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Identification of a chemokine receptor profile characteristic for mediastinal large B-cell lymphoma.

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Source

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Abstract

Mediastinal large B-cell lymphomas (MLBCLs) are considered as a subtype of diffuse large B-cell lymphoma; however, they exhibit completely different patterns of dissemination. Since they share a number of surface markers with thymic B cells, a close relationship was assumed. MLBCLs arise extranodally within the anterior mediastinum and have a low propensity to metastasize. To address the preferential positioning of MLBCL, we focused on homeostatic chemokines involved in B-cell compartmental homing in secondary lymphoid organs, which are also capable of shaping lymphoid niches in ectopic sites. Here, we applied immunohistochemistry to assess chemokine receptor and ligand expression in situ. Flow cytometry was used to identify the chemokine receptor profile on an MLBCL-derived cell line, Karpas1106 and on thymic B cells. Migration assays were performed to examine functionality of chemokine receptors. Electrophoretic mobility shift assay was applied to score for NF-kappaB activity. Using immunohistochemistry, we obtained an unexpectedly low-expression frequency for the chemokine receptors CXCR5 and CCR7 in primary lesions. Although the mature B-cell marker CCR6 was absent in most cases, the lineage aberrant marker CCR9 emerged in the majority of MLBCL cases. Given the role of NF-kappaB in the transcriptional activation of CCR7, we identified the involvement of the noncanonical activation pathway in MLBCLs. MLBCLs exhibit a diagnostic chemokine receptor profile that is instrumental in the discrimination from diffuse large B-cell lymphoma not otherwise specified and classical Hodgkin lymphoma. Furthermore, we suggest that low-abundance expression of CCR7 and CXCR5 may hinder lymphoma cells from nodal dissemination.

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