COMMENTARY

Classification of Cutaneous Lymphomas: An Update

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Challenges in the classification of cutaneous lymphomas

Primary cutaneous lymphomas are a rare heterogeneous subgroup of non-Hodgkin lymphomas affecting the skin and lacking extracutaneous manifestations at the time of diagnosis.[1,2] They are the second most common form of extranodal non-Hodgkin lymphomas, with an annual incidence of an average 1 case per 100,000 in the Western world.[3] The disease group is broadly categorized into cutaneous T-cell lymphomas (CTCL) and cutaneous B-cell lymphomas (CBCL), with each type further subdivided based on its clinical presentation and histological phenotype. Cutaneous lymphomas are usually characterized by a more indolent course than other lymphoid neoplasms and may remain restricted to the skin for a long time. Treatment options include mostly skin-directed therapies such as topical corticosteroids, topical chemotherapy, retinoids and phototherapy, as well as radiation therapy. Systemic treatments are the choice for advance disease and can be combined.[2]

Different subtypes of primary cutaneous lymphomas require distinct therapeutic approaches and hold varied prognostic implications. However, classifying and diagnosing cutaneous lymphomas is a complex task due to the heterogeneous nature of these malignancies, which can present with many different, but sometimes also overlapping clinical and histopathological features.[2,4] The challenge lies in the comprehensive integration of diverse diagnostic data, including clinical observations, histopathology, immunophenotyping and genotyping studies, to delineate precise subtypes and appropriately guide disease management.

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Recent updates in the classification of cutaneous lymphomas

Current classification of cutaneous lymphomas has undergone long evolution. Its basis was laid by the Revised European-American Classification of Mature Lymphoid Neoplasms published in 1994.[5] Subsequent revisions have been generated through continuous joined efforts of clinicians, hematopathologists and geneticists. Until 2005, cutaneous lymphomas were classified based on either the World Health Organization (WHO) criteria or the European Organization for Research and Treatment of Cancer (EORTC) classification. Then, the WHO-EORTC consensus classification was introduced to better reflect the characteristics of cutaneous lymphomas and eliminate inconsistencies in previous classification systems.[6] The definitions and diagnostic criteria continued to be refined in 2008 and 2017, and were presented in an updated version of the WHO-EORTC classification in 2018 and in the 4th edition of the WHO Classification of Skin Tumors Blue Book that serves as an accepted standard for the diagnosis and classification of lymphomas.[3,4]

Notably, over the last two years in 2022, two distinct classifications for hematological malignancies have been proposed, offering a comprehensive perspective on cutaneous lymphoid neoplasms. These two classifications are the 5th edition of the WHO classification of hematolymphoid tumors[7] and the International Consensus Classification of mature lymphoid neoplasms.[8] Compared to the previous 4th edition of the WHO classification, these new classifications introduce several changes, that are largely in harmony with each other, and emphasis particularly on alterations in terminology relating to skin lymphoid neoplasms. Common changes shared by both schemes include the reclassification of CD8+ acral T-cell lymphoma as CD8+ acral T-cell lymphoproliferative disorder, and the acknowledgment of entities that were previously considered provisional but have now been designated as definitive types. These recognized entities comprise primary cutaneous small or medium CD4+ T-cell lymphoproliferative disease (LPD), primary cutaneous gamma/delta T-cell lymphoma, primary cutaneous CD8+ aggressive epidermotropic cytotoxic T-cell lymphoma, and EBV+ mucocutaneous ulcer. Both classifications regard primary cutaneous marginal zone B-cell clonal neoplasms as predominantly indolent diseases but employ different terminology: the 5th WHO classification uses “primary cutaneous marginal zone lymphoma,” whereas the ICC classification opts for “primary cutaneous marginal zone lymphoproliferative disorder.” Furthermore, the 5th WHO classification introduces essential and desirable diagnostic criteria for each disease type, and includes dedicated chapters on reactive B- or T-cell-rich lymphoid proliferations, previously referred to as cutaneous pseudolymphomas. As in previous lymphoma classifications, the importance of a multiparameter approach that integrates clinical, histological, phenotypic, and molecular features remains the cornerstone for defining cutaneous (and extracutaneous) lymphomas.

Conclusion

The classification of cutaneous lymphomas is a dynamic and rapidly evolving field. Over the last few years, there has been significant progress in our understanding of these diseases, driven by clinicopathological, molecular and genomic data. These data have allowed for the refinement of diagnostic criteria for various entities, the establishment of previously provisional categories, and the discovery of new entities. The emergence of genomic data has particularly transformed our perspective on cutaneous lymphomas, with the potential to revolutionize diagnosis and management strategies in clinical practice. However, while the impact of these advances is undeniable, their successful integration into general practice will depend on continued research efforts and the establishment of clear guidelines. It is essential to strike a balance between innovation and validation to ensure that these advancements benefit patients and enhance our ability to effectively manage these complex diseases.

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