

A new therapeutic approach of radiation burns by mesenchymal stem cell transplantation

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The therapeutic management of severe radiation burns remains a challenging issue. Conventional surgical treatment (excision and skin autograft or rotation flap) often fails to prevent unpredictable and uncontrolled extension of the radiation-induced necrotic process. This is mainly due to two major causes on the first hand the difficulties to delineate extent and severity of radiation damages because of the unpredictable dynamic evolution of the lesions and on the other hand the very frequent delay in the recognition of the radiological nature of the lesions. Here we present two cases of radiation burns that occurred recently. The first accident occurred on December 15, 2005, in Chile, where a 27-year-old picked-up a gammagraphy source (¹⁹²Ir, 3.3 TBq) with his left hand and put it in the back left pocket of his trousers, where he kept it for approximately ten minutes before the alert was given. The patient rapidly exhibited multifocal lesions to the left hand and the buttock, and at the request of Chilean authorities, the patient was hospitalized at the burn treatment center of Percy military hospital on December 27, 2005. During this time, a physical reconstitution of the accident indicated more than 2000 Gy at the center of the buttock lesion. On the basis of the 20 Gy isodose determined by the physical dosimetry, an excision of the buttock radiation burn was made on day 21 post irradiation (PI), followed by a wound closure by a skin allograft, and in a second step by a skin autograft. However, due to a rapid lysis of the skin allograft together with an infected ulceration, a new therapeutic strategy was applied, using mesenchymal stem cell (MSC) autograft. For that purpose, a bone marrow harvest was made on day 75 PI, and MSC were expanded in vitro. A second excision was then performed on day 90 PI, followed by a second skin autograft together with local injection of 168×10^6 MSC. A second local transplantation of 226×10^6 MSC was made on 99 days PI and the lesion was further dressed with artificial derma. Following MSC injections, pain disappeared and the active clinical evolution was stopped. A complete healing was observed by 75 days post treatment (5.5 months PI) without any functional impairment.

The second case of radiation burns occurred in Dakar (Senegal) during June and July 2006. Following a technical failure, an iridium source was retained in the source ejection system. The material containing the source was stored near a work place during a 2-month period. The reconstitution of the accident allowed the identification of 63 potentially irradiated victims, of which 4 patients exhibited skin lesions of various severities. One of the most severely irradiated victims was hospitalized in Percy military hospital, 27 days after the discovery of the accident. At that time, a diagnosis of an acute irradiation syndrome together with a severe radiation burn to the left arm was evidenced. Biological dosimetry gave a mean global radiation of 2.6 Gy, but with strong evidence of heterogeneous exposure. The physical reconstruction of the radiation dose was not possible, due to the difficulty of defining a clear-cut scenario. The hematopoietic syndrome was evidenced by blood Flt3-ligand concentration of 2700 pg/ml, and was treated by G-CSF and EPO injections as soon as day 31. The hematopoietic syndrome resolved by day 35. By



contrast, the evolution of the radiation burn to the left arm was worse. After a period of dry desquamation followed by moist desquamation, ulceration appeared. A first excision was made on day 100, followed by a succession of two rotation flaps, 5 MSC transplantations and 2 skin allografts. The detailed evolution of the lesion will be presented. During one of the excision, a fragment of the humerus was harvested for ESR dosimetry. Results indicated that the humerus received a mean radiation dose of 40 Gy. However, more than 300 days post hospitalization the clinical evolution of the lesion was stopped and healing was observed, with some functional impairment due to the severity of the lesion.

Overall, these two cases of accidental irradiation showed opposite characteristics. In the Chilean case, the radiation was localized, and the radiological nature of the accident was recognized immediately. In the Senegal case, there was a combination of a global irradiation together with a localized burn, and the radiological nature of the lesions was recognized with a one month delay. However, in these two cases, the general therapeutic strategy was the same. Necrotic lesions were excised, the wound was covered with skin allograft, and autologous MSC were locally injected around the lesion. Results were similar in the two cases, with a first immediate effect which is the disappearance of pain. A second effect was observed, with a progressive healing of the lesions. Although there are only two cases of radiation burn treatment by local injection of autologous MSC, the comparison with historical cases strongly suggest that this therapeutic strategy may be highly efficient.