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Treatment of refractory systemic sclerosis with human umbilical cord-derived mesenchymal stem cell transplantation

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Systemic sclerosis (SSc) is a rare systemic disorder of connective tissue characterized by progressive fibrosis of skin and multiple organs and associated with high mortality. The immunosuppressive properties of MSCs make them particular attractive to treat severe autoimmune diseases such as refractory SSc. MSCs are not immunogenic and escape recognition by alloreactive T cells and natural killer cells. We report first SSc patient treated with transplantation of human MSCs derived from umbilicl cord. A 44-year-old man was admitted to our hospital on May 24, 2007 with a complaint of swelling and sclerosis of limbs together with Raynaud's phenomenon for 2 years. The disease course was characterized by progressive cutaneous and articular involvement, and ulcerations of bilateral tiptoes. He was diagnosed with SSc in March 2006. Despite aggressive immunosuppressive treatment including steroids, cyclophosphamide (CY), and D-penicillamine, even plasma exchange, his clinical status continued to deteriorate, leading to significant functional disability and leg ulcer. On examination, the patient had multiple irregular ill-defined white patches on the abdomen, back and the distal aspect of the hand. Skin of face, limbs and abdomen was smooth taut. It was firm and could not be picked up. Stiffness of phalangeal joints in both fingers and toes was observed. Flexure contracture producing shortened "claw-like" fingers and fingertip resorption were also present. Serological study indicated the positive test for anti-nuclear antibodies with a granular pattern and negative anti-Scl70. Serum complement 3 (C3) was 0.61g/L (normal range:0.8-1.6g/L).He was given human umbilical cord-derived mesenchymal stem cell transplantation on May 31, 2007 without conditioning regimen. These cells expressed CD73, CD90, CD105 but not CD11b, CD19, CD34, CD45 and HLA-DR. 1×10^6 cells per kg of the patient's weight was given intravenously. There was no toxicity after the infusion. Five weeks after transplantation, the Modified Rodnan skin thickness score (MRSS) decreased from 37 to 33 and the health assessment questionnaire-disability index (HAQ-DI) from 2.2 to 1.6. Interestingly, he had remarkably improvement in the ulcer. Eleven weeks later, the MRSS further decreased to 31 and the HAQ-DI decreased to 1.3. A serological study showed normal serum levels of C3 (0.8g/L). To our knowledge, this is the first human umbilical cord-derived MSCs transplantation performed to treat SSc. The long time effect need to be followed up.

***Keywords*:** systemic sclerosis, mesenchymal stem cell, transplantation

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