HYPERPLASIA OF MYOCARDIAL CELLS OF THE AURICLE OF THE HUMAN ATRIUM DURING HYPERTROPHY: POSSIBILITY AND MECHANISM

G. A. Mamyan

UDC 616.125-018.63-007.61

Measurement of the parameters of the myocardial cells and the DNA content of their nuclei demonstrated that hyperplasia of the cells could accompany their hypertrophy. A scheme of the successive stages of the hypertrophy and hyperplasia of the muscle cells is outlined.

Electron-macroscopic studies have shown that hyperplasia of the ultrastructures of the heart muscle cells can take place during their hypertrophy [3, 5, 8, 12].

However, the problem of hyperplasia of the cells themselves has not yet been settled. Some workers [1] deny that this can take place during hypertrophy of the myocardium, while others accept it only for the myocardium of the atrium [4] or for the myocardium of both atrium and ventricle if the weight of the heart reaches a high value – 500 g or more in man [7, 9, 10].

Hyperplasia of muscle cells must be preceded by DNA synthesis in the nuclei. The results of autoradiographic and cytophotometric studies of this problem are contradictory [4, 6, 11].

EXPERIMENTAL METHOD

Myocardial cells were studied in the auricle of the left atrium from 51 patients undergoing operative treatment of mitral valvular disease. The age of most patients was 30-40 years. Auricles of the left atrium from five persons killed accidentally were used as the control. Pieces of tissue were fixed in 7% TCA solution, 10% neutral formalin solution, and Carnoy's fluid and embedded in paraffin wax. Sections were stained with iron-hematoxylin by Heidenhain's method, with hematoxylin-eosin, and by Feulgen's method. Micrometric measurements were made with a screw-adjusted ocular micrometer and cytophotometric measurements on a type MUF-6 instrument adapted for work by the two-wave method. The DNA content was conventionally taken as equal to diploid if its increase compared with the DNA content in spermatids was not more than threefold.

TABLE 1. Results of Micrometric Investigation of Parameters of Cells and Nuclei in Biopsy Material from the Auricles of 23 Atria

	Transver. diameter (in μ), d	Number of measurements	%	Longitudinal diameter (in μ), l		%
Nucleus	2—4	7	3,5	6—10	32	16
	4—6	37	18,5	10—14	86	43
	6—8	58	29	14—18	55	27,5
	8—10	49	24,5	18—22	20	10
	10—12	30	15	22—26	6	3
	12—14	15	7,5	26—30	—	—
	14—16	3	1,5	30—34	1	0,5
	16—18	1	0,5			
Cell	8—12	30	15	47—67	47	23,5
	12—16	55	27,5	67—87	78	39
	16—20	64	32	87—107	42	21
	20—24	31	15,5	107—127	23	11,5
	24—28	11	5,5	127—147	7	3,5
	28—32	5	2,5	147—167	1	0,5
	32—36	4	2	167—187	2	1

EXPERIMENTAL RESULTS

The results of measurements of mononuclear myocardial cells with clearly distinguishable borders in the region of the intercalated disks in the biopsy material from the auricle fixed with TCA are given in Table 1. The relationship between the transverse diameter (d) of the cells and nuclei,

Department of Pathomorphology, Institute of Cardiology and Cardiac Surgery, Ministry of Health of the Armenian SSR, Erevan. (Presented by Academician of the Academy of Medical Sciences of the USSR, A. P. Avtsyn.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 73, No. 5, pp. 102-105, May, 1972. Original article submitted, November 12, 1970.

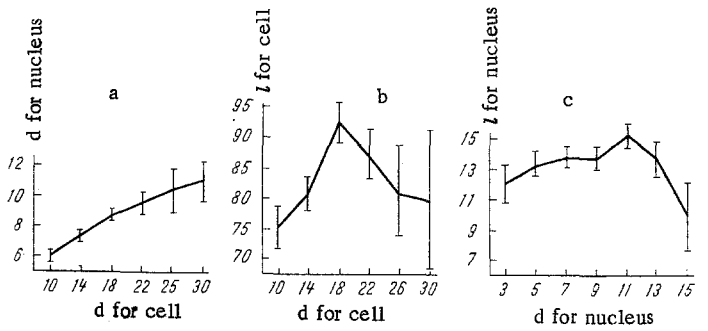

Fig. 1. Graphs showing relationship between parameters (in μ) of cells and nuclei during hypertropy: a) relationship between transverse diameters (d) of cell and nucleus; b) between transverse (d) and longitudinal (l) diameters of cell; c) between transverse and longitudinal diameters of nucleus.

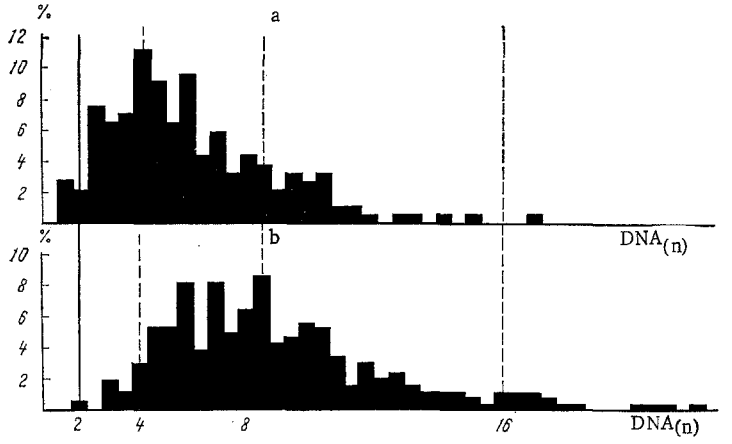

Fig. 2. DNA content in hypertrophied (b) and unhypertrophied (a) muscle nuclei in biopsy material from atrial auricle.

the transverse and longitudinal (l) diameter of the cells, and the transverse and longitudinal diameter of the nuclei can be seen in Fig. 1a-c. The value of d for the nuclei in the control with formalin fixation was 2-8μ, with a mean value of $4.3 \pm 1.5\mu$. Parallel measurement of d for the nuclei with different methods of fixation enabled the normal value of d for the nuclei with TCA fixation to be determined ($6.4 \pm 2\mu$). From Table 1, showing the relationship between d for the cell and d for the nucleus,the normal value of d for the cell for the same method of fixation was calculated ($15.9 \pm 3.8\mu$). The value of d for cells with amitotic figures of nuclear division (paired nuclei were taken as amitosis) in 8% of cases did not exceed 14μ, in 38% they did not exceed 20μ, and in 54% they exceeded 20μ. The total percentage of nuclei dividing by amitosis in the control group was 0.3. In the patients the percentage of amitosis in the hypertrophied nuclei varied from 1.5 to 6.9, with a mean value of 3.8. The DNA content in the hypertrophied and unhypertrophied muscle nuclei in the biopsy material from the myocardium is shown in Fig. 2a, b.

Taking $15.9 \pm 3.8\mu$ as the normal value of d for the cells after TCA fixation, it will be clear from the graph of the relationship between d and l for the cell that an increase in d of the cell to 18μ is accompanied by an increase in l for the cell: with a further increase in d for the cell, i.e. during its hypertrophy, the value of l for the cell is reduced. The percentage of these was 17.5 (with 25.5% of hypertrophied cells). A similar relationship was found between d and l for the nucleus: moderate hypertrophy of the nuclei was accompanied by an increase in the value of l for the nucleus, but with further hypertrophy the value of l for the nucleus decreased. The percentage of these nuclei was 8.5. The decrease in the length of the hypertrophied cells and nuclei is indirect evidence of their possible division. It is extremely difficult to record division of myocardial cells directly by the detection of newly formed intercalated disks, because even "old" intercalated disks cannot always be clearly identified in a sufficent number of cells lying in succession along the length of the fiber.

Judging from the patterns observed, the nuclei of the muscle cells divided by amitoses, although only provisional conclusions can be drawn about this. The overall index of amitoses in the patients, obtained from the percentage of amitoses in the hypertrophied nuclei (3.8) and the percentage of hypertrophied cells (25.5), was 0.97%, which is three times higher than the index of amitoses in the control. If the percentage of hypertrophied nuclei (49) was used for the calculation, the increase was sixfold. As a rule amitoses are observed in the cells for which the value of d reaches the upper limits of normal or beyond. In the hypertrophied nuclei of the myocardial cells, the tetraploid content of DNA was exceeded in 83% of cases, compared with only 47% in unhypertrophied nuclei.

Allowing for the percentage of amitoses (3.8), the percentage of nuclei with more than the tetraploid content of DNA (83), and the characteristics of the amitoses, in which the daughter nuclei are equal in size and in intensity of staining conventionally in only one-quarter of all cases, the index of amitoses with an adequate (not less than 2n) DNA content in the daughter nuclei was 0.8%. With an index of this order it is possible for the two cells to be provided with the proper nuclei, more especially since the rate of amitoses may be considerable [2].

It is also evident that some of the new muscle cells are formed by division of binuclear cells arising in the earlier stages of hypertrophy.

The following provisional scheme can thus be put forward to explain the process of hypertrophy and hyperplasia of the myocardial cell: hypertrophy of cell and nucleus – increase in polyploidy of nucleus – amitotic division of nucleus – binuclear cell – cell division.

LITERATURE CITED

1. A. I. Abrikosov, Special Pathological Anatomy [in Russian], No. 2, Moscow - Leningrad (1940).
2. Z. S. Katsnel'son, Arkh. Anat., No. 3, 3 (1954).
3. V. S. Paukov, Arkh. Pat., No. 9, 18 (1967).
4. P. P. Rumyantsev and V. O. Mirakyan, Tsitologiya, No. 10, 1276 (1968).
5. D. S. Sarkisov and B. V. Vtyurin, Electron Microscopic Analysis of Increased Tolerance of the Heart [in Russian], Moscow (1969).
6. W. Crane and L. Dutta, J. Path. Bact., 86, 83 (1963).
7. J. Linzbach, Arch. Path. Anat., 314, 595 (1947).
8. R. Poche, Arch. Path. Anat., 331, 165 (1958).
9. W. Sandritter and G. Scomazzoni, Nature, 202, 100 (1964).
10. J. Schoermackers, Arch. Path. Anat., 331, 3 (1958).
11. G. Wegner and E. Mölbert, Arch. Path. Anat., 341, 54 (1966).
12. A. Wollenberger and W. Schulze, in: Physiology and Pathology of the Heart [Russian translation], Moscow (1963), p. 126.