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Common clonal origin of an acute B-lymphoblastic leukemia and a Langerhans' cell sarcoma: evidence for hematopoietic plasticity.

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Source

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Abstract

BACKGROUND: The hierarchical organization of hematopoiesis with unidirectional lineage determination has become a questionable tenet in view of the experimental evidence of reprogramming and transdifferentiation of lineage-determined cells. Clinical examples of hematopoietic lineage plasticity are rare. Here we report on a patient who presented with an acute B-lymphoblastic leukemia and developed a Langerhans' cell sarcoma 9 years later. We provide evidence that the second neoplasm is the result of transdifferentiation.

DESIGN AND METHODS: B-cell acute lymphoblastic leukemia was diagnosed in an 11-year old boy in 1996. Treatment according to the ALL-BFM-1995 protocol resulted in a complete remission. Nine years later, in 2005, Langerhans' cell sarcoma was diagnosed in a supraclavicular lymph node. Despite treatment with different chemotherapy protocols the patient had progressive disease. Finally, he received an allogeneic peripheral blood stem cell transplant and achieved a continuous remission. Molecular studies of IGH- and TCRG-gene rearrangements were performed with DNA from the Langerhans' cell sarcoma and the cryopreserved cells from the acute B-lymphoblastic leukemia. The expression of PAX5 and ID2 was analyzed with real-time reverse transcriptase polymerase chain reaction.

RESULTS: Identical IGH-rearrangements were demonstrated in the acute B-lymphoblastic leukemia and the Langerhans' cell sarcoma. The key factors required for B-cell and dendritic cell development, PAX5 and ID2, were differentially expressed, with a strong PAX5 signal in the acute B-lymphoblastic leukemia and only a weak expression in the Langerhans' cell sarcoma, whereas ID2 showed an opposite pattern.

CONCLUSIONS: The identical IGH-rearrangement in both neoplasms indicates transdifferentiation of the acute B-lymphoblastic leukemia into a Langerhans' cell sarcoma. Loss of PAX5 and the acquisition of ID2 suggest that these key factors are involved in the transdifferentiation from a B-cell phenotype into a Langerhans'/dendritic cell phenotype. (Clinical trial registration at: Deutsches KrebsStudienRegister, http://www.studien.de, study-ID:8).

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