

Granular Cell Myoblastoma, an Electron Microscopic and Histochemical Study

Shigeo TAKEBAYASHI,*
Koichi MATSUDA** and Mikio MORI,*

*Department of Pathology,
Nagasaki University School of Medicine,
Nagasaki, Japan*

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A case of granular cell myoblastoma was studied histochemically and electron microscopically. The authors' opinion on the pathogenesis of this tumor was described after the review of literature.

Since myoblastoma was described by ABRIKOSSOFF in 1926, its histogenesis has been the subject of controversy. On the one side there is a group of authors who insist as origin the myoblast, adult striated muscle, or peripheral nerve, particularly the SCHWANN's cell, endoneural fibroblast and perineural fibroblast and others. On the other side there are people who advocate the fibroblast, histiocyte or myoepithelium as the origin of myoblastoma. There was established no final theory yet, but the neural origin is strongly supported by FUST and CUSTER¹⁰⁾, FEYRTER⁸⁾, FISHER⁹⁾, ASHBURN³⁾, and RATZENHOFER¹⁸⁾. There is an agreement, however, on the histochemical and other aspects of the specific granules.

The authors have a case of granular cell myoblastoma which was examined histochemically, not only under light microscope but also under electron microscope, to give light to its histogenesis, as reported here.

CASE REPORT

A 52-year-old policeman had been well until 3 months ago when he felt a foreign body at the left edge of his tongue. No change of taste or lingual motility, or speech disturbance was noticed. Since there was no subjective symptom except the feeling of foreign body, he ignored

* 竹林茂夫, ** 松田孝一, * 森 幹雄

** Department of Oto-Rhino-Laryngology, Nagasaki University School of Medicine,

it until a soy-bean-size mass was palpated in the depth of the tongue one month prior to admission and he was alarmed to visit a hospital.

Local and Operative Findings : Gross finding of the surface of the tongue looks normal without change of color, swelling or ulceration. On palpation there was felt a finger-tip size elastic solid tumor which is tender to pressure. Wedge resection of the tumor with surrounding normal tissues was performed. On the cut surface there was found a greyish round non-capsulated elastic solid granulomatous tumor of 0.4 x 0.5 x 0.5 cm was found. There was no sign of hemorrhage or necrosis.

Light Microscopic Findings : The specimen was fixed in 10 per cent formalin solution and whole sections were subjected to microscopic examination. The main part of the tumor was embedded in the layer of striated muscles, and only a part was in the submucosa. In hematoxylin-eosin staining the tumor cell contained a large number of slightly eosinophilic granules forming lines of irregularly interwoven fibers covered by fine collagens and of proliferated lymphocytes and reticular cells here and there. Most of the tumor cells were of large spindle-form containing numerous eosinophilic granules. Two or three independent moderately large oval nuclei of pale chromatin were located closer to the cell membrane rather than the center of the cell which formed a cluster with one another. No atypia or mitosis of the nucleus was noticed. The cell membrane was not so clearly distinguished. At the periphery of the tumor mass there were often found transition of a few fine muscle fibers into granule-filled cells, spreading like a bloom at the end (Fig. 3). When this portion was examined in PTAH staining or Gomoli silver staining, myofibrils in the striated muscle cell were scattered irregularly with their short axis of the cell elongated. These muscular components were finally replaced by countless pale eosinophilic granules (Fig. 1, 2). In silver staining, reticulum fibers surround the muscle cells, accompanied by dilatation of the cell body due to loosened myofibrils and presence of many granules in each muscle fiber (Fig. 5, 6). A sagittal section of the tumor cell shows a markedly long shape of the cell, the same size of their muscular cell (Fig. 5). Unmistakable peripheral nerve fibers and their branches were discovered in the tumor cell, but there was no sign, whether in hematoxylin-eosin staining or Gomoli silver, Luxol fast blue B, or PTAH staining, of myelin surrounding the granules, or any other finding which is common in the endoneurium, epineurium or perineurium. No morphological change was found in these nerve fibers (Fig. 7, 8).

The striated muscle outside the tumor was normal without myoblast-like finding as found in a fetus. There was neither hyperplasia nor atrophy of the epithelium overlying the mucous membrane of the tongue. Only pathologic finding beneath the mucous membrane was

that of mild inflammation accompanied by infiltration of lymphocytes and plasma cells.

As to the sensitivity of the granules to histochemical staining, they were negative to SUDAN dyes, as well as to Diastase test, although mild positive reaction to PAS was found in some of them. Toluidine blue staining (Ph : 4.1) in metachromasia was negative. Gomoli silver staining resulted in silver particle attachment to the granules even though in mild grade. They were light brown in PTAH staining and deep blue in Luxol fast blue B staining. Lipoid test by SMITH-DIETRICH method was slightly positive.

Electron Microscopic Findings : After being left in 10 per cent formalin solution for 30 hours, the specimen was fixed in the mixed solution containing the even amount of phosphoric acid stabilizer modified by Palade (Ph : 7.4) and 0.1 per cent osmium acid solution for 2.5 hours. This specimen was embedded in methacrylate plastic and sectioned by JUM Type 5 ultramicrotome, and then subjected to electron microscopic examination.

The granule in question is often irregular in shape with the size of 0.2 to 0.3 micron as shown in Figure 9, sometimes forming a mass of 1 micron. Electric density is usually high, but it is lower than a particle of fat (Fig. 11.). The content is not homogenous but consists of fine grains, forming granules of various shape. In the sarcoplasma the myofibrils become loose associated with disorganized myofilaments which disappear after being distorted. Above-mentioned particles appear in this portion of loose myofibrils. They increase in a single cell as the myofilaments disappear. The granule in question is obviously present in the sarcoplasma. However, resemblance or transition between the myofilament and granule failed to be demonstrated throughout the entire specimen. Myelinated nerve fibers were found under electron microscope, but the above-mentioned particle was not present in the Schwann cell covering the myelin sheath.

DISCUSSION

The origin of granules in granular cell myoblastoma has been hitherto discussed in many papers, which are summarized in Table 1. Included in these possibilities are the fetus myoblast²⁾, adult striated muscle^{6,7,14,15,18)}, myoepithelium¹⁷⁾, Schwann cell^{8,10,11)}, fibroblast¹⁶⁾, histiocyte^{12,13)} and epithelium cell¹⁷⁾. The nature of the granular cell is controvertially interpreted as degenerated myofilament, degenerated myelin, degenerated collagen, glucolipid, phospholipid, sphingomyelin, cephaline and lipoprotein, without any confirmative proof to support these hypotheses.

In the recent years increasing number of papers have advocated the theory of peripheral nerve^{3,8,9,10)}. In these reported cases, particularly

Table 1
Histogenesis of Granular Myoblastoma.

1. Neural theory
 - Schwann cell
 - Peri- & endoneurial fibroblast
2. Muscular theory
 - Striated muscle cell
 - Embryonal myoblast
 - Myoepithelium
3. Storage-cell theory
 - Histiocyte
 - Peri- & intraneural connective tissue
4. Epithelial (Epidermal) cell theory

those early cases in which original source is traceable, the granular cells are found in the nerve fibers, markedly in the SCHWANN cell and adjacent perimyelium fibroblast. From these findings it is suggested to call this tumor granular cell neuroblastoma. In the latest report of electron-microscopic study FISHER et al¹¹⁾ reported the presence of the granules in the SCHWANN cell. There are, however, a group of scholars who are in favor of the muscular cell theory since ABRIKOSOFF advocated it. MURRAY¹⁵⁾ reported that the growing state of the tumor cell resembles to the muscular cell of the skeleton muscle among all tissue cells comparatively studied. PEARSE¹⁶⁾ believes that the granules are the result of abnormal deposit of degenerated substance produced by metabolic disorder, and he regards the tumor cell as a form of fibroblast, because the tumor is benign with granulomatous slow growth. BANGLE^{4,7)} criticizes the theory of peripheral nerve because phagocytosis of the tumor cell is found in some cases and the tumor cell spreads along the interstitial cell presenting a striking similarity to the histiocyte. All authors agree in local invasiveness, slow growth, benignancy and granulomatous nature of this tumor.

Concerning the histochemical aspect of the granule, it is negative to SUDAN dyes, but occasionally it shows positive reaction. Some sections from paraffin block stain lightly in SUDAN staining, but some of them are stained only in SUDAN black staining. PAS reaction is varied from positive to weak positive or negative, but glycogen reaction is always negative. No paper reported of positive myelin staining. Positive reactions were reported to esterase, acid phosphatase and lipase tests. It is recognized from these reports that this granule varies from case to case in its reaction to lipid staining, PAS test, i. e., mucopolysaccharide to mucoprotein. In the pictures of granule illustrated in the literature advocating the nerve fiber theory, the granule is present along the nerve fibers or the cells related to the nerve fiber without question, although this is also true with other literature advocating other origin.

There is no room for doubt, however, if one looks at the granule inside the SCHWANN cell in the electron microscopic picture reproduced by FISHER et al. It is also true that the granule is present in the striated muscle cell in the authors' electron microscopic picture. Even if electron microscopic picture has not demonstrated unmistakable presence of granules in the fibroblast so far, there have been a few reliable report demonstrating the presence under light microscope.

Therefore, the authors reached the opinion that the granule in this tumor can be a lipid protein produced by a local metabolic disorder. It can not be a degenerated form of myofilament or myelin, as Fisher's and the authors' cases show. It is hardly conceivable that this disease is a genuine tumor, something which multiplies through cell dividing process owing to coherent autonomic pathological growth of the cell itself. It should belong to the group of pseudotumor having a granulomatous type of growth. The matrix varies from case to case, some are from a cell related to the nerve fiber some are from the striated muscle fiber, and others are from fibroblast. Those who advocate the theory of peripheral nerve emphasize their finding of granular cells in the peripheral nerve, but they fail to pay a due attention to the growth of fibroblast along the interstitial tissues, an incompatible fact with the view to regard the SCHWANN cell as the origin, to occasional finding of phagocytosis, to those cases showing a close relationship to muscular cells, and to the invasion along the muscle sheath. It seems that they based their opinion on the typical findings of a few cases and ignored many contradictions, insisting one system or one type of cells as the origin of the granule. It helps understanding if one does not stick to any one particular type of cells as the sole origin of the granule, although the true pathogenesis of this disease is still unknown. FISHER's report of impressive finding of virus under electron microscope was not confirmed in the authors' case.

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EXPLANATION OF FIGURES

- Fig. 1. Granular cell myoblastoma. Cells are of large elongated form containing numerous eosinophilic fine granules. Nuclei are round or oval, multiple as striated muscle. H. and E.
- Fig. 2. Leaving loosened myofibrils are scattered in the granule-filled cells, yet. PTAH.
- Fig. 3. There are found transition of few fine muscle fibers into granule-filled cells spreading like a bloom at the end. Cross striated fibrile of individual cells are disappeared there. PTAH.
- Fig. 4. Proliferation of granulo-fibrous tissue with lymphoid follicle are recognized in central area of the tumor mass. H and E.
- Fig. 5. There are a large amount of reticulum fibers around individual granule-filled cells as same as striated muscle fiber. Gomoli's reticulum stain.
- Fig. 6. Same section and staining in fig. 5. Striated muscle fibers and granule-filled cells are covered by same reticulum membrans. Gomoli's reticulum stain.
- Fig. 7. Nervous fiber passed through the tumor mass are well preserved and no granule is seen. Luxol fast B stain.
- Fig. 8. Same nervous fiber as fig. 7. In left under corner the granule-filled cells are distinguished but not invated to the epi- and endoneurium. Luxol fast Blue B stain.
- Fig. 9. Electron micrograph of the granules. Fine irregular granules are 0.2 to 0.3 micron in diameter. These electric density is moderated increased. $\times 12500$.
- Fig. 10. Electron micrograph. The granules appeared between myofibriles. $\times 12500$.
- Fig. 11. Electron micrograph. Lipid particles are seen and these distinguished from the granule. $\times 7400$.
- Fig. 12. Electron micrograph. Myofilaments turn to broken and then di appear but no evident transforming to granule. $\times 21800$.
- Fig. 13. Electron micrograph. Degenerated myofilaments and lipid particles. $\times 20300$.
- Fig. 14. Electron micrograph. Same pattern as fig. 13. $\times 12500$.









