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

Alain Chapel¹, A Semont¹, N Mathieu¹, C Linard¹, L Douay^{2, 5}, N C Gorin^{2, 5}, M Mothy^{2, 5}, J M Simmon³, H Rouard^{2, 5}, J J Lataillade⁴, J Voswinkel³, R Tamarat¹ and M Benderitter¹

¹Institute of Radiological Protection and Nuclear Safety, France

²Saint Antoine Hospital AP-HP, France

³Pitié-Salpêtrière University Hospital, France

⁴Percy Military Hospital, France

⁵UPMC University, France

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 sequela does not exist. Our group has demonstrated in preclinical animal models that systemic MSC injection is a promising 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 four first 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 was infused intravenously to the patients. Pain, hemorrhage, frequency of diarrheas and fistulisation 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. At the beginning, fistulisation 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 1st 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 fistulisation. For patients with refractory chronic inflammatory and fistulising bowel diseases, systemic MSC injections represent a safe option for salvage therapy.

Biography

Alain Chapel is a Scientific Investigator at IRSN, Laboratory of Radiopathology and Experimental Therapies. For 20 years, he has been developing gene and cell therapy using non-human primates and immune-tolerant mice and rats to protect against the side effects of radiation. He has developed representative experimental models of SAI to investigate the effect of radiation on both radiosensitive hematopoietic cells and their bone marrow microenvironment. In collaboration with Saint-Antoine Hospital (Paris, France), 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. Currently his work focuses on the development of radio-induced bone marrow aplasia using human hematopoietic stem cells derived from human IPS. He is a Member of various learned national and international societies: European Bone Marrow Transplantation Group (EBMT), American Society for Hematology, International Society of Stem Cell Research, Société Française de Greffe moelle et de thérapie cellulaire. He is an Associate Editor of five international journals: World Journal of Stem Cells, World Journal of Gastrointestinal Surgery, World Journal of Radiology, The Open Gene Therapy Journal and Journal of Clinical Rehabilitative Tissue Engineering Research.

alain.chapel@irsn.fr

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