Autotransplantation of bone marrow endotelioblasts of cd133+ for the patient with chronic critical ischemia of the lower extremity

Abstract

Within the first year after the diagnosis of critical ischemia big amputation of an extremity is carried out at 25% of patients. In this regard certain hopes are laid on a new method of treatment – therapeutic angiogenesis. The early clinical trials demonstrate improvement of perfusion of an extremity and clinical efficiency of a method. Terms of control of patients make at most 2 years, in our Center results of application of stimulators of angiogenesis in more remote period are analysed (up to 10 years). The clinical case of the isolated application of autotransplantation of bone marrow endotelioblast of CD133+ for the patient with critical ischemia of the lower extremity showing safety and efficiency of this method is presented in article.

Keywords: chronic critical ischemia of the lower extremities, cellular therapy, therapeutic angiogenesis

Abbreviations: CILE, the chronic ischemia of the lower extremities; ABI, the ankle brachial pressure index; TcO2, transcutaneous monitoring of partial oxygen pressure; MDW, the maximum distance of walking

Introduction

The chronic ischemia of the lower extremities (CILE)-the frequent reason of decline in quality of human life. Critical ischemia is a terminal stage of chronic ischemia and constitutes serious danger not only to the patient’s extremity, but also to his life. At a decomposition of an arterial blood flow by the end of the first year of 25% of patients it will be subjected to amputation of an extremity and 25% - will die from the cardiovascular reasons.1 By the main methods of treatment of CILE remain a surgical and endovascular revascularization of an extremity, but according to a number of authors, improvement of haemodynamics in the affected extremity by a surgical way perhaps only to 70% of cases in connection with insolvency of the distal arterial course (ways of outflow) and anatomo-functional inadequacy of collateral ways of a blood-flow.2 In this regard, certain hopes are laid on therapeutic angiogenesis – exogenous stimulation of formation and development of collateral blood vessels. A large number of experimental studies and the early clinical trials demonstrate improvement of perfusion of an ischemic extremity and clinical efficiency. Terms of control of patients make at most 2 years. Our research on application of autotransplantation of bone marrow endotelioblasts of CD133+ at chronic critical ischemia of the lower extremities have been begun in 2003 therefore we managed to analyse a condition of patients in more remote period – more than 10 years.3,4

Case presentation

The patient G., 44 years, within 3 years noted the appearance of chronic ischemia of the right lower extremity. Progressing of a disease happened gradually. At inspection, already concerning critical ischemia, for the patient it has been diagnosed atherosclerotic “multystoried” inoperable damages of arteries of the right lower extremity (occlusion of a superficial femoral artery and diffusion occlusion/ stenosis of a popliteal artery from the level of a crack of a knee joint and arteries of a shin). The patient was observed on an ambulatory, received standard angiotropny therapy without significant improvement. At the time of inclusion in a research of the patient the right lower extremity pains when walking on the minimum distances, paresthesia at rest. At survey noted cyanosis of the right foot when lowering an extremity, paleness – at her raising in horizontal position. Tropic ulcers haven’t been revealed. The pulsation of arteries on the right lower extremity distally the common femoral artery wasn’t defined. Careful survey of the patient and an additional examination have been conducted. After signing of a voluntary consent to the patient autotransplantation of bone marrow endotelioblasts of CD133+-is carried out intramuscular (in gastrocnemius muscle) (from 40ml of bone marrow 2,2million cells are received and transplanted). Pospital monitoring of the general condition of the patient, condition of the lower extremity, laboratory indicators was during the day carried out. Any deviations it hasn’t been established. Further, according to the protocol, it was carried out control inspection in 1, 3, 6 months, further–annually. The protocol included ultrasonic Doppler sonography with measurement of the ankle brachial pressure index (ABI) at rest, transcutaneous monitoring of partial oxygen pressure (TcO2) in the 1st inter digital interval of the right foot, the treadmill-test (v of the movement of a cloth of 3,2km/h, without angle, was measured by MDW (the maximum distance of walking), standard laboratory researches, the questionnaire on quality of life of SF-36 was filled. Within the first year the patient received only basic anti agregantny therapy, further – standard angiotropny therapy, including infusional 1-2time/year (without use of prostaglandins).

Results

Completion of critical ischemia has been noted by 3rd month

Paresthesia in the right foot at rest have disappeared, the walking...
distance, indicators of ABI and TcO2 on foot has increased (Table 1). At annual control surveys in the remote period the achieved result is stable. According to an angiography of the right lower extremity the collateral network in the pool of a deep femoral artery of the right lower extremity has significantly increased (+2 on classification of Tateishi-Yuyama published in 2002) in comparison with an initial picture (Figure 1). During the entire period of observation of pathological states and diseases it hasn’t been established.

**Table 1 Results of noninvasive methods of inspection of the patient after autotransplantation of bone marrow endotelioblasts of CD133+**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>ABI</th>
<th>TcO2, mm Hg</th>
<th>MDW, Min</th>
</tr>
</thead>
<tbody>
<tr>
<td>In 1 month</td>
<td>0.28</td>
<td>23</td>
<td>43</td>
</tr>
<tr>
<td>In 3 months</td>
<td>0.34</td>
<td>32</td>
<td>75</td>
</tr>
<tr>
<td>In 6 months</td>
<td>0.32</td>
<td>34</td>
<td>84</td>
</tr>
<tr>
<td>In 1 year</td>
<td>0.36</td>
<td>40</td>
<td>191</td>
</tr>
<tr>
<td>In 5 year</td>
<td>0.38</td>
<td>46</td>
<td>215</td>
</tr>
<tr>
<td>In 10 year</td>
<td>0.45</td>
<td>52</td>
<td>340</td>
</tr>
</tbody>
</table>

ABI, an ankle brachial pressure index at rest; TcO2, partial oxygen pressure (TcO2) in the 1st interdigital interval of the right foot; MDW, the maximum distance of walking.

**Figure 1** Results of angiography of the right lower extremity initially, in 3 months and in 1 year after autotransplantation of bone marrow endotelioblasts of CD133+.

### Discussion

The isolated autotransplantation of bone marrow endotelioblasts of CD133+ to the patient with critical ischemia of the right lower extremity caused by significant inoperable defeat of the distal arterial course safely has allowed to keep an extremity not only in the next, but also in remote (in 10 years) the period. The received clinical result completely correlates with dynamics of indicators of tool researches, including an angiography, is caused by development of collateral network that is result of therapeutic angiogenesis. This clinical case confirms the general tendency in results of application of autotransplantation of bone marrow endotelioblasts of CD133+ in the research conducted in NSPC of AN Bakulev. The results received by us demonstrate that application of cell therapy at observance of indications and contraindications at patients inoperable chronic critical limb ischemia is an effective and safe method of treatment. The clinical trials conducted now will allow to include cell therapy in National recommendations about treatments of patients with vascular arterial pathology of lower extremity.

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### Conflict of interest

The author declares no conflict of interest.

### References