



UKE Paper of the Month February 2025

Reconstructing skeletal homeostasis through allogeneic hematopoietic stem cell transplantation in myelofibrosis

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ABSTRACT:

Myeloproliferative neoplasm-associated myelofibrosis is a clonal stem cell process characterized by pronounced bone marrow fibrosis associated with extramedullary hematopoiesis and splenomegaly. Allogeneic hematopoietic stem cell transplantation (allo-HSCT) represents the only curative treatment leading to bone marrow fibrosis regression. Here we provide an in-depth skeletal characterization of myelofibrosis patients before and after allo-HSCT utilizing clinical high-resolution imaging, laboratory analyses, and bone biopsy studies. Despite unimpaired bone microarchitecture at peripheral skeletal sites, we observe a marked increase in bone mineral density at the lumbar spine and proximal femur, which is histologically related to severe bone marrow fibrosis and osteosclerosis, fully normalizing after allo-HSCT. Importantly, the regression of fibrosis is accompanied by vanishing osteosclerosis along with restored osteoclastic resorption activity and whole-body calcium homeostasis. Together, our results provide evidence for an extensive reconstruction of skeletal homeostasis by allo-HSCT in MF, leading to rapid resolution of osteosclerosis.

STATEMENT:

This study is a comprehensive assessment of bone mass, microarchitecture, matrix quality and turnover trajectories in patients with myeloproliferative neoplasm-associated myelofibrosis undergoing allo-HSCT. We demonstrate that allo-HSCT leads to rapid normalization of osteosclerosis, accompanied by restoration of osteoclast function and systemic calcium homeostasis. This is the first time that researchers have demonstrated that allo-HSCT heals not only the bone marrow but also the bone in patients who have myelofibrosis.

BACKGROUND:

This work is the result of excellent internal UKE collaboration between the Department of Stem Cell Transplantation, the Institute of Osteology and Biomechanics, and the Department of Trauma and Orthopaedic Surgery, under the supervision of Prof. Nicolaus Kröger, Prof. Michael Amling and Dr. Tim Rolvien. First authors are Mathias Schäfersküpper and Alexander Simon, who performed this work as part of their MD (Dr. med.) and PhD thesis, respectively.