Bone marrow megakaryocytes in human ontogenesis

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Abstract

The aim of the study was a histomorphometric evaluation of bone marrow megakaryocytes (MK). The study was based on bone marrow histological evaluation. Morphometric evaluation was carried out with the aid of the MicroImage Olympus computer image analysis software. We evaluated the amount of megakaryocytes (MK) per 1 mm^2, MK area, the nuclear-cytoplasmatic (N/C) ratio and circular deviation (CD). Bone marrow was examined in premature newborns, full-term newborns and adults. The obtained data were statistically analysed with the aid of the Statistica PL computer software. Statistically significant differences were found in MK quantity, their distribution in relation to non-haematopoietic elements of haematopoietic microenvironment of sinusoid vessels system. To a smaller extent, did the differences refer to MK area, the N/C ratio or shape.

Key words: bone marrow, megakaryocytes, histomorphometric features, human ontogenesis.

Introduction

Human haematopoesis begins at about 2-6 week of intrauterine life in the wall of the yolk sac of the foetus. The blood islets belong to the, so-called, mesoblastic period of haematopoiesis. From the 6th to the 16th week of prenatal development, the main site of haematopoesis is the liver and, to a smaller extent, the spleen. Liver-spleen haematopoesis in physiological conditions does not occur in postnatal development [1, 2, 3]. Since the 20th week of prenatal life, the bone marrow starts its haematopoietic functions and remains the only site of haematopoesis in further developmental periods. Bone marrow can be found in marrow cavities of spongy bones, in the stroma, consisting of reticular tissue. It is full of sinusoid blood vessels of up to 30 μm in diameter. Till the 5th year of postnatal life, this red bone marrow presents main haematopoietic properties. In further stages of ontogenesis, there is more and more yellow bone marrow which, till the 18th year of life, replaces 50% of the red bone marrow. In adults, the red bone marrow is mostly located in sternum, ribs, and vertebrae, pelvic and cranial bones and in the epiphyses of humeral and femoral bones. The amount of the red bone marrow undergoes further reduction with age.

Proper haematopoietic activity, together with the efficient blood / bone marrow barrier, condition certain cell properties of individual developmental lines in peripheral blood and maintain the organism homeostasis. Developmental disorders in megakaryocytic line belong to the most common causes of the clotting system dysfunctions and may result in death. They are usually manifested by haemorrhagic diathesis or thrombosis, which often result from the syndrome of disseminated intravascular clotting (DIC). This syndrome occurs in various stages of human ontogenetic development and is characterised by high mortality. The disorders, observed in the course of DIC, may result, among others, from immaturity of the megakaryocytic bone marrow system [4, 5].

The aim of the study was a histomorphometric evaluation of bone marrow megakaryocytes (MK) in selected stages of human ontogenesis.

Material and Methods

The study was based on bone marrow histological evaluations. Biopsy examination was performed within 12 hours after

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Table 1. Histomorphometric features (mean± standard deviation) of age groups

Age Groups	N	Number of MK		Area of MK		N/C		CD	
		X	SD	x	SD	x	SD	x	SD
NN	6	20.0	3.6	287.7	40.6	0.29	0.04	0.78	0.06
ND	6	23.2	4.0	298.8	25.1	0.26	0.02	0.79	0.04
< 10	6	21.2	5.9	224.7	65.1	0.33	0.13	0.73	0.04
11-20	6	18.7	5.1	255.2	51.0	0.39	0.23	0.80	0.08
21-40	6	17.2	3.9	216.3	64.1	0.37	0.16	0.82	0.06
41-60	6	17.2	3.1	197.5	42.5	0.32	0.12	0.82	0.07
> 60	6	16.7	3.3	180.0	52.2	0.40	0.13	0.84	0.03

N/C-nuclear-cytoplasmatic ratio
CD-circular deviation

death. Bone marrow was collected from sternum at II intercostal space. The material was fixed in the 'Oxford' fixing agent for 48 hours. After fixing, it underwent standard histological processing. Morphometric evaluation was carried out with the aid of the MicroImage Olympus computer image analysis software. We evaluated the amount of megakaryocytes (MK) per 1 mm^2, MK area, nuclear-cytoplasmatic (N/C) ratio, cellular shape, disorder-circular deviation (CD). Bone marrow was examined in premature newborns, (N=6), full-term newborns (N=6) and adults (N=30), divided into age groups (1mth - 10 yrs, 11-20, 21-40, 41-60, and over 60 yrs).

Results

It was found that the highest number of megakaryocytes per 1 mm^2 occurred in full-term newborns and amounted to the mean value of 23,2 (±4.0), while the lowest number was found in the group of adults over 60 and amounted to the mean value of 16.7 (±3.3). Similar relations were observed, regarding the MK area. In the group of full-term newborns, the value was the highest and amounted to the mean value of 298.8 mm2 (±25.1) and, in the oldest age group, it was the lowest and amounted to the mean value of 180.0 mm^2 (±52.2). The nuclear-cytoplasmatic (N/C) ratio was the lowest in the group of full-term newborns and the highest in the group over 60. CD coefficient was the lowest in the groups of newborns and children up to the 10^{th} year of life and then, it gradually grew in the consecutive groups. Detailed data are presented in Table 1. The obtained data were statistically analysed with the aid of the Statistica Pl computer software. The mean values of the examined parameters were compared in individual groups. Statistically significant differences were found in MK quantity in the compared groups. It was observed that in preterm newborns the percentage of MK, occurring in the direct vicinity of sinusoid vessels, was the highest and amounted to 6-10%, the mean value- 8.4%, in full-term newborns - 4-7%, the mean value - 5.5% and, in the other groups - 3-5%, the mean value- 4.5%. The differences were less significant, regarding the MK area, N/C relation or CD.

Discussion

The obtained results indicate considerable morphological differentiation of the bone marrow MK system in the examined groups. The to-date's studies and developmental standards refer mainly to the percentage composition of individual bone marrow developmental lines [6, 7, 8]. The aim of the study, beside the morphometric evaluation of MC, was also an analysis of the topographic localisation of megakaryocytes. It was observed that, in neonatal period, MK were located closer to sinusoid vessels and were composed into bunches, their surface being more irregular. In the course of development, the examined cells were dispersed in the marrow stroma. A presence of cell nuclei of other developmental lines, mostly leukocytes, was observed in megakaryocytes cytoplasm. With progression of age this phenomenon (so-called, emperipolesis) in the marrow of adults and elderly people was scarce. It is difficult to make a clear-cut definition of the above phenomenon, but it may result from the functional immaturity of MK, which may clinically result in worse quality platelets and clotting system disorders, as mentioned above. Further studies of the observed topographic changes in bone marrow are essential.

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