SOME ASPECTS OF THE FINE STRUCTURE OF GIANT CELLS ON THE SURFACE OF FOREIGN BODIES

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UDC 616-018.1-02:616-003.6

Although during the period of almost 100 years of study of the giant cells arising around foreign bodies they have been the subject of numerous investigations [5, 8, 11], the fundamental problems of the biology of these cells—their sources and genetic pathways, their potential—still remain unsolved [10]. This state of affairs, like all aspects of the reaction of the living organism to a foreign body, has now become especially important. This is because during the last decades certain foreign bodies have been found to possess carcinogenic activity [1, 4, 13].

The cytology of foreign body giant cells has been inadequately studied. So far as the use of modern methods of application in their study is concerned, only isolated reports may be found in the literature [8, 12, 16].

Theobject of the present investigation was to make an electron microscopic study of the giant cells arising after implantation of glass disks into the abdominal cavity, and to compare their ultrastructure with data obtained by the methods of classical cytology by means of intravital phase-contrast observations.

EXPERIMENTAL METHOD

Multinuclear cells developed on the surface of glass disks introduced into the abdominal cavity of albino rats. For electron microscopic purposes pieces of glass slides measuring 1.5 · 1.5 cm were introduced into the abdominal cavity. The experiments lasted 5 and 7 days (4 and 5 animals respectively). The cells were fixed to the surface of the disks by Sjöstrand's method and the specimens were embedded in butyl-methyl methacrylates. Sections were cut on a type LKB microtome to a thickness of 150-200 A and contrasted with a 5% aqueous solution of uranyl acetate for 3-5 h. The investigations were conducted on a model IEM-6c electron microscope with an instrumental magnification of 4500 and 20,000.*

To study the giant cells by means of phase contrast and the methods of ordinary optical cytology (staining by Heidenhain's method for detecting mitochondria, impregnation by da Fano's method) 96 rats were used. Disks made from glass cover slips were introduced into their abdominal cavity.†

EXPERIMENTAL RESULTS

During encapsulation of the glass disks in the abdominal cavity giant cells developed from three sources: histiocytes, fibroblasts, and cells of the mesothelium. Their formation was usually associated with amitotic division of the nuclei. The multinuclear cells arising from the different sources varied in their overall pattern of morphological, histochemical, and functional signs. However, they all possessed one common feature, certainly connected with their long stay on the surface of the glass disk: most of the multinuclear cells had projecting processes of cytoplasm. They were most completely visible in vivo by means of phase contrast, and in fixed and stained preparations the number and size of the cytoplasmic processes were considerably reduced. In some cases they attained a length of several tens of microns, and in width they varied from 1 to 5-6 μ (Fig. 1, 1).

The electron microscope revealed new structural details of the peripheral zone of the cytoplasm of the giant cells. The multinuclear cells were found to possess a vast number of long, very thin processes, derivatives of the cytoplasmic membrane (Fig. 1, 2). They were found all over the periphery of the giant cell, but in their density

* The sections and electron micrographs were prepared by A. F. Bykovskii in the laboratory of morphology of viruses and electron microscopy of the N. F. Gamaleya Institute of Epidemiology and Microbiology, and the author is grateful to him for his help.

† For a more detailed account of the technique, see [2].

Department of Histology and Embryology, Leningrad Veterinary Institute (Presented by Academician V. N. Chernigovskii). Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 62, No. 11, pp. 107-112, November, 1966. Original article submitted April 10, 1965.

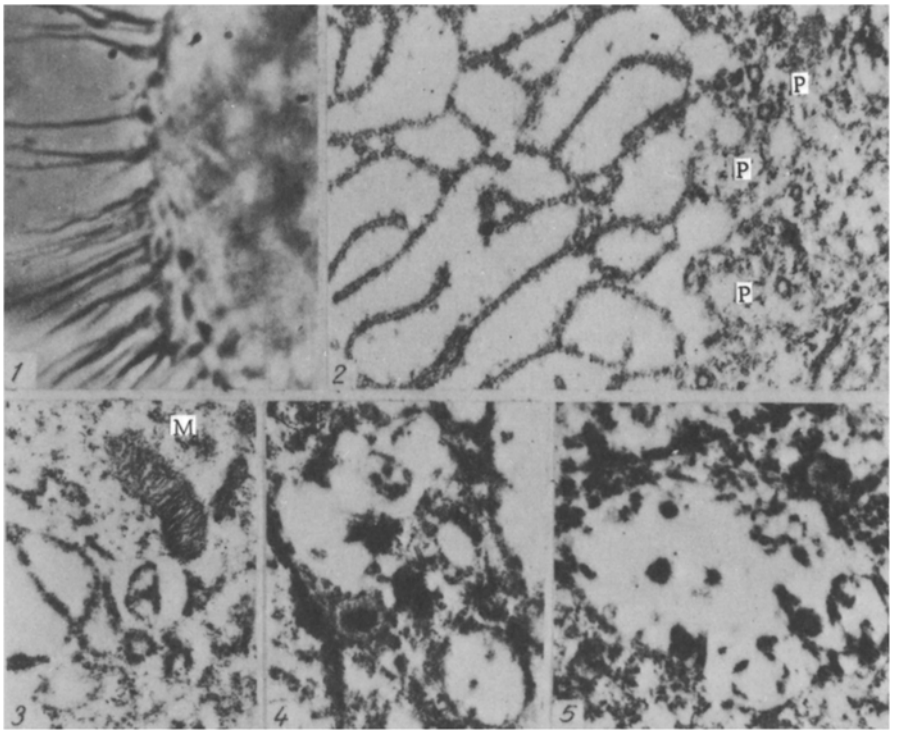

Fig. 1. Morphology of the peripheral zone of the cytosome of foreign body giant cells. 1) Cytoplasmic processes of a giant cell. Phase contrast. Immersion. Objective 90 ×, ocular 15 ×; 2) system of cytoplasmic processes: P) pinocytotic vacuole, magnification 15,000 ×; 3) phagocytic vacuole; M) mitochondrium, magnification 17,000 ×; 4 and 5) phagocytic vacuoles arising as a result of fusion of small vacuoles, magnification 17,000 ×.

of distribution and in their length they showed considerable variation. These processes were also found on the larger processes of cytoplasm, containing elements of the endoplasmic reticulum and mitochondria. The width of the thin cytoplasmic processes was fairly uniform, varying from 650 to 800 A. Numerous anastomoses were present between the processes, leading to the formation of a complex wide-looped reticulum. In the zones of the cytoplasm with the most highly developed cytoplasmic processes many invaginations or indentations of the cytoplasmic membrane were observed. Numerous smooth-walled vesicles, bounded by a dense, single membrane, were also found here constantly (Fig. 1, 2). They were fairly uniform in size, varying from 0.12 to 0.2 μ. On progressing deeper into the cell from the peripheral zone of the cytoplasm, their number fell rapidly. No fusion of these vesicles, with the dimensions and morphology of the pinocytotic vacuoles, was observed. Occasionally larger pinocytotic vacuoles were seen, measuring up to 0.4-0.5 μ, but in these cases, too, their contents were homogeneous. No connection was observed between the pinocytotic vesicles and the typical phagocytic vacuoles.

The phagocytic vacuoles were a constant component of the foreign body giant cells. The electron microscope showed that the vacuoles arose as a result of the invagination of the cytoplasmic membrane and at first they remained connected with the external medium (Fig. 1, 3). The larger vacuoles arose as a result of fusion of several smaller ones (Fig. 1, 4). Many ingested particles of different size and density were found in the large vacuoles (Fig. 1, 5). Vacuoles often were found in the immediate vicinity of the nuclei.

The endoplasmic reticulum of the foreign body giant cells was well defined in all parts of their cytosome, and its special feature was that dilatations of the tubules of the reticulum (cisternae) were frequently present (Fig. 2, 1). The multinuclear cells were characterized by a cytoplasm with high RNA content. Corresponding to the high RNA concentration, there were numerous ribosomes, localized not only on the membranes of the tubules, but also in the matrix of the cytoplasm. Clusters of ribosomes were constantly found here (Fig. 2, 2). This type of localization of the ribosomes is characteristic of many fast growing cells—embryonic or cancer cells [14]. In the paper cited it is suggested that ergastoplasm of this type be called "unorganized ergastoplasm." The membranous elements of the endoplasmic reticulum in the areas of the most widely dilated tubules were poorly developed. This may be due to the degree of stretching of the tubules, for in such cases the membrane structures are ill-defined even in cells in which normal conditions they stand out particularly clearly [12].

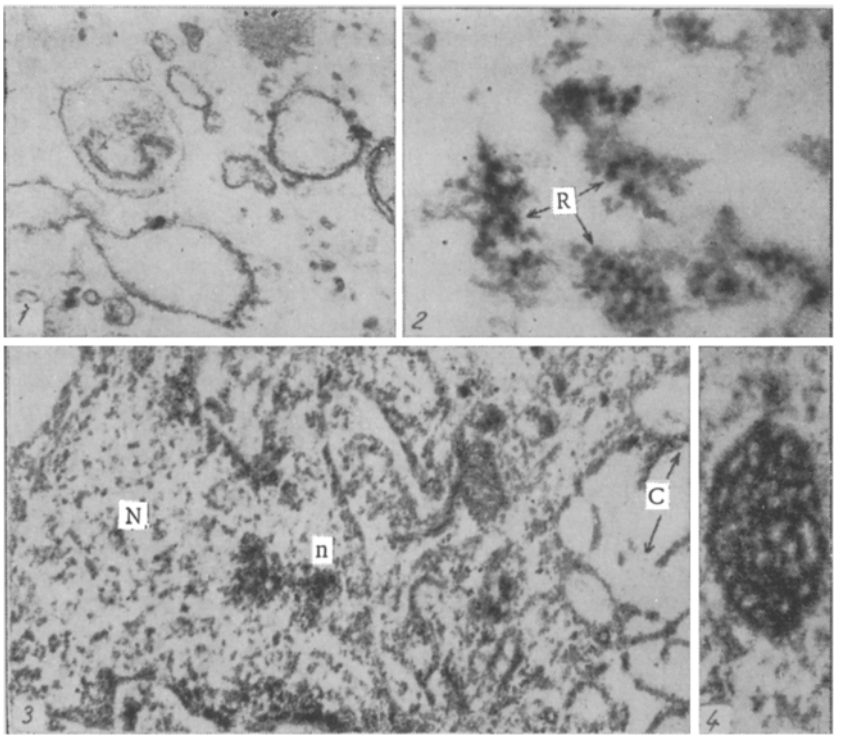

Fig. 2. The endoplasmic reticulum and nuclei of the giant cells. 1) Cisternae of the endoplasmic reticulum, magnification 85,000 ×; 2) clusters of ribosomes (R) in the matrix of the cytoplasm, magnification 140,000 ×; 3) multilobular nucleus: N—nucleus, n —nucleolus, C—cytoplasmic processes, magnification 15,000 ×; 4) nucleolus, magnification 20,000 ×.

As a rule the nuclei of the giant cells were oval or round in shape. The electron microscope revealed that irregular nuclei, with many projecting processes, were present in these cells (Fig. 2, 3). A constant characteristic of the nuclei of the giant cells at times up to 15-20 days was the presence of large nucleoli, rich in RNA. In most cases the electron microscope revealed a nucleolonema with a complex system of anastomoses in the nucleoli; the nucleolar filament was clearly granular in character (Fig. 2, 4).

The results of optical microscopy, obtained after impregnation with silver nitrate, demonstrated the high degree of development of the Golgi apparatus of the giant cells. In the multinuclear cells the Golgi apparatus was usually fragmented into dichthyosomes. A large part of the dichthyosomes consisted of two components—a centrally situated argentophobic and a peripheral argentophilic (Fig. 3, 1), Each type of multinuclear cells was characterized by a special form of localization of the individual elements of the apparatus in the cytoplasm. Experiments in which colloidal dyes were injected into the abdominal cavity have demonstrated the high level of functional activity of the Golgi apparatus of giant cells. The triad of signs discovered by D. N. Nasonov [6] was clearly visible in the multinuclear cells: the appearance of the first granules of dye in the Golgi zone and their close contact with the dichthyosomes, reduction of the substance of the apparatus in the cells with large numbers of granules, and the greater or lesser degree of argentophilia of these granules.

The electron microscope revealed a correlation between the submicroscopic form of organization of the Golgi apparatus and the data obtained by the methods of optical cytology. The Golgi apparatus of the giant cells was found to possess a structure similar in its general features to the cells of most animals and plants [3, 10]. The Golgi complexes consisted of a system of triple membranes (3 or 4 flattened sacs), small vesicles, and several larger vacuoles (Fig. 3, 2). The membranous character of the elements of the complex was very noticeable. Points of transition between the membranes of the elements of the Golgi complex and of the endoplasmic reticulum could be seen. A special feature of the Golgi complex of the multinuclear cells was the predominance of the system of flattened sacs. In the opinion of some investigators these sacs correspond to the dicthyosomes revealed by the methods of optical cytology [9, 16]. Hence, the results obtained by means of the electron microscope demonstrated the dominant position of the dichthyosomes in the Golgi complexes of the foreign body giant cells.

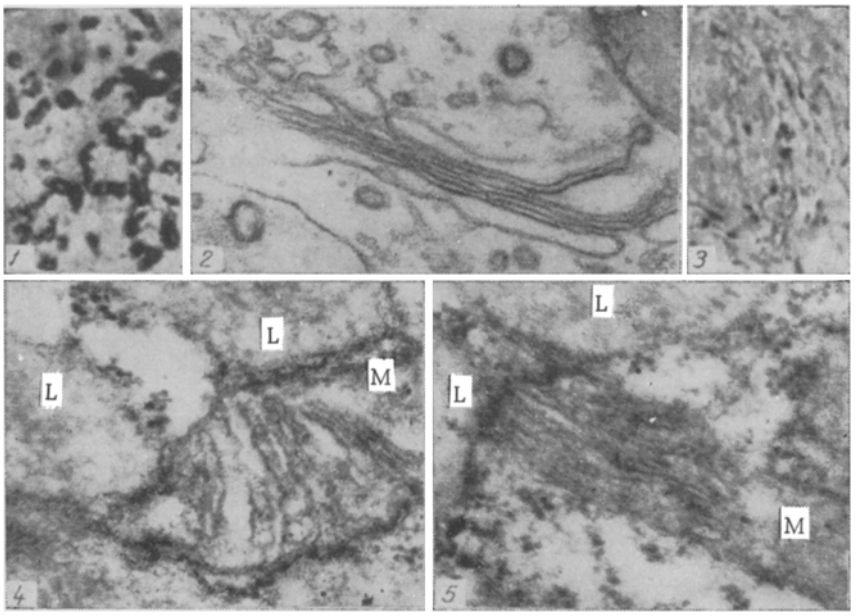

Fig. 3. The Golgi apparatus and mitochondria of the giant cells. 1) A group of dicthyosomes of the Golgi apparatus. Impregnation by da Fano's method. Immersion. Objective 90 ×, ocular 15 × ; 2) Golgi complex of a giant cell, magnification 85,000 ×; 3) area of a giant cell with mitochondria, phase contrast. Immersion. Objective 90 ×, ocular 15 ×; 4) area of a mitochondrium with transverse cristae and lipid granules close to them: M—mitochondrium, L—granules of lipids, magnification 140,000 ×; 5) area of a mitochondrium with longitudinal cristae, showing its contact with granules of lipids, magnification 140,000 ×.

One of the important characteristics of the giant cells around foreign bodies is the abundance of mitochondria in their cytoplasm, visible both in fixed, stained preparations and intravitally (Fig. 3, 3). Submicroscopically, the mitochondria are characterized by the well marked membranous character of the structure of their external envelope and their system of cristae. The latter may be arranged both longitudinally and transversely (Fig. 3, 4, and 5).

Granules of lipids were constantly found in the cytoplasm of the giant cells. They possessed an ill-defined membrane, and their ground substance was of uneven density and honeycombed. Ribosomes were frequently localized on their membranes. A noteworthy feature was the close contact between the lipid granules and the mitochondria (Fig. 3, 4, and 5). These contacts evidently were not accidental, for many authors have described the important role of the mitochondria in the genesis of the lipid granules [3, 7].

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