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PRIMARY CUTANEOUS LYMPHOMAS

Epidemiology

Primary cutaneous lymphomas (PCL) are non-Hodgkin lymphomas that present in the skin with no evidence of extracutaneous disease at the time of diagnosis. The estimated annual incidence is 1/100 000 in Western countries. PCLs comprise cutaneous T cell lymphoma (CTCL), accounting 75-80% of cases, and cutaneous B cell lymphoma (CBCL) subtypes, acconting 20-25% of cases. The most common CTCL subtype is represented by mycosis fungoides (MF).

Signs and symptoms

Patients with PCLs usually present with various types of skin lesions, ranging from patches, plaques in MF covering various percentage of skin surface, to generalized erytroderma in Sezary Syndrome (SS). Skin lesions may be itching and may be associated to loco-regional involvement of lymph nodes. The characteristic of skin lesions depends on the type of CTCL or CBCL subtype and may be solitary or multifocal. Systemic symptoms (loss of weight, fever, night sweats, fatigue) are rare and confined in advanced stages of disease.

Diagnosis and risk stratification

The diagnosis of PCLs should always be based on a combination of clinical, histological, immunophenotypical and genetic data. Demonstration of clonal T cell receptor or immunoglobulin gene rearrangements in lesional skin or peripheral blood may be a valuable adjunct in selected cases. However, clinical, and histopathological features are, in most cases, the most important deciding factors for therapeutic planning. In all cases, adequate staging should be carried out to exclude the presence of extracutaneous disease. Flow cytometry of the peripheral blood is recommended for all stages of MF. Computed tomography (CT) and/or positron emission tomography (FDG-PET) scans are optional in early-stage MF. Initial work-up for patients with a PCL other than MF/SS also includes complete physical examination, representative skin biopsy, complete and differential blood cell count, routine serum biochemistry with lactate dehydrogenase (LDH) and appropriate imaging studies (CT and/or FDG-PET scans).
Prognosis is extremely variable depending on the type of PCLs and the stage of disease. For clinical staging of MF and SS, the revised tumour, node, metastasis, and blood (TNMB) staging system should be used. Clinical stage has the most relevant prognostic influence. Other factors with prognostic relevance in MF are older age, large cell transformation and increased LDH values.

Treatment

The choice of treatment depends on the type of PCL and the stage of disease. A stage-adapted conservative therapeutic approach is recommended for MF. Patients with only patches and/or plaques (stage IA o IB) should be treated with skin-directed therapies, including topical steroids, psoralens plus ultraviolet A (PUVA),
narrow-band ultraviolet B (nb-UVB). In patients developing one or few infiltrated plaques or tumours (stage IIB), additional low-dose local radiotherapy (RT) may suffice. For patients with more extensive infiltrated plaques and tumours, or refractory to skin-directed therapies, systemic therapy with interferon alpha (IFNa) or retinoids (including bexarotene), commonly combined with PUVA or other skin-directed therapies, or a combination of IFNa and retinoids or total skin electron beam therapy (TSEBT), can be considered.

Our treatment approach is based on International guidelines (i.e. ESMO doi.org/10.1093/annonc/mdx223).
In case of relapsed or refractory MF expressing CD30 the antibody-drug conjugate Brentuximab Vedotin is an effective option. An alternative approach is represented by single-agent chemotherapy with Gemcitabine. In relatively young patients with refractory, progressive MF or with SS, allogeneic stem cell transplantation (alloSCT) should be considered.