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# Central Neurocytoma

## An Electron-microscopic Study of Two Cases*

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**Summary.** The authors report two cases of a rare tumor in adults which were inserted on the fornix and caused a frontal syndrome. By light microscopy, the tumors, highly calcified, were composed of small clear cells forming dense areas in a patchy fibrillary stroma. Electron microscopy revealed a striking neuronal differentiation with numerous synapses. These tumors, for which the term neurocytomas was proposed, were compared with the other CNS neuronal tumors described in the literature.

**Key words:** Central neuronal tumor – Third ventricle tumor – Synapses – Electron microscopy

True neuronal tumors of the central nervous system (CNS) are rarely observed, and their identification by light microscopy is often controversial. Except for ganglioneuroma (Robertson et al. 1964), ganglioglioma (Rubinstein and Herman 1972; Probst et al. 1979) or complex neurectodermal tumors (Gambarelli et al. 1981) which contain typical ganglion cells, other tumors like supratentorial neuroblastomas (Horten and Rubinstein 1976) or primitive neurectodermic tumors (Boesel et al. 1978) are considered as only potential neuronal tumors without any constant and definite morphological proof of differentiation. The two present cases strikingly similar to each other, showed some particular clinical and topographical features and morphologically corresponded to mature neuronal tumors, the actual site of origin of which remaining problematic.

## Material and Methods

Tumor fragments from the two cases were fixed for classical histological study and stained by the following methods: hematoxylineosin (HE), Gomori method for reticulin, Bodian's silver impregnation for neurofibrils, and Grimelius method for neurosecretion. For immunocytochemistry, routinely fixed and paraffin-embedded sections were stained according to the unlabeled antibody peroxidase-antiperoxidase (PAP) method (Sternberger 1979). Specific anti-GFA serum kindly donated by Dr. L. Eng (Stanford, CA, USA) was used at a dilution of 1/100°. Normal rabbit serum was used for negative control. Some other tumor fragments were fixed in 2.5% glutaraldehyde in cacodylate buffer, postfixed in 1% osmic tetroxide, dehydrated, and embedded in araldite for electron microscopy. Ultrathin sections were stained with lead citrate-uranyl acetate and photographed with an EM 300 Philips electron microscope.

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## Case Reports

*Clinical Story*

*Case 1.* A 32-year-old man was hospitalized for progressive loss of memory, lack of initiative, apathy, and disorientation in time and space. The trouble had started more than 1 year ago. Neurologic examination was normal. Fundus showed a bilateral edema. At EEG, there were right anterior frontal disturbances. Radiography of the skull showed a huge calcified mass projecting in suprasellar area. On CT scan, the tumor was located in the third ventricle and occupied a part of the right lateral ventricle (Fig. 1a). Iodine injection did not enhance the contrast. At the operation the tumor destroyed the fornix and widened the foramen of Monro. It was easily removed. Postoperative radiotherapy was applied (55 rays on the brain, 35 rays on the spinal cord). However, a ventriculo-peritoneal shunt was needed by a hydrocephalia. A meningitis occurred parallely to a medullary aplasia. The patient died 14 months after the operation without any tumor recurrence on CT scan.

*Case 2.* A 39-year-old man was hospitalized for a 3-year clinical history made of loss of memory, apathy, and intracranial hypertension. CT scan had previously revealed a calcified mass in the head of the caudate nucleus and a hydrocephalia (Fig. 1b). After the installation of a shunt, the clinical signs had decreased. At the present hospitalization, the patient again presented a complete loss of memory and apathy. Neurologic examination showed dysesthesia of the extremities of upper limbs. A stereotactic biopsy was performed, followed by a complete surgical removal. The postoperative course has been uneventful until now, 2 years after surgery.

*Light Microscopy*

The morphological features were strictly similar in both cases and deserve a common description.

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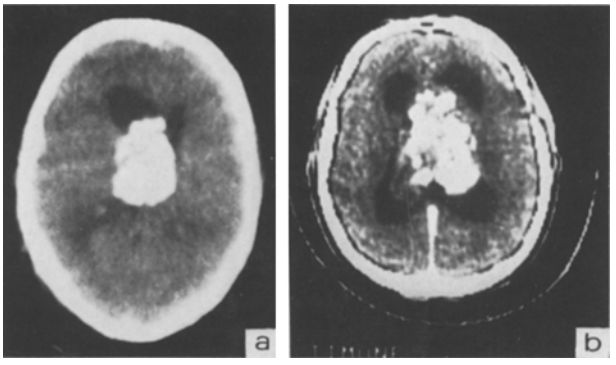


**Fig. 1 a, b.** CT scans of central neurocytoma developing in the third ventricle. **a** Case 1. **b** Case 2

The major part of the tumor was characterized with an extensive fibrillary stroma through which the tumor cells were sparsed or grouped into small clusters (Fig. 2a). The tumor cells were round showing a central regular nucleus and a clear cytoplasma. Mitosis were unfrequent and there was no cell pleiomorphism. In some dense areas, the aspect was reminiscent of an oligodendroglioma (Fig. 2c). No Homer-Wright rosettes were seen, but in some instances tumor cells were disposed around wide fibrillary patches sometimes including a vessel (Fig. 2b). Bodian's staining showed very few argentophilic processes (Fig. 2d). Achucarro's staining for pineocytes and Grimelius staining for neurosecretion were negative. GFAP immunostaining failed to show any astrocytes. Blood vessels were numerous and outlined some incomplete partitions, enhancing the histological similarities with oligodendroglioma. Numerous calcifications were found through the tumors, either in the vessel walls or in the stroma (Fig. 2e). Moreover, in case 2, some of them displayed an osseous metamorphism (Fig. 2f).

*Electron Microscopy*

Only one cell type was observed in both cases (Fig. 3). Tumor cells showed nuclei with a clear finely dispersed chromatin and a neat nucleolus. The cytoplasm contained some parallel ergastoplasmic channels, an abundant Golgi apparatus, and dispersed lysosome-like structures (Fig. 3a). These osmiophilic inclusions were irregular, ovoid, or dumb-bell shaped (Fig. 3d). The thin cell processes formed a dense neuropile (Fig. 3e). They showed 20 nm parallel microtubules but no filament. The most striking feature corresponded to typical synapses joining the processes (Fig. 4) or the processes and the tumor cell perikarya (Fig. 3b, c). Presynaptic bags were filled with 40 nm clear vesicles, or 50–60 nm dense-cored vesicles (Fig. 4a). Various synaptic abnormalities were seen: (1) pre- and postsynaptic membranes showed a similar osmiophilic densification (Fig. 4b); (2) clear and dense-core vesicles were present in both pre- and postsynaptic bags (Fig. 4d, e); (3) some presynaptic bags disclosed only punctae adherentiae or no contact at all with the surrounding processes (unattached synapses) (Fig. 4e); (4) numerous processes were enlarged and filled with an accumulation of dense-core vesicles. At last some simple zonulae adherentes were observed between processes and/or perikarya (Fig. 4c). No glial cells were seen. Blood capillaries were normal. Calcified fragments were not studied by electron microscopy.

## Comments

These two cases showed numerous striking similarities. Both developed in young men with a several-month clinical history of amnesic and behavioral troubles evoking a frontal syndrome. In both cases, the tumor was located in the third ventricle, destroying the anterior part of the fornix, the septum lucidum, invading a lateral ventricle. At last, both tumors were highly calcified, surgically totally removed, and showed an identical morphological pattern which raised some problems of histogenesis.

First, by light microscopy, the association of small, regular, and clear cells, a capillary network forming incomplete septa and numerous calcifications could suggest an oligodendroglioma. The ventricular site of the tumors, the patchy fibrillary stroma, as well as the electron microscopy findings excluded this diagnosis.

The second possibility was that of a pineocytoma. The arrangement of tumor cells into large ill-defined rosettes favored this hypothesis (Rubinstein 1972; Herrick and Rubinstein 1979). Moreover, ultrastructural findings, particularly synapses, were similar to those reported by Herrick and Rubinstein (case 27, 1979) in a case with neuronal and glial differentiation. Here, only neuronal features were present, the absence of GFAP immunostaining by light microscopy ruling out any astrocytic component. Electron microscopy of the two other human pineocytomas described in the literature failed to show any definite neuronal differentiation (Nielsen and Wilson 1975; Neuwelt et al. 1979). In the present cases, in spite of some similarities with the tumor described by Herrick and Rubinstein (1979), the clinical, tomodensitometric, and peroperative observations permitted to assert that the pineal body was intact. CT scan displayed a normal median and posterior calcification in pineal area. The tumors were only attached to the anterior part of the fornix. These features were not compatible with the diagnosis of pineocytoma, unless these tumors were true "ectopic" pinealomas. In fact, it is difficult to establish any correspondance between these rare reports and the ultrastructure of mammalian pineal. Normal pineocytes are not neurons and do not form classical synapses. Only synaptic ribbons have been described in their cytoplasma (Kappers 1976; Welsh and Reiter 1978).

A third comparison with cerebral neuroblastomas could be done by light microscopy. However, the absence of Homer-Wright rosettes, the clear cytoplasma of tumor cells, the age of the patients, and even the ventricular site of the tumors were not classical features of this rare tumor (Horten and Rubinstein 1976). On the other hand, central neuroblastomas presented as immature neurectodermal tumors by electron microscopy (Yagishita et al. 1978; Rhodes et al. 1978; Boesel et al. 1978) though they could support some neurosecretion activity (Vuia and Hager 1975; Azzarelli et al. 1977; Pearl et al. 1981). On the contrary, extensive complete or unattached synapses were de-

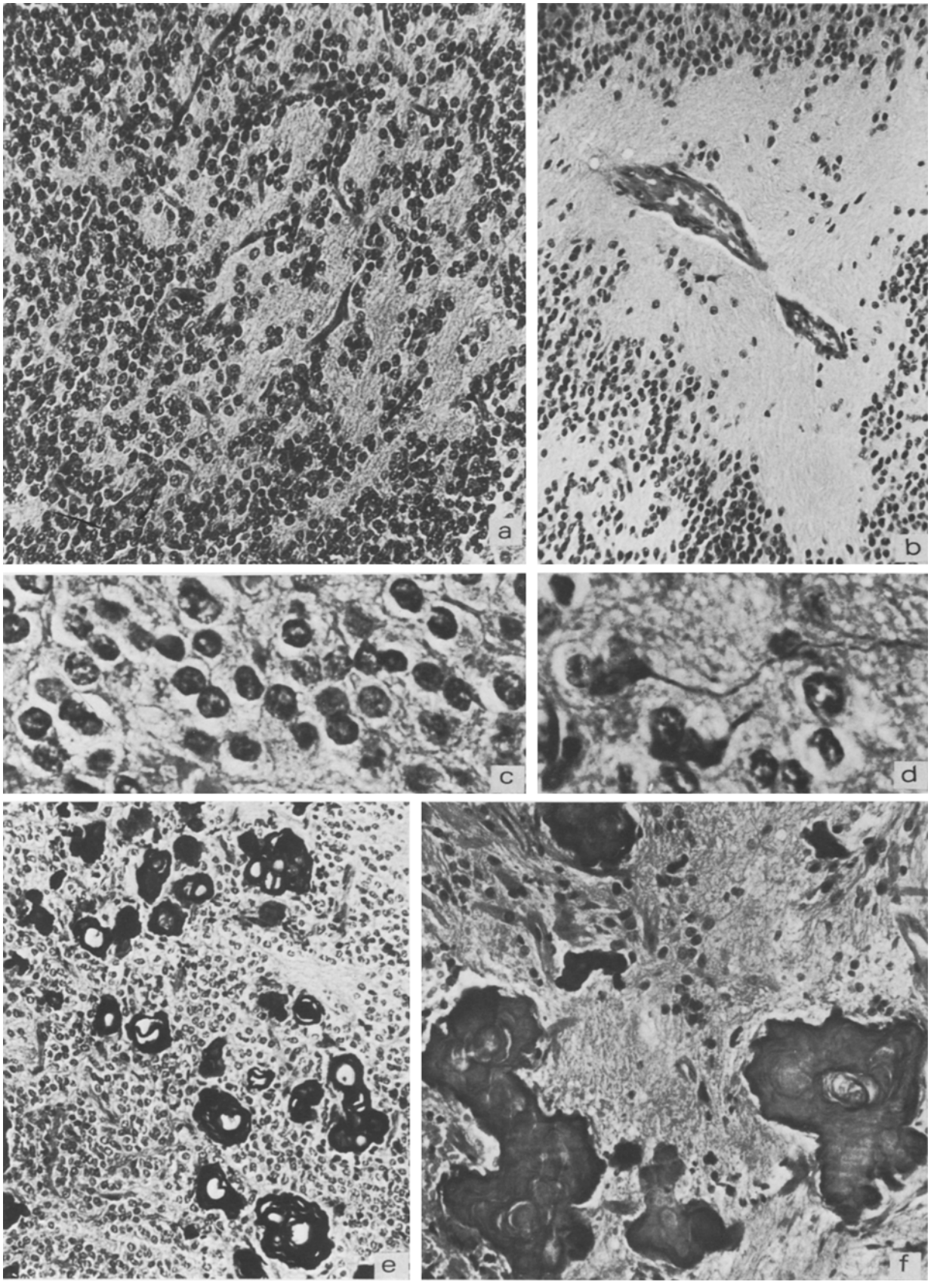


**Fig. 2a–f.** Histological features of central neurocytomas. **a** Case 1: Tumor cells sparsed through a fibrillary stroma, HE ( × 250). **b** Case 2: Fibrillary area including capillaries, HE ( × 100). **c** Case 1: Clear tumor cells resembling tumor oligodendrocytes, HE ( × 950). **d** Case 1: Bodian's staining showing neuritic processes ( × 1,000). **e** Case 1: Sparsed calcifications, HE ( × 100). **f** Case 2: Calcifications and osseous metamorphism, HE ( × 250)

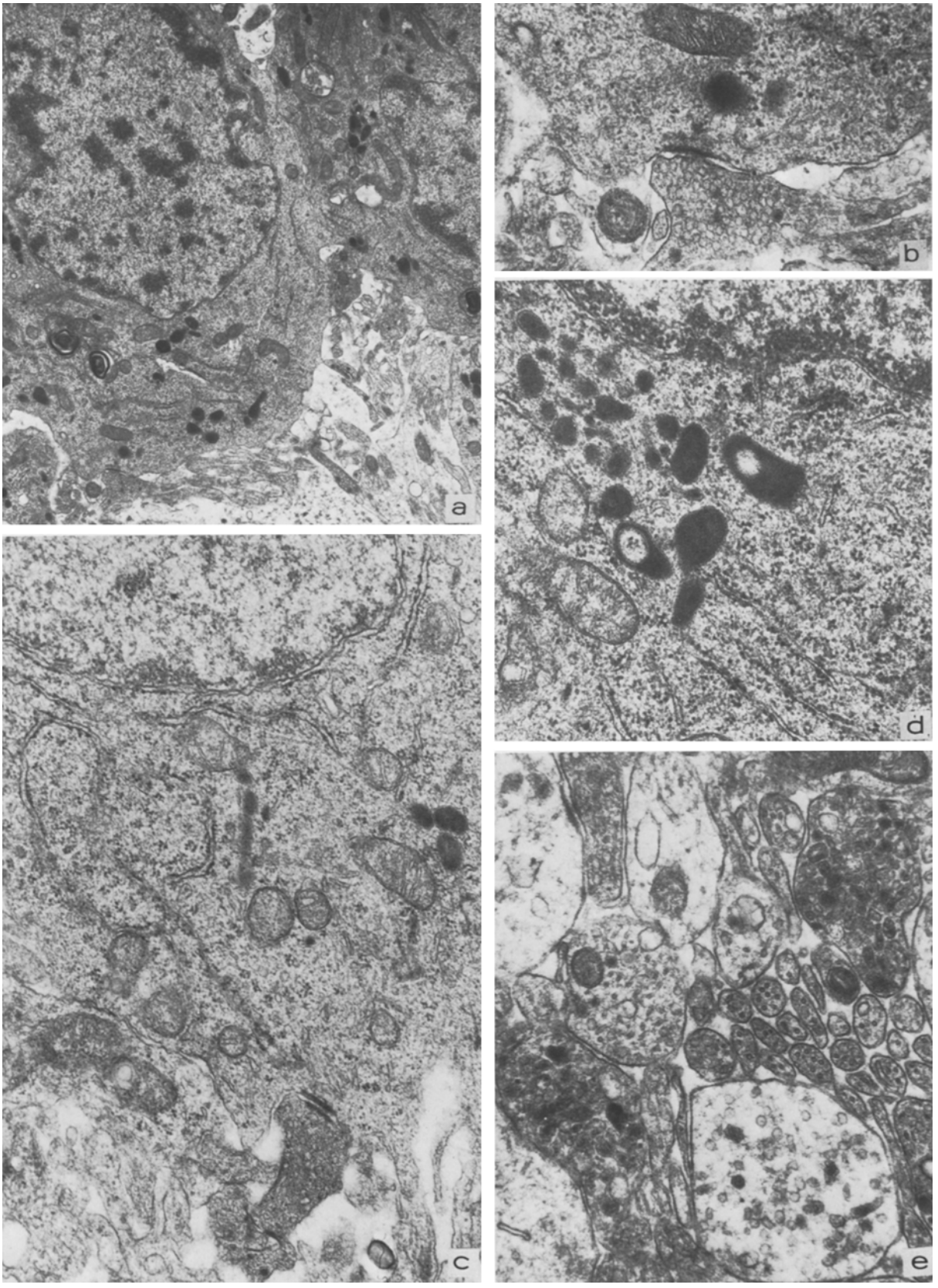


**Fig. 3a—e.** Electron microscopy of central neurocytomas. **a** Case 2: Neuronal tumor cells showing indented nuclei, lysosome-like inclusions and thin processes ( × 20,700). **b** Case 2: Detail of "a": synapse between a cell process and a perikaryon ( × 32,500). **c** Case 1: Tumor cell showing ergatoplasmic channels, lysosome-like structures and presenting an axo-somatic synapse ( × 28,000). **d** Case 1: Detail of pleiomorphous lysosome-like structures ( × 36,500). **e** Case 2: Tumor cell processes including microtubules, clear and dense-core vesicles ( × 36,000)

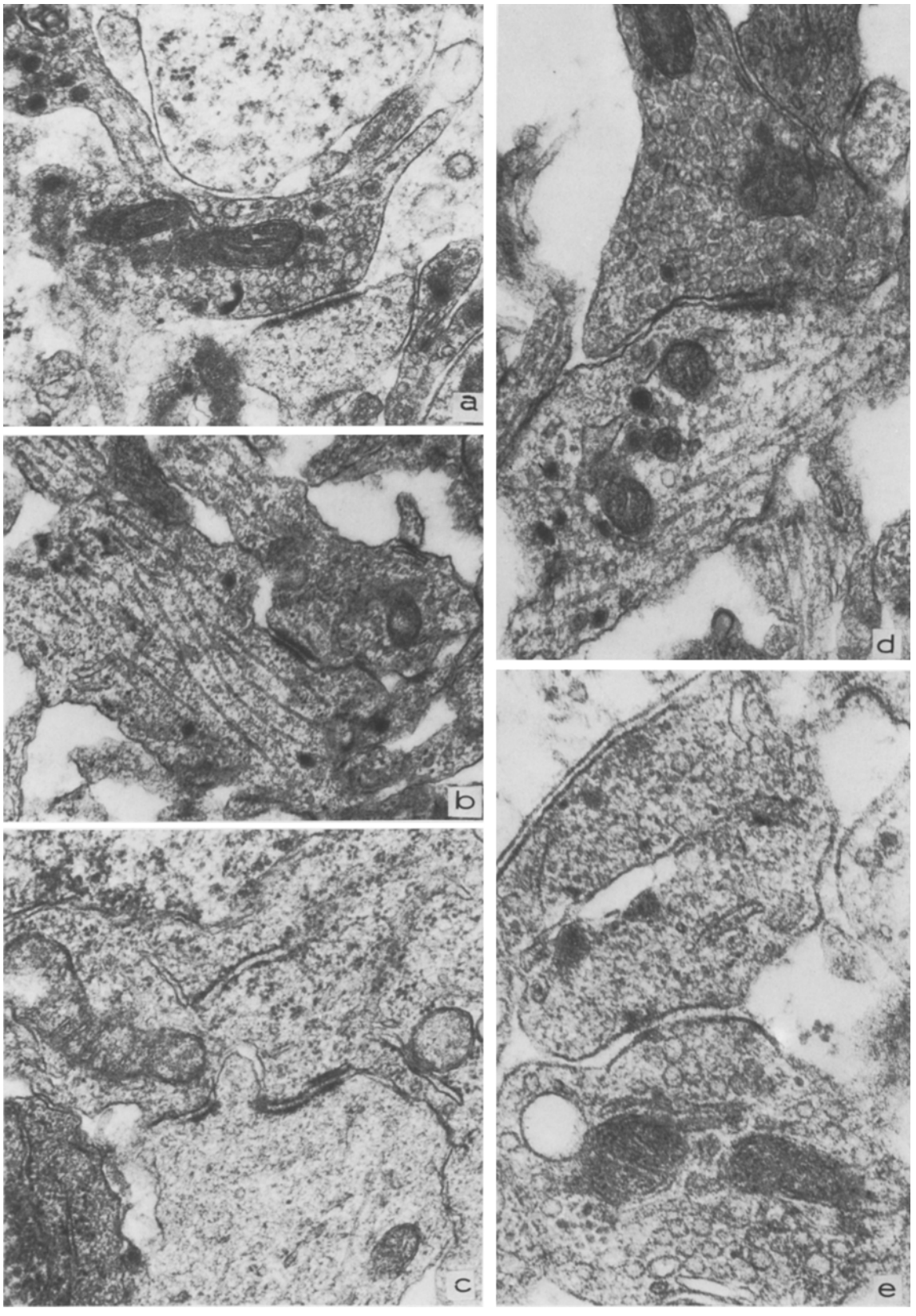


**Fig. 4a–c.** Synapses and junctions in central neurocytomas (see the text). **a** Typical synapse (case 2, ×36,500). **b, d,** and **e** Various synaptic abnormalities (**b**: case 1, ×36,500; **d**: case 1, ×45,000; **e**: case 2, ×57,600). **c** Zonula adherentia between a cell process and a perikaryon (case 1, ×41,000)

scribed in three cases of children cerebellar neuroblastoma (Shin et al. 1978; Hirano and Shin 1979; Yagishita et al. 1980; Pearl and Takei 1981). These differentiated cerebellar tumors could develop from granule cells or represent an advanced maturative stage of medulloblastomas. Like the present cases, these tumors should rather be called neurocytomas.

The actual origin of the two ventricular neuronal tumors in adults reported herein remains obscure. In spite of a negative Grimelius staining, pleiomorphous lysosome-like inclusions and dense-cored vesicles proved the neurosecretory activity of tumor cells. A possible source could be the nuclei of septum lucidum, this hypothesis supporting the medial anterior site and the clinical expression of the tumors.

To summarize, these two cases correspond to a very specific tumor for which we propose the term supratentorial neurocytoma. The clinical course, fatal in the first case with a intercurrent ventriculitis, cannot be precise, but it seems that the development of the tumors was long and insidious before the emergence of the first dramatic signs of a brain neoplasia.

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