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Stem cell therapy for the treatment of severe tissue damage after radiation exposure

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The late adverse effects of pelvic radiotherapy concern 5 to 10% of them, which could be life threatening. However, a clear medical consensus concerning the clinical management of such healthy tissue sequelae does not exist. Our group has demonstrated in preclinical animal models that systemic MSC injection is a promise approach for the medical management of gastrointestinal disorder after irradiation. We have shown that MSC migrate to damaged tissues and restore gut functions after irradiation. The clinical status of first four patients suffering from severe pelvic side effects resulting from an over-dosage was improved following MSC injection in a compassionate situation. A quantity of 2×10^6 - 6×10^6 MSC /kg were infused intravenously to the patients. Pain, hemorrhage, frequency of diarrheas and fistulization as well as the lymphocyte subsets in peripheral blood were evaluated before MSC therapy and during the follow-up. Two patients revealed a substantiated clinical response for pain and hemorrhage after MSC therapy. In one patient pain reappeared after 6 months and again substantially responded on a second MSC infusion. A beginning fistulization process could be stopped in one patient resulting in a stable remission for more than 3 years of follow-up. The frequency of painful diarrhea diminished from an average of 6/d to 3/d after the first and 2/d after the 2nd MSC injection in one patient. In all patients, prostate cancer remained in stable complete remission. A modulation of the lymphocyte subsets towards a regulatory pattern and diminution of activated T cells accompanies the clinical response in refractory irradiation-induced colitis. No toxicity occurred. MSC therapy was safe and effective on pain, diarrhea, hemorrhage, inflammation, fibrosis and limited fistulization. For patients with refractory chronic inflammatory and fistulizing bowel diseases, systemic MSC injections represent a safe option for salvage therapy. A clinical phase II trial will start in 2018.

Biography

Alain Chapel has been developing gene and cell therapy using non-human primates, immune-tolerant mice and rats to protect against the side effects of radiation, for 25 years. He collaborates with clinicians to develop strategies for treatment of patients after radiotherapy overexposures. He has participated in the first establishment of proof of concept of the therapeutic efficacy of mesenchymal stem cells (MSCs) for the treatment of hematopoietic deficit, radiodermatitis and over dosages of radiotherapy. He has contributed to the first reported correction of deficient hematopoiesis in patients (graft failure and aplastic anemia), thanks to intravenous injection of MSCs restoring the bone marrow microenvironment, mandatory to sustain hematopoiesis after total body irradiation. He is Scientific Investigator of clinical phase II trial evaluating the efficacy of systemic MSC injections for the treatment of severe and chronic radiotherapy-induced abdomino-pelvic complications refractory to standard therapy (NCT02814864/Hirsch Index 26). His research interests are regenerative medicine, cell therapy, scaffold and radiotherapy.

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