The "Lemmocyte" in Peripheral-Nerve Tumors

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Based on tissue-culture studies, Murray and Stout in 1940 demonstrated that the Schwann cell has an active role in the formation of primary tumors of peripheral nerves. They further suggested, and supported the suggestion with good evidence, that reticulin and collagen can be formed by Schwann cells as well as by fibroblasts.

An extensive cytologic study of Schwann-cell tumors made by del Río-Hortega, using his method, prompted him to support the above views and to point out that the fibroblast is of secondary importance in the formation of these tumors. A recent electron-microscope description of tumors of the human acoustic nerve led to the conclusion that the principal cells in these tumors and those described by Murray and Stout, and by del Río-Hortega, were probably the same as those said to be of schwannian origin. Present submicroscopic observation of other peripheral-nerve tumors appears to provide more information regarding this subject.

Current workers continue to examine and compare structures visualized by methods of metallic impregnation utilizing the light microscope and the electron microscope. Since few papers have dealt with this subject, the present report is based upon an extension of these studies and is designed to examine the structural aspects as seen by silver-carbonate techniques. Particular interest was focused upon the principal cell of these tumors, the lemmocyte, which term is used as synonym for derivatives of Schwann cells since these elements originate from embryonal cells, termed lemmoblasts by Antoni, of the neural crest.

No attempt has been made to discuss or examine the theoretical neuroectodermal origin of these cells, a subject of long controversy. Such origins will be discussed later when other ultrastructural aspects of these tumors, which favor this concept, will be presented. The works of Masson, Murray and Stout, del Río-Hortega, Kersting and Finkemeyer, and others appear to have provided satisfactory evidence for this hypothesis.

Material and Methods

Specimens of peripheral-nerve tumors were fixed in a solution of 10 per cent formalin with an alkaline-lithium reaction. Frozen sections, 20 to 25 µ in thickness, were cut, impregnated by one or two passages through a solution of silver carbonate (employing both cold and heat methods) and reduced with 1 per cent neutral formalin. A double impregnation with a solution of 5 per cent silver nitrate and silver carbonate also was used.

Some sections were passed through a brew of gold chloride, and all sections were exposed to a solution of 5 per cent hyposulphite. Preparations were dehydrated with alcohol at 95° and 100°, cleared with creosote and mounted.

Additional paraaffin-embedded sections were prepared and stained with hematoxylin and eosin, Bodian, Wilder and periodic-acid Schiff methods.

Observations

Grossly, the tumors presented a rubbery consistency and a white glistening appearance on their cut surface. Histologically, in all methods used, tumors consisted of numerous cellular elements of characteristic shape and form, with abundant intercellular substance. Ample fibers of collagen, crossing irregularly throughout the neoplastic tissue, were present.

The cellular component predominated in the tumors. The cells characteristically were thin or elongated in outline and contained large, small, oval or round nuclei. Some of these cells showed features indicating them to be fibroblastic or histiocytic elements (Fig. 1). Histiocyte-like cells were fewer in

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number. Their nuclei were rounded and smaller, resembling at times lymphocytic elements. Their cytoplasm was abundant.

A third cellular element, however, preponderated in the microscopic appearance of the tumors. These cells were oblong in shape and contained elongated nuclei often of bizarre conformation (Fig. 2). The poles of the cells were elongated and these extensions were easily confused within the collagenic substance when viewed in hematoxylin and eosin preparations. In other areas, cells were clearly outlined and were closely related to existing nerve fibers. Based on their morphological appearance alone, these cells often resembled the Schwann cells of the myelinated and unmyelinated neural axons (Fig. 9) and it is proposed that they are the principal cells of the peripheral-nerve tumor.

**Principal Cells.** The silver-carbonate preparation caused the principal cells to appear unusually clear-cut and demonstrated their cytoplasmic processes particularly well. The nuclei were usually elongated with a smooth

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**Fig. 1.** The cells found in peripheral-nerve tumors present different sizes and shapes. The principal cell exhibits an elongated nuclear appearance. Bands of collagen can be seen crossing the field. Silver carbonate, cold method, X 1350.

**Fig. 2.** The principal cell, the lemmocyte (1 arrow) has characteristic filiform processes (2 arrows) called neuritides. Silver carbonate, double impregnation, X 1400.
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or irregular outline. In portions of the tumor, which consisted of a loose network of tissue, nuclei were sausage-shaped while, in more compact areas, nuclei exhibited a more bacillus-like appearance with tapered ends. Occasionally bizarre shapes of oblong appearance and exhibiting broad and irregular segments were noted (Fig. 3). Usually the nucleus was evenly impregnated with the metallic salts and definite structures could be readily identified.

The cytoplasm was scanty around the nucleus, but far-ranging, extensive processes drawn out from the poles of the cells were visualized. These processes were clearly seen to be independent of fibers of collagen (Figs. 4 and 8) since these two structural components appeared as overlapping structures when in close apposition.

The filiform-appearing cytoplasmic processes were identified without difficulty as extensions of the cell body. However, in areas where unmyelinated fibers could be observed, the processes could not be easily distinguished from them. The axons commonly showed intermittent, pale, widened areas not seen in processes. Additionally the filiform appendices of the principal cells were more abundant than were axons, and the constant criss-cross of these wire-like processes served to identify them, especially when observed in areas of loose structure. They could be traced out often as single bipolar extensions, but occasionally two processes could be discerned originating from one of the poles of the cell. Rarely the cell was multipolar in our preparations.

Polymorphism of the principal cells was seen sporadically, and careful scrutiny was necessary to differentiate such forms from other cellular components of the tumor.

**Fibroblasts.** Fibroblasts were identified easily with the silver-carbonate method since, with this technique, the cytoplasm was shown never to exhibit filiform processes as in the principal cells. The general appearance was that of an oval or rounded contour with abundant cytoplasm surrounding the nucleus (Fig. 5). The cytoplasm at times assumed an irregular or stellate form (Fig. 6). When they existed, bipolar processes of fibroblasts could be differentiated from those

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Fig. 3. Different forms and shapes of tumoral lemmocytes can be identified (A, B, C). The neuritides (1 arrow) are thickened and show slightly irregular contour. Silver carbonate, double impregnation, X1400.
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Fig. 4. The lemmocytes are seen to intertwine with the waved collagen material (arrow a). The processes of the principal cells are not visualized here. Few fibroblasts (arrow b) and histiocytes (arrow c) are also present. Silver-carbonate impregnation. Heat method, ×1350.

of the principal cells since the former were neither far-ranging nor filiform. The nucleus was large, rounded or oval in shape.

Histiocytes. Histiocyte-like cells were seen to have a small, round nucleus (Fig. 7). When the cytoplasm was visualized, it appeared abundant usually containing some phagocytized material.

Collagen. Collagen was plentiful throughout the tumor. The filiform processes of the principal cells were delineated and observed to be separated from the collagenic structure (Fig. 8).

Nerve Fibers. Associated myelinated and unmyelinated nerve fibers could be differentiated readily from the surrounding neuritide processes. The periodic-acid Schiff stain demonstrated regressive changes of the myelin. Some axons appeared abnormally irregular. Schwann cells were observed around the periphery of myelinated (Fig. 9) and unmyelinated nerve fibers. They resembled closely the principal cells of the tumors.

Discussion

The principal cells of these tumors have been propagated in tissue cultures by Murray and Stout. According to these authors, the characteristic tumor cells invariably grew out from transplants of neurilemmoma, and appeared to resemble the Schwann cells grown from nerve cultures. The cells were described as long, thin, and compact and were shown to possess bipolar, often filiform cytoplasmic processes. Kersting and Finkemeyer, with the same method of culture, were able to differentiate between the “neurinoma” cells and large fibroblasts on the basis of the distinctive appearance of the two types of cells.

The morphological characteristics of these cells observed in tissue culture were similar to those visualized microscopically after impregnation with the silver-carbonate method described here. Other staining procedures were found not so effective in bringing out cellular detail. Usually the lemmocyte can be identified by its shape even in routine
Fig. 5. Fibroblasts exhibit different characteristics. (A) The nucleus is rounded and cytoplasm exhibits faint multiple expansions (arrow). Two lemmocytic nuclei are shown in the left upper corner. (B) These four fibroblasts...
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Fig. 6. This fibroblast contains an indented oval nucleus. Its cytoplasm exhibits three short processes distended with dark granules. Silver carbonate, double impregnation, X1700.

Fig. 7. These histiocyte-like cells contain round nuclei within cytoplasm which contains abundant protoplasmic particles. Note smoothly rounded cytoplasmic outline. Silver carbonate, double impregnation X1850.

preparations. Its long cytoplasmic extensions, however, can be visualized only in metallic preparations (Fig. 3). These wire-like cytoplasmic processes were quite similar to the neurites or axons for which reason del Río-Hortega named them neuritides. The term "neuroid" was used by him to describe the surrounding wave-like connective tissue which was independent both of the neurites or the neuritides (Figs. 4 and 8). The lemmocytes observed in the present study showed the same characteristics as were originally reported by del Río-Hortega,10 Polak,9 and Pineda.6 Fibroblasts and histiocyte-like cells show abundant cytoplasm extending into wide processes. (C) The cytoplasm of the fibroblast is here irregular suggesting pseudopodia (arrow a) and it contains clear ring-like structures (arrow b). Silver carbonate, double impregnation, X1850.
Fig. 8. Neuritide processes (arrow a) are shown here together with unmyelinated axons (arrow b). Both are seen to be independent from the collagen visualized faintly in the background. Silver carbonate, double impregnation, $\times 1350$.

Fig. 9. Myelinated nerve fibers and Schwann cells (arrow a) can be seen in a neurilemmal sheath. The nucleus of these cells hardly can be differentiated from the lemmocytic nucleus (arrow b) here also observed. Some fibroblasts (x) and histioocyte-like cells (y) are also present in the field. Silver carbonate, double impregnation, $\times 1350$. 
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usually encountered in these tumors presented quite different features (Figs. 5 and 7), which are described for the first time in this study using silver-carbonate methods.

Summary

A morphological description is given of the cellular components of peripheral-nerve tumors using silver-carbonate techniques.

The so-called lemmocyte is particularly well stained by this method. The morphology of these cells so stained appears to be quite similar to cells of these tumors grown in tissue culture by other authors, and correlates with structure of cells identified as lemmocytes in electron-microscopic descriptions of neoplasms of the acoustic nerve. The fibroblast and histiocyte-like cells usually found in peripheral-nerve tumors by the above methods are described also.

References


Addendum

The cells described here as histiocyte-like elements were identified as mast cells when studied with the electron microscope: PINEDA, A. The presence of mast cells and their ultrastructural characteristics in peripheral nerve tumors. Arch. Neurol., Chicago. (In press)