Karolinska Institutet

Institutionen för Kliniska Vetenskaper, Danderyds Sjukhus, Enheten för Dermatologi

Cutaneous lupus erythematosus; epidemiology, association with SLE and comorbidity

AKADEMISK AVHANDLING
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ABSTRACT

Lupus erythematosus (LE) is a disease that includes a broad spectrum of symptoms, from localized cutaneous LE (CLE) to severe systemic LE (SLE). Based on histopathological changes, the skin manifestations of LE can be divided into LE-specific (=CLE) and LE-non-specific manifestations. CLE is a chronic, inflammatory skin disease with a wide range of manifestations that can be seen in patients with or without SLE. As defined by clinical symptoms, average duration of symptoms, histological and serological findings, CLE can be further divided into three main subsets (acute CLE [ACLE], subacute CLE [SCLE] and chronic CLE [CCLE]). All four studies in this thesis focused on CLE and different comorbidities: the classification of cutaneous manifestations in SLE patients, the risk for progression to SLE, risk for cancer among CLE patients and the association between drug exposure and the development of subacute CLE.

In study I we investigated the frequency of cutaneous manifestations in a cohort of 260 SLE patients. We compared clinical and serological manifestations in SLE patients with and without CLE. LE-non-specific skin manifestations (43 %) were almost twice as frequent as CLE (23 %). Raynaud's phenomenon was significantly more common but arthritis and serositis were less common in the CLE group than in the non-CLE group. Of the SLE patients, 42 % had symptoms consistent with polymorphic light eruption.

In study II a cohort study of 1,088 CLE patients from the National Patient Register was undertaken to calculate the incidence of CLE in Sweden. The incidence rate was estimated to 4.0/100,000 inhabitants. We also calculated age- and gender-specific incidence rates for different CLE subsets (i.e. discoid LE, SCLE and other local LE). We estimated the probability of also being diagnosed with SLE during the first 3 years after diagnosis of CLE. We found the cumulative probability of receiving an additional diagnosis of SLE to be 18 %, highest for women and the SCLE subset.

In study III we evaluated the overall and specific cancer risks in CLE patients. In a cohort of 3,663 CLE patients we found increased risks for cancer overall (hazard ratio 1.8 (95 % confidence interval 1.5-2.2) and about a fourfold increased risk for buccal cancer, lymphomas, respiratory cancer and non-melanoma skin cancer. The elevated risks remained when we excluded patients also diagnosed with SLE.

In study IV, we performed a case-control study to examine the association between previously dispensed drugs and a subsequent development of SCLE in a group of 234 incident SCLE patients. We found increased relative risks for exposure to terbinafine, TNF-α inhibitors, antiepileptics, proton pump inhibitors, thrombocyte inhibitors, ACE -inhibitors and NSAIDs 0-6 months before the diagnosis of SCLE. About one third of all SCLE cases could be attributed to previous drug exposure.

This thesis adds to previous knowledge about epidemiology, prognosis, disease progression to SLE, comorbidity and the association with certain drugs in CLE. Swedish population-based epidemiological data on CLE will potentially be useful in the planning of health care as well as clinical trials. For prospective studies, especially of the intermediate group between CLE and SLE, population-based quality registers will be needed to further improve the health care for CLE patients.

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