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Dysplastic Gliosis (Spongioblastosis) and the Rosenthal Fibres

Pathogenetic Contributions

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Summary. The material obtained from 11 cases of gliosis and 4 cases of tumours associated with Rosenthal fibres was studied under optical and electron microscope.

Ultrastructurally the Rosenthal fibres appear in the form of osmiophil amorphous masses deposited in the cellular cytoplasm among the glial filaments, the latter showing no degenerative phenomena.

The development of Rosenthal fibre-forming gliosis is closely linked to dysplastic processes, resulting in discontinuity of the ependymal epithelium, concomitantly affecting the normal embryonic development of the subependymal glial system.

The spongioblast, a Rosenthal fibre-forming element, represents the type of dysplastic, subependymal glial cell with fibrillofoming and proliferative potentiallites (Bielschowsky, Hallervorden, Schlote). The presence of osmiophil bodies next to Rosenthal fibres forms the specific ultrastructural properties of the spongioblastic cell in contrast to the situation in normally differentiated astrocyte.

Rosenthal fibres described by this author in 1898, in blastomatous gliosis, around a syringomyelia cavity have been of late the subject of detailed studies in the electron microscope (Schlote, 1966, 1967; Hager 1968; Herndon *et al.* 1970). Even if today the intimate structure of these formations has been fully established, the way in which they are produced still gives rise to many different interpretations

Thus Hallervorden (1961) believes that the formation of Rosenthal fibres is closely linked to a certain type of cell which he considers to be the sprongioblast, the cell preceding the astrocyte and oligodendroglia. Russell and Rubinstein (1971), on the other hand, consider that the cell forming Rosenthal fibres may be assumed, in view of its fibrillogenetic activity, to be a pilotcytic astrocyte. Since the term of piloid gliosis was first used by Penfield (1932) to designate isomorphus fibrillary gliosis it is obvious that, according to this concept, the property of forming Rosenthal fibres actually belongs to the fibrillary astrocyte (Russell and Rubinstein, 1971). The results of these investigations are not yet conclusive. The question appears to be whether formation of the Rosenthal fibres is a characteristic of the fibrillary astrocyte and therefore an altogether unspecific degenerative product of isomorphus (piloid) fibrillary gliosis or else belongs to a cellular system with a more or less specific mechanism.

This is the question to which we have tried to find an answer in the present work.

Material and Method

The autopsy material at our disposal consisted of 250 brains received over a 2 year period from patients who died from different cerebral diseases. To this may be added 800 biopsy specimens representing the operative material from different cases of tumours of the nervous system.

In 11 of the autopsy cases gliosis foci with the formation of Rosenthal fibres were found. These cases together with those which served as controls are described in the following table.

Table 1

Case sex, age (years)	Diagnosis	Presence of rosenthal fibres	Localization	Observation
1. B.H. m, 30	Craniopharyngioma of 3rd ventricle	+++ accompanied by cellular proliferation with fibrilloforming bipolar processes	In the vicinity of the tumoral inclusions, in the subependymal tissue of the 3rd ventricle	
2. B.M. m, 25	Craniopharyngioma of 3rd ventricle	+++ accompanied by proliferation of bipolar fibrillogenetic cells forming the stroma of the epithelial tissue	In the subependymal tissue around the intracerebral inclusions of the tumor	
3. R.O. m, 4	Malformation of 4th ventricle with int. noncommunicating hydrocephalus	++accompanied by cellular proliferation with elongated nuclei and abundant fibrillary proliferation	In the subependymal tissue around the 3rd ventricle	No R. Fibres were found in the subependymal tissue of the lateral ventricles
4. L.J. m, 21	Malformative dilation of the 4th ventricle	+accompanied by fibrillocellular multiplication	Idem	Idem
5. G.K. f, 64	Cyst of the lateral foramina, Generalised internal hydrocephalus	+ accompanied by proliferation of elongated fibrillogenetic cells	Idem	Idem
6. F.S. f, 14 months	Cyst of the 4th ventricle with obstruction of Magendie and Luschka's foramina.	+ accompanied by proliferation of elongated cells with moderate fibrillogenetic activity.	In the subependymal tissue arond the 4th ventricle.	Idem
7. S.F. m, l	Hydromyelia	++ cells with elongated nucleus, some with round nuclei and others with monstrous nuclei.	In the subependymal tissue around the hydromyelic cavity	

Table 1 (continued)

Case sex, age (years)	Diagnosis	Presence of rosenthal fibres	Localization	Observation
8. O.A. f, 20	Spongioblastosis with intramedullary cyst	+++ accompamied by elongated fibrillo-forming cells	In the nervous tissue surrounding the intramedullary cavity	
9. E.C. f, 8	Micronodular encephalitis	+ accompanied by proliferation of elongated fibrillo-forming cells.	In the subependymal tissue below the floor of the 4 th ventricle	Dysraphism of t h 4 th ventr.
10. R.H. m, 37	Chronic meningo-arteritis, probably syphilitic	++ accompanied by elongated fusiform cells and glial fibrosis	Ependymal granulation	R. Fibres also present in gliosis of the epiphyseal gland
11. S.A. m, 39	Intraventricular and meningeal melanoblastosis	+++ in elongated bipolar cells	In the reactive subependymal tissue	R. fibres not found in subpial gliosis. Abundant around a cyst of the epiphyseal gland.

V = ventricle; R = Rosenthal fibres; + = rare R. fibers; ++ = R. fibres in moderate amounts +++ = abundant R. fibres.

Control Cases. Two cases of craniopharyngioma that developed strictly intraventricularly; in the subependymal fibrillary gliosis no Rosenthal fibres were found. Fifteen cases of chronic internal hydrocephalus of various origin (tumours, encephalitis, abiotrophic disease — Huntingtou chorea — demyelinating diseases, senility). In spite of the presence of accentuated subependymal fibrosis no evidence was found of Rosenthal fibres at this level.

Rosenthal fibres were detected in 3 cases of cerebrellar spongioglastomas (the so-called cerebrellar astrocytoma) and 1 case of diffuse spongioblastomatosis of the brainstem with selective subependymal development in the cerebrellum up to the thalamus. To these may be added 2 cases of diffuse spongioblastosis with Rosenthal fibres associated with intracerebral dermoid cysts, which however have been studied separately (Vuia, 1973).

The biopsy material of 3 tumours and one intramedullary spongioblastosis associated with Rosenthal fibres was fixed directly in glutaraldehyde and embedded for examination in the electron microscope.

The autopsy material was embedded in paraffin and stained by the hematoxylineosin, Goldner and Heidenhain methods; Rosenthal fibres showed a marked tincorial affinity for the two staining methods.

Results

In the optical microscope Rosenthal fibres resemble knob or rod-like formations, amorphous masses staining rose with eosin or bright red with Goldner, distributed among the glial fibres of the cellular processes and rarely observed in the perikaryon cytoplasm. (Fig. 1). The cells in contact with the Rosenthal fibres appear to be elongated with bipolar processes; next to them, cells with nuclear anomalies, others with round clear nuclei or multipolar astrocyte cells were noted.

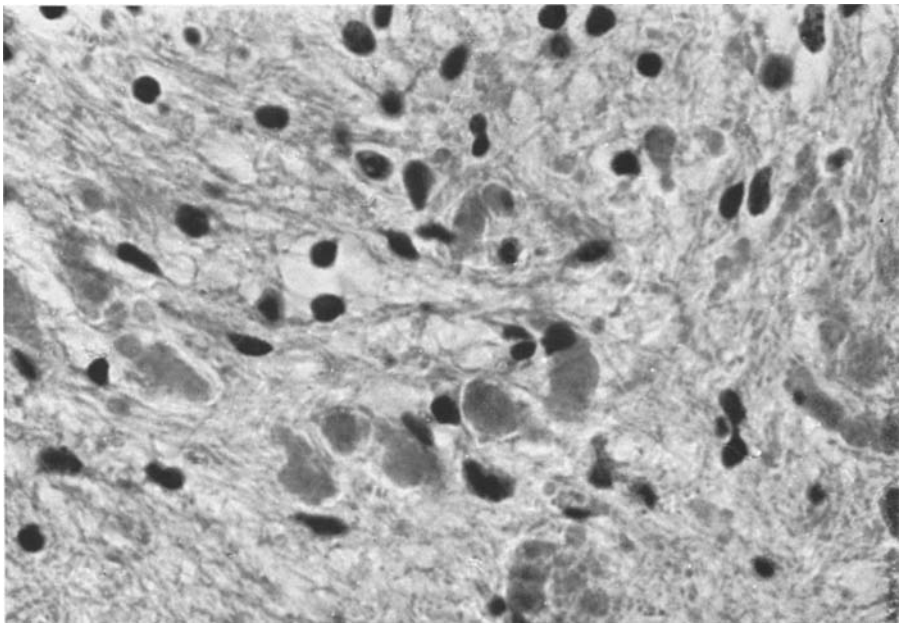

Fig. 1. Subependymal gliosis and Rosenthal fibres around the malformative dilation of the 4th ventricle. H. E. × 40

In the electron microscope the Rosenthal fibres appear as amorphous osmiophil masses in the cytoplasm of the cellular processes and more seldom in the cytoplasm surrounding the nucleus. The amorphous osmiophil masses, that are not delimited by a membrane, develop among the glial filaments which do not exhibit degeneration phenomena. Intact glial filaments without alterations or interruptions can be clearly discerned among the mass of amorphous deposits (Fig. 2). In the cellular cytoplasm, in the neighbourhood of the osmiophil masses, constant evidence was found of mitochondria with manifest dystrophic alterations: tumefaction, destruction of the internal cristae and accentuated osmiophilia of the content. The Rosenthal fibres-forming cell appears as a glial element with a brisk fibrillogenetic activity, abundant filaments being found both in its processes and in the perikaryon. In the basal cytoplasm evidence was found of various organelles, such as mitochondria, lysosomes, ribosomal granules and a granular free canallicular system (Golgi system) (Fig. 3). Rarely found in connection with this system, more frequently free in the cytoplasm were small particles with a filamentous structure, delimited by a membrane. The characteristic feature of this cell is the abundance of a series of osmiophil bodies, diffusely distributed both in the perikaryon and in the processes, around the Rosenthal fibres included. Cells whose cytoplasm is predominantly charged with these elements were seldom observed (Fig. 4). In some fields we were able to follow up in these osmiophil bodies the transformation of mitochondria, on the one hand, and of the particles with a filamentous content on the other. The latter frequently presented a deposit of small osmiophil granules, proof

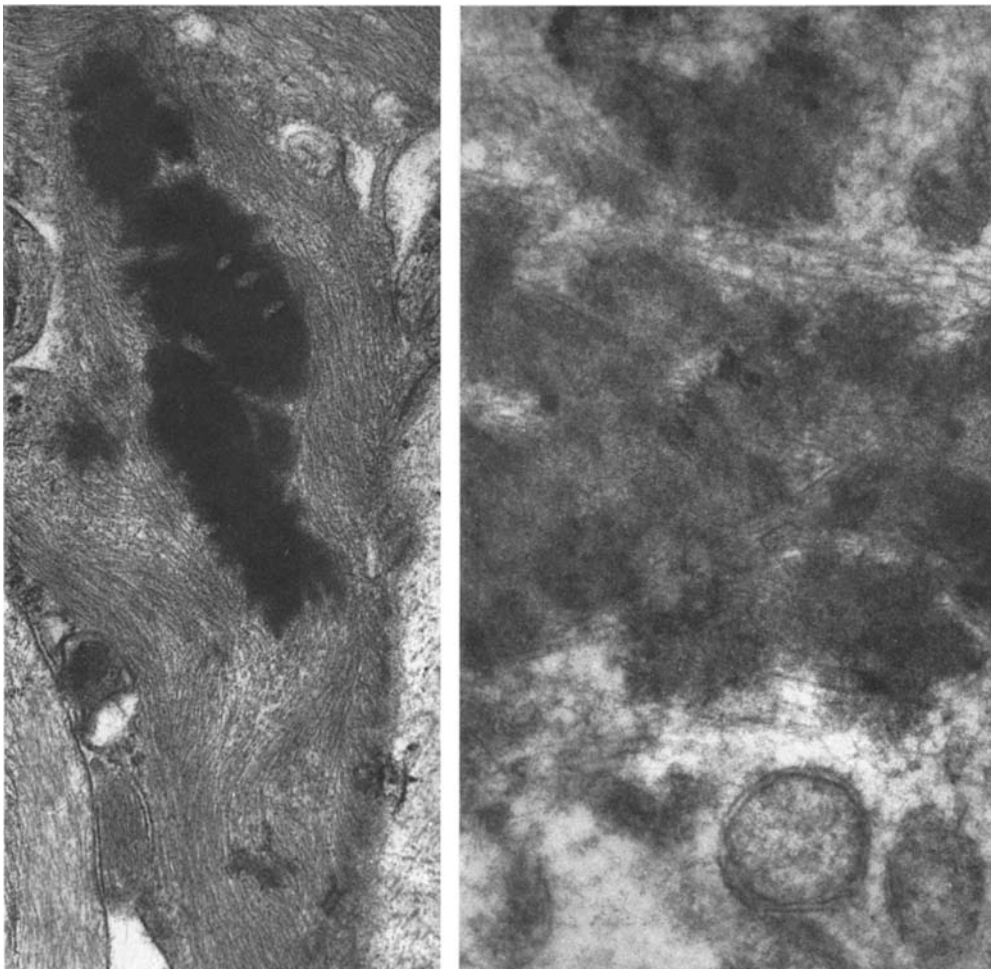

Fig. 2a and b. Ultrastructural aspect of Rosenthal's fibres: a) osmiophil mass deposited between the glial filaments, multiplying abundantly; b) among and within the osmiophil mass, glial filaments without degenerative phenomena can be seen. a × 10500; b × 22500

of an evident fatty degeneration. The osmiophil bodies did not seem to be directly connected with the amorphous masses, both developing independantly in the cellular cytoplasm (Fig. 5).

Interpretation of the Results. Discussion

The ultrastructural aspect of Rosenthal's fibres corresponds to that described by Schlote (1966) and Hager (1968); amorphous mass deposited among the glial filaments, not delimited by a membrane but always present in the cellular body, never free. These deposits appear more frequently in the cellular processes and rarely in the perikaryon. In all the cases studied by us the glial filaments do not

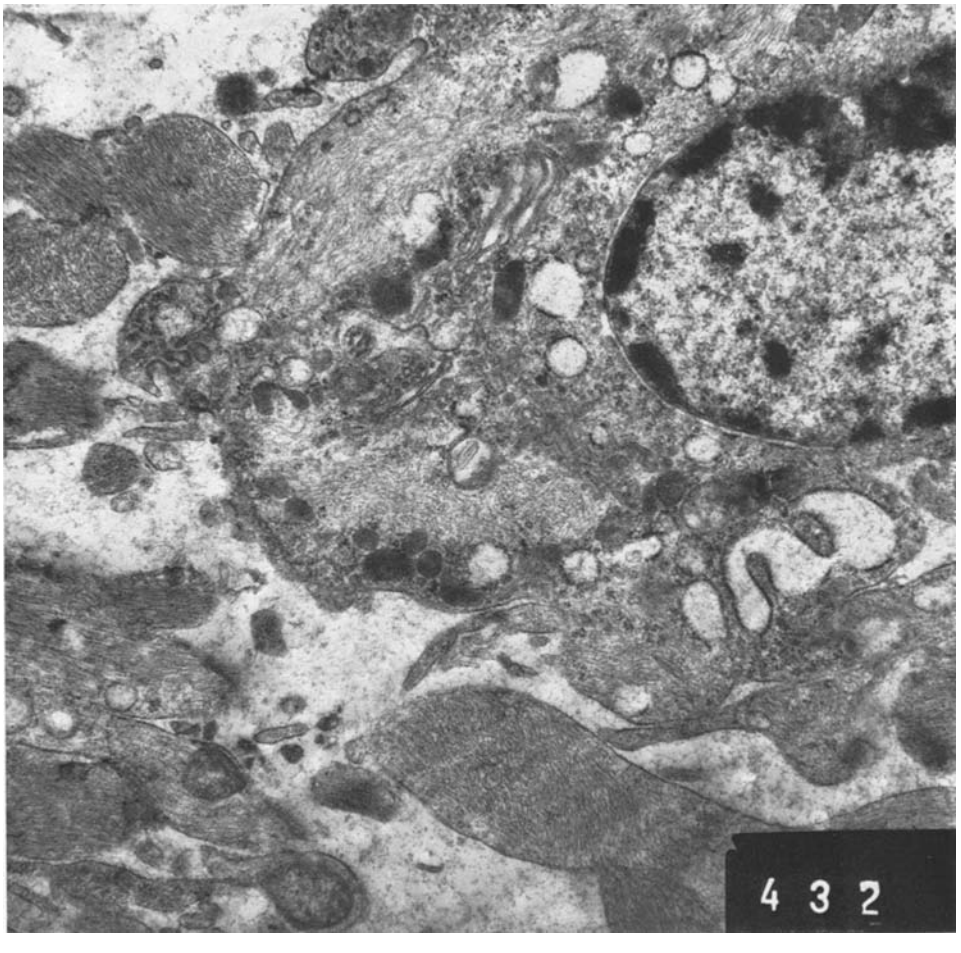

Fig. 3. a) Ultrastructural aspect of the Rosenthal fibre-forming cell. Cell with round nucleus rich in chromatin. The organelles may be discerned in the cytoplasm (mitochondria, lysosomes and reticulum of the Golgi type). Multiple bands of glial filaments and a series of corpuscular formations with a fine fibrillary content can be seen. × 7500

exhibit degenerative phenomena, therefore the osmiophil masses do not appear as a degeneration product of the glial filaments, as sustained by some authors (Herndon *et al.* 1970; Gullottta and Fliedner, 1972) but as a product of the basal cellular cytoplasm. Lending support to this assumption are the alterations of the cellular organelles (mitochondria) constantly made evident araound these osmiophil masses.

The cells forming Rosenthal fibres closely resemble a glial cell and exhibit intense fibrillogenetic activity, the Rosenthal fibres appearing in the cytoplasm of cells with a particularly intense fibrilloforming activity (Spongioblastische filamentbildende Zelle Schlote, 1967).

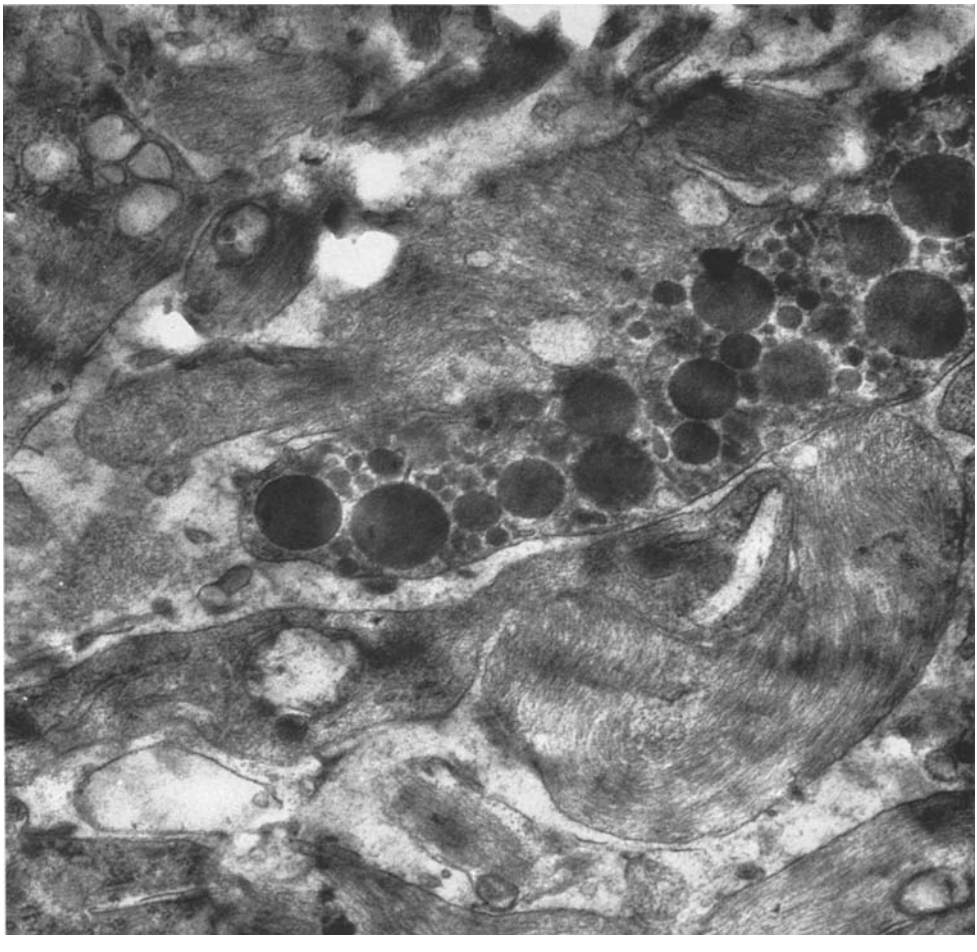

Fig. 4. Characteristic of the Rosenthal fibres-forming cell is the presence of osmiophil bodies in the cytoplasm, which in some cells completely fill the cellular cytoplasm. × 6750

The presence of osmiophil bodies appears to be a characteristic of this type of cell, first noted by Hossmann and Wechsler (1965) and also confirmed in tissue cultures (Gullotta and Fliedner, 1972). The presence in small amounts of osmiophil bodies is a feature of mature glial or tumoural cells, as well as of any other cell with an intense proteinogenetic activity.

In the case of Rosenthal fibre-forming cells the abundance of osmiophil bodies becomes striking, evidently expressing deviation of the protein metabolism. Lending support to this point of view is also the transformation of the mitochondria in these formations and the presence of degeneration phenomena at the level of the small filamentous structures.

As regards their relationship with the Rosenthal fibres, the osmiophil bodies do not take part in the formation of the osmiophil masses deposited between the fibres,

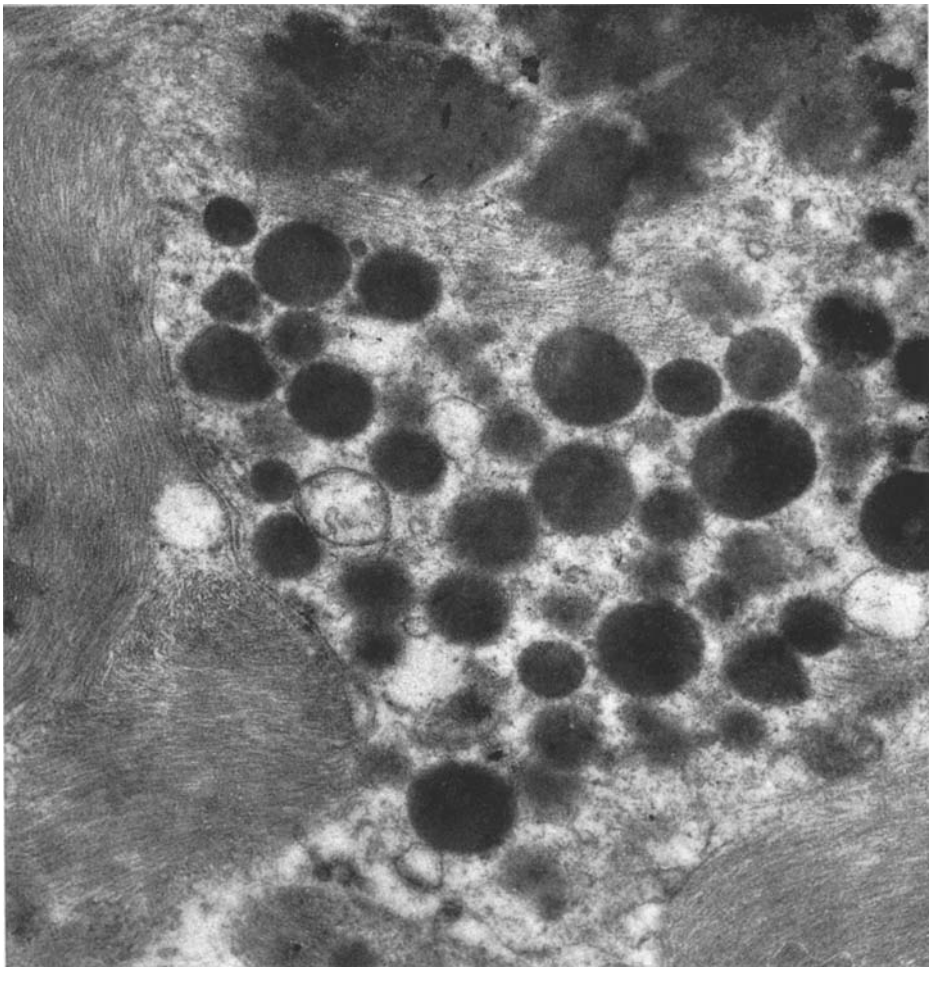

Fig. 5. Next to the osmiophil masses and osmiophil bodies in the basal cytoplasm note the presence of a degenerated mitochondria. × 12000

the two processes actually being two separate dystrophic phenomena that occur in the cytoplasm of the same cell.

In all the cases studied by us the way in which the Rosenthal fibre-forming glial cell appears seems to be a process constantly linked to the activity of the subependymal glia; a phenomenon first described by Zülich (1959).

The conditions under which the Rosenthal fibre-forming cells develop seem to be met with, on the one hand, in tumours with a starting point from this subependymal glia, and, on the other ,in a glial proliferative process developing subependymally around a series of pathologic processes. In our cases these appear to have been the following:

A. Craniopharyngioma associated to gliosis with Rosenthal fibres in 2 cases. This association was also reported by Hallervorden (1961) and by Russell and Rubinstein (1971) and more recently by Ghatak, Hirano and Zimmermann (1971) in the electron microscope. Worthy of note in our cases is that Rosenthal fibres only developed when epithelial inclusions developed in the nervous parenchym, in which case glial fibrosis with Rosenthal fibres forms a veritable stroma around the epithelial formations. B. In 4 cases of malformations of the 4th ventricle and 2 of intramedullary cysts, Rosenthal fibres appear in the subependymal area around the malformed tissue. In the other cases of internal hydrocephalus of nonmalformative origin no Rosenthal fibres were found in the subependymal gliosis.

In all these cases the basic process was evidently a dysplasia. In 3 cases the basic disease had a different character: subacute nodular meningoencephalitis, chronic meningoarteritis probably of syphilitic origin and diffuse intraventricular metastases of a melanoblastoma. In case 2 it may be seen that the Rosenthal fibres developed in the ependymal granulations as reported by Opalski (1934) in a case of cerebral cysticerosis and by Dietzel and Rottman (1958) in a tb meningoencephalitis.

A more detailed study in the first case revealed dysraphism of the 4th ventricle ependyma, gliosis, with Rosenthal fibres being present only at this level. In the other 2 cases, Rosenthal fibres were also made evident in the pineal gland that did not exhibit a tumoural or inflammatory invasion but presented a series of dysraphic ependymal cysts. This demonstrates that neither in these 2 latter cases does the formation of Rosenthal fibres appear as the expression of a reactive glial fibrosis but is related to a preexisting characteristic of the local, glial system. The association of the Rosenthal fibres-forming process with dysraphism was also emphasized by Hallervorden (1961).

From these data it may clearly be seen that Rosenthal fibre-forming gliosis accompanies malformative lesions characterized by embryonic discontinuity of the ependymal epithelium, a process also concomitantly affecting during the foetal life the normal development of the subependymal glial tissue. The embryonic glia described by Bergstrand (1932, 1937), arrested in its normal development, will give rise to falsely differentiated dysplastic elements, manifested structurally by elongated cells with a spongioblastic character, next to other cells with nuclear anomalies and finally others resembling the embryonic glia (cells with a round, clear nucleus.) The cellularity of Rosenthal fibre-forming gliosis is another characteristic of this process which pleads for its intense activity, and makes it at times so difficult to differentiate a purely reactive subependymal process from a tumoural-proliferative one (Russell, and Rubinstein, 1971).

Ultrastructurally, the formation of Rosenthal fibres and osmiophil bodies represents the ultrastructur specific of the dysplastic glial cell as compared to the normally differentiated astrocyte.

On the basis of these we consider that the term of spongioblast given to the Rosenthal fibre-forming subependymal cell is the most suitable since it is a fibrillo-forming dysplastic cell, standing at the basis of a series of processes characterized by a cellular malfomation with a tendency to lent proliferation (as Gliadysgenesien mit blastomatösem Einschlag described by Bielschowsky) today called phacomatosis (Kissel and Dureux, 1963).

In relation to the apparently primary and diffuse subependymal Rosenthal fibre-forming spongioblastosis a question arises concerning its relationship to the subclinical form of Alexander's disease. Thus, Tihen (1972) found in a case of central pontine myelinosis an obviously independent process, developing diffusely, subependymally, with Rosenthal fibres. The author rightly speaks in his case of a subclinical form of Alexander's disease.

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