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ORIGINAL ARTICLE

Quality of long-term cryopreserved umbilical cord blood units for hematopoietic cell transplantation

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Abstract The aim of this study was to evaluate the quality of long-term cryopreserved umbilical cord blood (CB) units for hematopoietic cell transplantation (HCT). The recovery of the number of total nucleated cell (TNC), hematopoietic progenitor cells (HPCs; CD34+ cells, colony-forming units-granulocyte/macrophages [CFU-GMs]), and the percentage of viable cells, CD34+ CD38− cells, and CD34+ CXCR4+ cells of CB units cryopreserved for 10 years for HCT were examined. Eighteen CB units cryopreserved for 10 years (as the study group) and for 1 month (as the control group), respectively, were analyzed. The recovery rate of TNC, CD34+ cells and CFU-GMs were 88.72 ± 16.40, 68.39 ± 18.37 and 42.28 ± 38.16% for the study group and 80.17 ± 14.46, 72.67 ± 20.38 and 49.61 ± 36.39% for the control group ($p = 0.106$, $p = 0.513$ and $p = 0.559$, respectively). There were no significant differences in the recovery rate of TNC, CD34+ cells and CFU-GMs between the study group and the control group. The mean basal percentage of viable cells, CD34+ CD38− cells, and CD34+ CXCR4+ cells after thawing were 83.69 ± 9.45, 9.11 ± 4.13 and 81.65 ± 10.82% for the study group. These results indicate that long-term cryopreservation does not negatively affect the quality of CB units for HCT.

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Keywords Umbilical cord blood · Long-term cryopreservation · Quality assurance · Cord blood transplantation · Cord blood bank

1 Introduction

Umbilical cord blood (CB) is increasingly used as a source of alternative hematopoietic stem cells for transplantation [1–3]. Most CB units in the world's CB banks are cryopreserved in liquid nitrogen in individual bags for several years and then are quickly thawed just prior to hematopoietic cell transplantation (HCT). CB units, many of which have been cryopreserved for more than 10 years, are available for HCT in many worldwide CB banks. However, little information is available on the long-term survival of cryopreserved CB cells. Most reports focus on relatively short storage intervals [4–11]. Although a few reports are available on effects of long-term cryopreservation on CB cells [12–16], these CB units have used only for study not for HCT. The CB bank network was established in Japan in 1998, and CB units cryopreserved more than 10 years are considered for public cancellation. No reports have focused on the quality of long-term cryopreserved CB units for HCT, and it is not clear whether long-term cryopreservation affects the quality of CB units for HCT. Therefore, this study analyzed the effect of long-term cryopreservation on hematopoietic cells of CB units that were cryopreserved 10 years ago for HCT. The number of total nucleated cell (TNC) count, CD34+ cells count, colony-forming units-granulocyte/macrophage (CFU-GM) assay, viability of mononuclear cells were evaluated before cryopreserving and after thawing. The CD34+ CD38− phenotype identifies a UCB primitive subpopulation of hematopoietic stem cells that have a higher proliferative potential in response

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High incidence of fatty liver and insulin resistance in long-term adult survivors of childhood SCT

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Overweight/obesity among adult survivors of childhood SCT has been considered to be predictive of eventual development of metabolic abnormalities. Fatty liver is increasingly recognized as a major cause of liver-related morbidity and mortality in the general population. However, the real incidence of fatty liver in adult survivors of SCT has not been fully elucidated. We determined whether adult survivors are at risk for overweight/obesity, metabolic abnormalities and fatty liver and whether these risks are associated with cranial radiotherapy (CRT) before SCT. Among the 51 patients (30 males), only two male patients were overweight/obese at the last evaluation. On the other hand, 9 male (30%) and 15 female (71%) patients were underweight. Fatty liver was diagnosed in 11 male (37%) and 10 female (48%) patients during the follow-up period, although patients who had fatty liver did not tend to be overweight/obese. Significantly more patients who received CRT before SCT developed fatty liver with insulin resistance than those who did not ($P<0.05$). Even patients who are not overweight/obese may develop fatty liver and metabolic abnormalities. We recommend that healthcare professionals recognize these risks and give life-long attention to detecting, preventing and treating late complications after SCT.
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Introduction

The number of long-term surviving SCT recipients has increased steadily and attention is now extended to the late endocrine complications of this procedure.[1] Overweight/obesity has been identified as a potential late effect of therapy in survivors of acute lymphoblastic leukemia (ALL) treated with conventional therapy,[2] and cranial radiotherapy (CRT) during ALL treatment has been implicated as a potential cause of excess weight gain among these survivors. Although the mechanism by which CRT leads to overweight/obesity is unknown, hypothalamic damage leading to GH deficiency and/or leptin insensitivity has been suggested.[3,4] Overweight/obesity in childhood, adolescence and young adulthood after SCT treatment is an important predictor of eventual development of hyperinsulinism and its attendant metabolic syndrome.[5] Specifically, excessive accumulation of visceral fat within the abdomen is strongly and independently associated with metabolic syndrome,[6,7] and the storage of fat in non-adipose tissue such as the liver is known to cause insulin resistance in mouse models.[8]

Fatty liver is increasingly recognized as a major cause of liver-related morbidity and mortality[9] because of its potential to progress to cirrhosis and liver failure.[10] This disease is often associated with metabolic abnormalities characterized by obesity,[11] type II diabetes mellitus,[12] dyslipidemia,[13] and hypertension,[14] and, finally, each of these abnormalities also carries a cardiovascular disease risk. Whether the risk for these metabolic abnormalities is increased in adult survivors of childhood SCT recipients has, however, not been fully elucidated. There is a possibility that identification of the risk factors for development of fatty liver in survivors is, therefore, critical for the development of strategies for prevention of and intervention in cardiovascular disease.

Although overweight/obesity in adult survivors of childhood ALL has been well evaluated, no longitudinal study that investigated metabolic abnormalities in survivors of childhood SCT has been reported,[15,16] and the mechanism of these conditions has not been completely understood. A longitudinal retrospective study of a cohort of adult

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