Intracranial Cyst Lesions

> Edited by Anthony J. Raimondi Maurice Choux Concezio Di Rocco



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Head Injuries in the Newborn and Infant

The Pediatric Spine I: Development and Dysraphic State The Pediatric Spine II: Developmental Anomalies The Pediatric Spine III: Cysts, Tumors, and Infections

Cerebrovascular Diseases in Children

Intracranial Cyst Lesions

Posterior Fossa Tumors

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With 232 Figures



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Series Preface

It is estimated that the functionally significant body of knowledge for a given medical specialty changes radically every 8 years. New specialties and "sub-specialization" are occurring at approximately an equal rate. Historically, established journals have not been able either to absorb this increase in publishable material or to extend their readership to the new specialists. International and national meetings, symposia and seminars, workshops, and newsletters successfully bring to the attention of physicians within developing specialties what is occurring, but generally only in demonstration form without providing historical perspective, pathoanatomical correlates, or extensive discussion. Page and time limitations oblige the authors to present only the essence of their material.

Pediatric neurosurgery is an example of a specialty that has developed during the past 15 years. Over this period neurosurgeons have obtained special training in pediatric neurosurgery and then dedicated themselves primarily to its practice. Centers, Chairs, and educational programs have been established as groups of neurosurgeons in different countries throughout the world organized themselves respectively into national and international societies for pediatric neurosurgery. These events were both preceded and followed by specialized courses, national and international journals, and ever-increasing clinical and investigative studies into all aspects of surgically treatable diseases of the child's nervous system.

Principles of Pediatric Neurosurgery is an ongoing series of publications, each dedicated exclusively to a particular subject, a subject which is currently timely either because of an extensive amount of work occurring in it, or because it has been neglected. The two first subjects, "Head Injuries in the Newborn and Infant" and "The Pediatric Spine," are expressive of those extremes.

Volumes will be published continuously, as the subjects are dealt with, rather than on an annual basis, since our goal is to make this information available to the specialist when it is new and informative. If a volume becomes obsolete because of newer methods of treatment and concepts, we shall publish a new edition.

The chapters are selected and arranged to provide the reader, in each instance, with embryological, developmental, epidemiological,

clinical, therapeutic, and psychosocial aspects of each subject, thus permitting each specialist to learn what is most current in his field and to familiarize himself with sister fields of the same subject. Each chapter is organized along classical lines, progressing from Introduction through Symptoms and Treatment, to Prognosis for clinical material; and Introduction through History and Data, to Results and Discussion for experimental material.

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Cytogenesis and Developmental and Functional Anatomy of the Glia and Ependyma

Eiichi Tani

Early Development of the Neural Tube

The central nervous system (CNS) of mammalian embryos is first shown as the neural plate. The lateral edges of the neural plate soon become elevated to form the neural folds, and the depressed region between the folds becomes the neural groove. Further development results in the formation of the neural tube, with a long caudal part (spinal cord) and a broader cephalic portion (brain vesicles). The neural tube is composed of three different zones:^{1,2} ependymal, mantle, and marginal zones. The ependymal zone borders the lumen of the neural tube and consists of high columnar epithelial cells and large round cells. The round cells are referred to as the germinal cells and develop into neuroblasts, whereas the columnar epithelial cells give rise to spongioblasts. Both the neuroblasts and the spongioblasts migrate to a densely packed nuclear zone, the mantle zone. The marginal zone is the outermost layer of the neural tube and consists of the peripheral processes and axons of the neuroblasts.

However, serious criticism of the germinal cell theory has been raised repeatedly,^{3–5} suggesting that the large round cells adjacent to the lumen are simply dividing epithelial cells and that both cell types are in fact the same. Figure 1.1 summarizes schematically the observations obtained with the following techniques: colchicine,^{6–8} autoradiography,^{8–14} and electron microscopy.^{15,16} The cells in the wall of the neural groove or of the early

neural tube are considered to form a homogeneous population that consists of only one cell type, the neuroepithelial cells, because no differentiation into neuroblasts and spongioblasts can be observed. The neuroepithelial cells form a pseudostratified epithelium and extend over the entire thickness of the wall. They are connected to each other by terminal bars in the juxtaluminal zone. During DNA synthesis the cells are wedge-shaped, with the broader part containing the nucleus in the outer zone and a slender cytoplasmic part extending toward the inner surface. Soon after DNA synthesis, the nucleus begins to move toward the lumen, while the cells contract toward the terminal bars. During metaphase the cells are round and in broad contact with the lumen, thereby often squeezing the slender cytoplasmic processes of the neighboring nondividing cells. The terminal bars do not break down during division. Soon after mitosis, the daughter nuclei return toward the outer zone and the cells assume their original wedge shape.

Gliogenesis

Astrocytes and Oligodendrocytes

Using silver techniques, Ramón y Cajal¹⁷ noted two different cellular elements derived from the neuroepithelial cells in the spinal cord of the chick embryo. First to appear are the apolar neuroblasts. The second type, defined as the neuroglial cells, becomes visible some time later, and is considered to be dislo-



Figure 1.1. Schema of transverse section through the wall of the neural tube just after closure of the tube. According to Hardesty² the cell membranes are disappearing and the cells form a syncytium.

cated and greatly transformed neuroepithelial cells and classified as embryonal or modified astrocytes. Consistent with Ramón y Cajal's interpretations are the recent electronmicroscopic observations of monkey fetuses, that these cells show relatively electron-lucent cytoplasm, shafts filled with microtubules, lamellate expansions at a right angle to the main radial process, and glycogen granules in the expanded end-feet.¹⁸ The third type defined with silver carbonate technique by del Rio-Hortega¹⁹ consists of two different types of well-branched cells, which he named oligodendroglial and microglial cells.

Recently, the immunocytochemical method has been used as a valuable adjunct to the traditional morphological techniques for the identification of cell types in the developing CNS. Golgi, immunohistochemical, and electron-microscopic studies of gliogenesis in the developing CNS reveal an orderly sequence of events characterized by the formation of radial glial cells and astrocytes and subsequently by the appearance of oligodendrocytes in the cerebrum, cerebellum, and spinal cord of humans.²⁰⁻²⁴ It thus appears that the earliest glial cells that form within the developing CNS are radially organized and show the ultrastructural and immunocytochemical features of astrocyte differentiation in human fetal cerebrum at 12 weeks of gestation (Figure 1.2) and in human fetal spinal cord at 10 weeks of gestation. In addition, radial glia and radial glia-derived cells also give rise to differentiated astrocytes, indicating that cells of astrocyte lineage are being generated while active neurogenesis is still taking place.22

Although the formation of compact myelin sheaths is accomplished by more differentiated oligodendrocytes, the presence during development of cell forms intermediate electron microscopically and immunocytochemically between those of oligodendrocyte and astrocyte suggests not only a close and dynamic ontogenetic relationship between, but also a common cell lineage for, the two cell types.^{25,26} Others have also described the presence of 0–



Figure 1.2. Glycogen granules (gly), glial filaments (gf), and a few microtubules are shown in the large electron-lucent glial process (GP). A 17-week-old human fetal cerebrum. (\times 31,000.) [Reprinted with permission from Choi and Lapham.²⁴]

2A progenitor cells that differentiate into both astrocyte and oligodendrocyte in cultures of immature glial cells,^{27–32} as described later. It is suggested, therefore, that these early radially organized glial cells may be the ultimate source of all macroglial cell types, including astrocytes, oligodendrocytes, and ependymal cells.

Ependymal Cells

The innermost cells of the matrix in the neural tube are bordering the cerebrospinal fluid and can be regarded as a primitive ependyma. In some cells of the ependymal zone the basal process continues to grow while the nucleus remains in the ventricular region. These cells become the so-called ependymal tanycytes.³³ In higher vertebrates, the ependymal processes are disconnected and replaced by free astrocytes with increasing thickness of the brain.

Microglial Cells

During development, the microglial cells appear first below the pia and only later in the vicinity of the ventricles.^{19,34} The two main sources of origin are found at the attachment of the tela chorioidea and at the pia covering the cerebral peduncle. Small numbers also arise from the pia throughout the brain and spinal cord and from the adventitial cells of the large- and medium-sized blood vessels, suggesting that the microglial cells originate from mesenchymal elements. During their migration the microglial cells have a somewhat rounded appearance with pseudopodia.

General Histology

Astrocytes

Ramón y Cajal's work on the neuroglia is one of the most thorough studies ever made on the form and structure of astrocytes, and together with del Rio-Hortega's work, has become the standard reference for the appearance of astrocytes.

Fibrous and Protoplasmic Astrocytes

Several types of astrocytes exist, of which the most common are the fibrous and the protoplasmic (Figure 1.3). The cytoplasmic processes 20 to 50 altogether, issue directly from the cell body, in most instances in radial array, giving the cells a star-like shape. The fibrous astrocytes differ from the protoplasmic astrocytes in that their processes are fewer and longer and branch less frequently and at a more acute angle.

Fibrous astrocytes are widely distributed in the CNS, predominantly in the white matter. The inferior olivary nucleus is exceptional in that it contains a particularly heavy complement of fibrous astrocytes.35,36 Protoplasmic astrocytes are located solely in the gray matter, and imposed by adjustments to the surface of neuronal elements. Three main classes of protoplasmic astrocytes in the gray matter may be distinguished on the basis of location: (a) neuronal (perisomatic) satellites, which are in close contact with neuronal cell bodies and with the proximal part of the axon and the dendrites; (b) interneuronal astrocytes, which are at some distance from cell bodies; and (c) vascular satellites, which lie next to vessels.37

Astrocyte density differs in different regions of the CNS.^{38,39} For instance, the ratio of glial cells to nerve cells in the human striatum is 4:1; glial cells take up 20% of the volume of the striatum, and three-fourths of this volume is occupied by glial processes. Corresponding values for the pallidum are 100:1, 40%, and 95%.⁴⁰ The cytoplasmic processes of cerebellar Bergman and Fañanas glia occupy nearly 20% of the total space in the neuropil of the molecular layer.⁴¹

Fibrous astrocytes form a reticular layer over most of the surface of the cerebrum, and are called marginal astrocytes. They are closely applied to the undersurface of the pia and send out fibrous expansions parallel to the pia (Figure 1.4) and down into the cerebral tissue. These astrocytes may have perivascular endfeet, but many possess a short robust pial end-foot.⁴² The end-feet participate in the formation of the external glial-limiting mem-



Figure 1.3. Fibrous astrocytes of the spinal cord of the monkey (A). Long astrocytic processes are located between groups of nerve fibers and directed to the pia. Protoplasmic astrocytes of the human cerebral cortex (B). A few astrocytic end-feet are to be seen. Some of the nerve cells appear to be impregnated. (Golgi-Hortega-Lavilla method.) [Reprinted with permission from Polak, Haymaker, Johnson, and D'Amelio.⁹⁰]



Figure 1.4. Schema of astrocyte.

brane, and a thin basement membrane adheres closely to the pial surface of these end-feet. The cytoplasmic processes of astrocytes in the cerebral parenchyma have endfeet that form a glial-limiting membrane around the adventitia of large vessels. This membrane has a basement membrane such as is present at the pia. Other astroglial cells have processes, which are implanted on the capillary wall by means of a conical suckerfoot (Figure 1.4). The astroglial end-foot is not directly applied to the capillary wall, for a space 40 to 100nm in width lies between it and the basement membrane of the capillary. Sometimes more than one process of a given astrocyte is so implanted. In addition, the neural processes are shown to be insulated from each other by the astrocytic processes (Figure 1.4).

1. Cytogenesis and Anatomy of the Glia and Ependyma



Figure 1.5. Type 1 (A) and type 2 (B) astrocytes in culture of newborn rat optic nerve.

Type 1 and Type 2 Astrocytes

Recently, it has become more and more clear that astrocytes can no longer be considered as a homogeneous cell population. Two distinct types of glial fibrillary acidic protein-positive astrocytes (type 1 and type 2) can be distinguished in cultures of developing rat optic nerve by a combination of morphological and antigenic criteria (Figure 1.5).^{27,43,44} Type 1 astrocytes have a fibroblast-like morphology, proliferation in culture [especially in response to epidermal growth factor (EGF) or bovine pituitary extract], and do not bind detectable amounts of tetanus toxin or A2B5 antibody, which recognizes complex gangliosides.⁴⁵ Type 2 astrocytes have a processbearing morphology, resembling neurons or oligodendrocytes, divide infrequently in culture (even in the presence of EGF or bovine pituitary extract), and bind tetanus toxin and A2B5 antibody.

In culture, the two types of astrocytes derive from different cell lineages: type 1 astrocytes develop from their own precursor cells, whereas type 2 astrocytes develop from a bipotential precursor cell, which also gives rise to oligodendrocytes and has therefore been called an 0–2A progenitor cell.^{27,44} In vivo, cells with the antigenic phenotype of type 1 astrocytes first appear at embryonic day 16, whereas cells with the antigenic phenotype of type 2 astrocytes do not appear until the beginning of the second postnatal week.⁴⁶ However, there are still no antibodies that unambiguously distinguished type 1 and type 2 astrocytes.

There is increasing, indirect evidence that the two types of astrocytes in perinatal optic nerve cultures correspond to distinct types of astrocytes in the adult optic nerve. Type 1 astrocytes in vitro apparently correspond to astrocytes in vivo that have most of their processes oriented radially in the nerve, ending mainly on blood vessels or the pial surface (Figure 1.6).⁴⁷ Type 2 astrocytes in vitro, by contrast, apparently correspond to astrocytes in vivo that have most of their processes oriented longitudinally, associated mainly with nodes of Ranvier, suggesting that they may collaborate with oligodendrocytes to ensheathe axons and construct nodes of Ranvier



Figure 1.6. Schema of type 1 and type 2 astrocytes in adult rat optic nerve.



Figure 1.7. Fibrous astrocyte in rat corpus callosum. A large number of small vesicles are scattered throughout the cytoplasm. Seven lysosomes are found with polymorphic appearance. Glial filaments are visible in the perinuclear region and the cell processes. (×16,000.)

in the white matter tracts (Figure 1.6).⁴⁷ In view of the close developmental²⁷ and functional⁴⁷ relationship between oligodendrocytes and type 2 astrocytes, it is intriguing that these two types of glial cells seem to be connected by gap junctions at nodes of Ranvier.^{48,49} Thus, type 2 astrocytes seem to be a novel type of glial cell not previously recognized as a distinct cell type.

Ultrastructure of Astrocytes

The nuclei of astrocytes have a thin rim of fairly dense chromatin along their mem-

branes, and the chromatin is rather evenly distributed throughout the remainder of the nuclei. A nucleolus is usually well developed. There are differences as well as similarities in the perikaryon of fibrous (Figure 1.7) and protoplasmic astrocytes. In both types the perikaryon is electron-lucent, though owing to the sparsity of ribosomes, it is lighter in protoplasmic than in fibrous astrocytes. They also differ with respect to their cytoplasmic filament content, fibrous astrocytes having by far the greater number.

In fibrous astrocytes the filaments are present throughout the perikaryon and extend as parallel arrays into the processes. Usually, they are assembled in bundles, and each filament measures about 6 to 9 nm in diameter. At high magnification, they are found to be round with a clear center and have a beaded wall. As viewed in longitudinal sections, the filament is seen as two parallel dense lines separated by a light core. In fetal stages of development, microtubules in fibrous astrocytes are quite numerous, but they decline in number after birth. 50

Mitochondria are usually abundant in both the fibrous and protoplasmic astrocytes and are seen in the perikaryon and in the larger cytoplasmic processes. The cristae of mitochondria in astrocytes are often of the prismatic type.⁵¹ Endoplasmic reticulum (ER) is sparse. In fibrous astrocytes the cisternae of ER are unevenly but prominently studded with ribosomes. In protoplasmic astrocytes the ribosomes are fewer.⁵⁰ Small aggregates of glycogen granules are distributed in the cytoplasm of both astroglial types. Lysosomes are found in both fibrous and protoplasmic astrocytes.^{51,52} A further point of interest is the frequent presence of centrioles in the cytoplasm of fibrous astrocytes. Cilia may also be found, one per cell, and they contain nine peripheral pairs of microtubules but no central pair.53

In addition to adherent junctions (Figure 1.4 and 1.8), interastroglial gap junctions are



Figure 1.8. Two gap (arrows 1) and four adherent junctions (arrows 2) are found between adjacent astrocytes. (\times 9,000.) [Reprinted with permission from Tani and Ametani.⁹¹]



Figure 1.9. An astrocyte in freeze-fracture replica is characterized by irregular shape of cell body, scanty cytoplasmic organelles, and presence of glial filaments. A gap junction (arrow 1) is found between adjacent astrocytes, and reveals an aggregation of particles and pits in faces P and E, respectively (inset). The top surface of the particles occasionally displays a central electron-opaque (arrow 2) or white dot (arrow 3). A pit is replaced by a particle (arrow 4), which shows a central electron-opaque region in its top. (\times 53,000; inset \times 117,000.) [Reprinted with permission from Tani, Ikeda, Nishiura, and Higashi.⁷¹]

1. Cytogenesis and Anatomy of the Glia and Ependyma

often noted between two cell bodies, between two processes, and between a cell body and a cell process (Figures 1.8 and 1.9). The interspace of 10 to 20 nm in that region is narrowed to a constant width of 2 to 3nm, the gap continuous with the wider interspace.^{54–56} The gap junctions are usually hexagonally packed in a crystalline array with a center-to-center distance of 85 nm.^{48,57}

Numerous astrocyte-to-oligodendrocyte gap junctions are also identified.⁴⁸ These gap junctions occur between cell bodies, between processes, and between cell bodies and processes, as do the interastrocytic gap junctions. In addition, astrocytic cell processes form gap junctions with the outer turn of the myelin sheath at the level of cytoplasmic pockets, the outer loops, and the paranodal loops. In the astrocyte-oligodendrocyte gap junctions, with few exceptions, the connections are closely packed but not crystalline. The center-tocenter spacing is 11 nm.

Oligodendrocytes

Light Microscopy of Oligodendrocytes

Oligodendrocytes are small cells whose soma averages 6 to 8 μ m in diameter. The nuclei are round or oval and relatively dense, and the cytoplasms form a narrow rim. In sections stained by silver techniques, oligodendrocytes appear as spheroidal, polygonal, or piriform cells having several slender processes that occasionally appear thorny (Figure 1.10). Oligodendrocytes are distributed in both gray and white matter, and in the gray matter they appear as neuroal (perisomatic) satellites or are found next to nerve fibers or blood vessels. In the human precentral cortex, oligodendrocytes make up 51% of the perineuronal glial population.^{58,59} Interfascicular oligodendrocytes are by far the most common cell type in the white matter. Their processes tend to run parallel to nerve fibers, and give off branches that partly or completely encircle nerve fibers. In the rat corpus callosum 69.8% of the glial cells are oligodendrocytes.⁶⁰ In the rat spinal cord (anterior horn and midzone),



Figure 1.10. Oligodendrocyte in human corpus callosum. Oligodendrocyte has slender processes originating from spheroidal body. (Golgi-Hortega-Lavilla method.) [Reprinted with permission from Polak, Haymaker, Johnson, and D'Amelio.⁹⁰]

60% of the glia have been found to be oligodendrocytes.⁶¹

Ultrastructure of Oligodendrocytes

Oligodendrocytes have many ultrastructural features in common regardless of their location (Figure 1.11). The nucleoplasm has an electron density greater than that of astrocytes. The cytoplasm is electron dense.⁵⁰ Free ribosomes also abound, and the cytoplasm is rich in granular ER. The cisternae of ER are generally arranged in a circumferential manner around the nucleus but predominate on one side of the nucleus. The Golgi apparatus is usually well developed, and its cisternae and vesicles are present throughtout the perikaryal cytoplasm. Mitochondria are rather inconspicuous. Microtubules are numerous and are concentrated at the sites of origin of the cytoplasmic processes and in the cytoplasmic processes themselves. Filaments are rarely seen, and the cytoplasm contains no glycogen granules. Lysosomes sometimes encountered in the perikaryal cytoplasm have either a homogeneous appearance or contain granules, membranous components, filaments, and droplets, or even exhibit one or two clear rectangular areas. 50,62