 7 had HM and SLE concurrently. HM after malignancy group confirmed previous findings of the predominant cell type, DLBCL, and their poor prognosis. The new information provided here describes a more favourable prognosis observed in HM before SLE and patients with concurrent HM/SLE who are usually omitted from previous reports that eliminate prior or concurrent malignancy in patients who are diagnosed with SLE. It is perhaps not surprising that those who developed HM prior to the diagnosis of SLE had a more favourable prognosis as they survived their HM and then remained alive long enough to develop SLE. Two patients with SLE who received a renal transplant for end-stage renal disease secondary to SLE developed late HM, which was described as post-transplant lymphoproliferative disorder (PTLD). These patients may be

very different than those patients with SLE not undergoing transplant, and the relationship and/or mechanism of the relationship between SLE and HM is likely to be different. The authors also raise the possibility that SLE is a paraneoplastic syndrome when HM and SLE are diagnosed concurrently.

The authors have broadened the spectrum of HM in SLE raising new questions about mechanisms and the impact of treatment in HM before SLE and patients with SLE who later develop PTLD. Assuming HM before patients with SLE were treated for HM that included immunosuppression for early-stage disease and many achieved remission, then why do these patients still develop SLE later including nephritis? What does this tell us about implicating genetic, immunological or environmental factors as contributors to either or both conditions? Are SLE transplant patients who subsequently develop PTLD different from other transplant recipients who do not have SLE but presumably are exposed to similar immunosuppression following renal replacement or does the underlying SLE predispose to PTLD irrespective of treatment?

Although new observations were made in this retrospective study, we still need to make progress in gaining additional insight as to the mechanism behind the coexistence of these two diseases. What is the driver or the important interactions between genetics, medications, immune dysfunction or the environment (eg, infections, hormones)?

Competing interests None.

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