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Letter to Editor

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The Healing of Ulcus Cruris by Mesenchymal Stem Cells: No delay in wound healing by high-dose and standard chemotherapy

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A 61-year-old male patient with T-cell NHL PTCL type (CD30-, Alk-), st. II.BE (oesophagus, mediastinum) was treated with 6 cycles of CHOP from June to October 2012. After the completion of 6 cycles, the CT images showed a mild progression of the disease. The patient received 2 cycles of ICE (ifosfamide, carboplatin, etoposide) (11-12/2012) + radiotherapy on mediastinum TD 30 Gy. After the second cycle of ICE, peripheral blood stem cells were collected ($4.5x10^6$ CD34+/kg body weight). The patient had a partial remission.

In 02/2013, the patient received BEAM (BCNU, etoposide, ara-C, melphalan) regimen with autologous stem cell transplantation (SCT). On day +26, he was discharged from the hospital (WBC $7.2x10^9$/l, Hb 96 g/l, PLT $20x10^9$/l –without substitution).

In 02/2014, the patient was in CR (PET confirmed). His blood counts were all in the normal range.

The problem of the patient was ulcus cruris appeared on his left leg in 2001, remaining stationary despite a trial of conservative treatment. After obtaining approval from Ethics Committee, a total of $20x10^6$ allogeneic adipose tissue- derived mesenchymal stem cells (MSCs) were applied locally (circumferentially) in 12 different punctions (Fig.1a). This occurred during the first cycle of ICE in 11/2012. No adverse reaction was observed during and after the application.

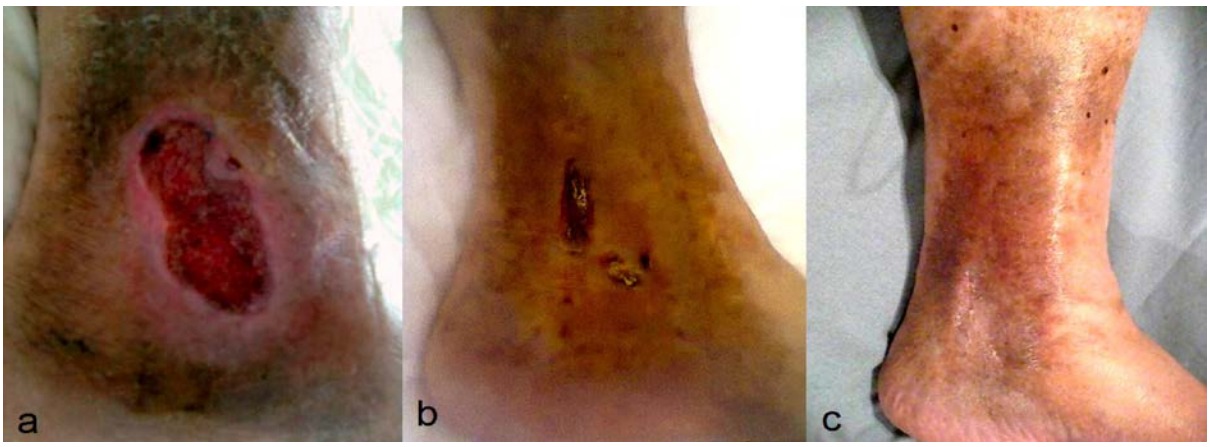

Figure 1. Healing of the ulcus after MSC application
a) 11/2012 day after application, b) 02/2013 d+25 after SCT, c) 05/2013

MSCs were obtained from adipose tissue of a volunteer donor and fulfilled the criteria provided by the International Society for Cellular Therapy.[1] Briefly, MSCs are defined by their plastic-adherent properties under standard culture conditions, by their ability to differentiate in to osteocytes, adipocytes and chondrocytes in vitro under a specific stimulus and by positive (CD105, CD73, and CD90) or negative (CD45, CD34, CD14 and HLA-DR) expression of specific surface markers.

Fig.1b shows the progression of leg healing on day 25 post-transplant. The complete healing of ulcusis is shown in Fig. 1c.

We decided to use MSCs in the treatment of the patient with ulcus cruris for the following two reasons:

I) There was an eleven-year history of unsuccessful attempt to treat the wound.

ii) High dose therapy was recommended for the patient and the wound was expected to heal before HDT.

Finally, the patient received myeloablative regimen on 02/2013. The ulcus shrinked before high-dosetherapy and continued to heal by day 25 post-transplant (Fig. 1b). Despite the use of 2 cycles of ICE and BEAM (HDT) regimen, no effect on the healing was observed. There was no difference in the speed of ulcus cruris healing between patients who did not receive HD or standard therapy and the patient reported in this study[2] (unpublished data). The results of the study indicated that the treatment with MSCs was safe and the ulcus healing progressed "normally" during the standard and high-dose therapies. Therefore, we concluded that the healing process triggered by MSCs was not influenced by high-dose chemotherapy and standard chemotherapy. The status was achieved on 05/2013 and persisted up to 04/2014.

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