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The Fine Structure of Meningiomas: An Attempted Classification

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Summary. We examined 23 meningiomas by electron microscopy. In each case it was possible to distinguish certain cells with epithelial features (desmosomes, microfilaments, interdigitating extensions) and others with fibroblastic features (collagen fibers). Others cells of transitional form were also seen. The proportion of these cellular types is variable, making it possible to classify meningiomas into seven types progressing gradually from a purely epithelial type to a purely fibroblastic one. – We found no important ultrastructural abnormalities in the cells.

These case reports confirm the uniqueness of meningiomas, which are composed of variously shaped cells but have their origin from a single cellular type. This has double potentiality for fibroblastic and epithelial differentiation.

Key words: Meningioma – Ultrastructure – Classification.

Introduction

The term meningioma has been widely accepted since Cushing (1922) used it to delineate a group of tumors arising from the meninges, or more accurately from the leptomeninges. They are benign tumors which are slow growing and may be found anywhere in the meninges. Their microscopical appearances are characteristic; more or less spherical masses which are well demarcated and whose diameter usually lies between 1 and 5 cm. More rarely plate-like forms occur. The tumors are extraparenchymatous and adherent to the dura mater. By light microscopy, meningiomas show very varied features. This polymorphism results from variability in the shape and size of the cells, their organisation, their vascularity and finally to the presence of secondary structures including pigment, and calcium, etc. This diversity is closely linked to the large number of proposed classifications.

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The results of a number of studies suggest that three schools of thought exist on the classification of meningiomata.

1. Those who consider there are two main types, fibroblastic and endotheliomatous.

2. Those who consider that there is only one type, with variable differentiation of the component cells.

3. Those who consider that there is only one type with variable histological arrangement of the component cells.

Methods

After surgical removal, each tumor was minced into small fragments. Some pieces were fixed with glutaraldehyde (4%) in phosphate buffer (pH=7.4) followed by osmium tetroxyde (1%) in the same buffer. After araldite embedding the sections were cut with a Reichert ultramicrotome; semithin sections were stained with toluidine blue and viewed through a light microscope; thin sections were stained by uranyl acetate and lead citrate (Reynolds, 1963) before electron microscopic observations (Philips EM 200). For routine histological examination other fragments were stained with hematoxylin and eosin.

Case Reports

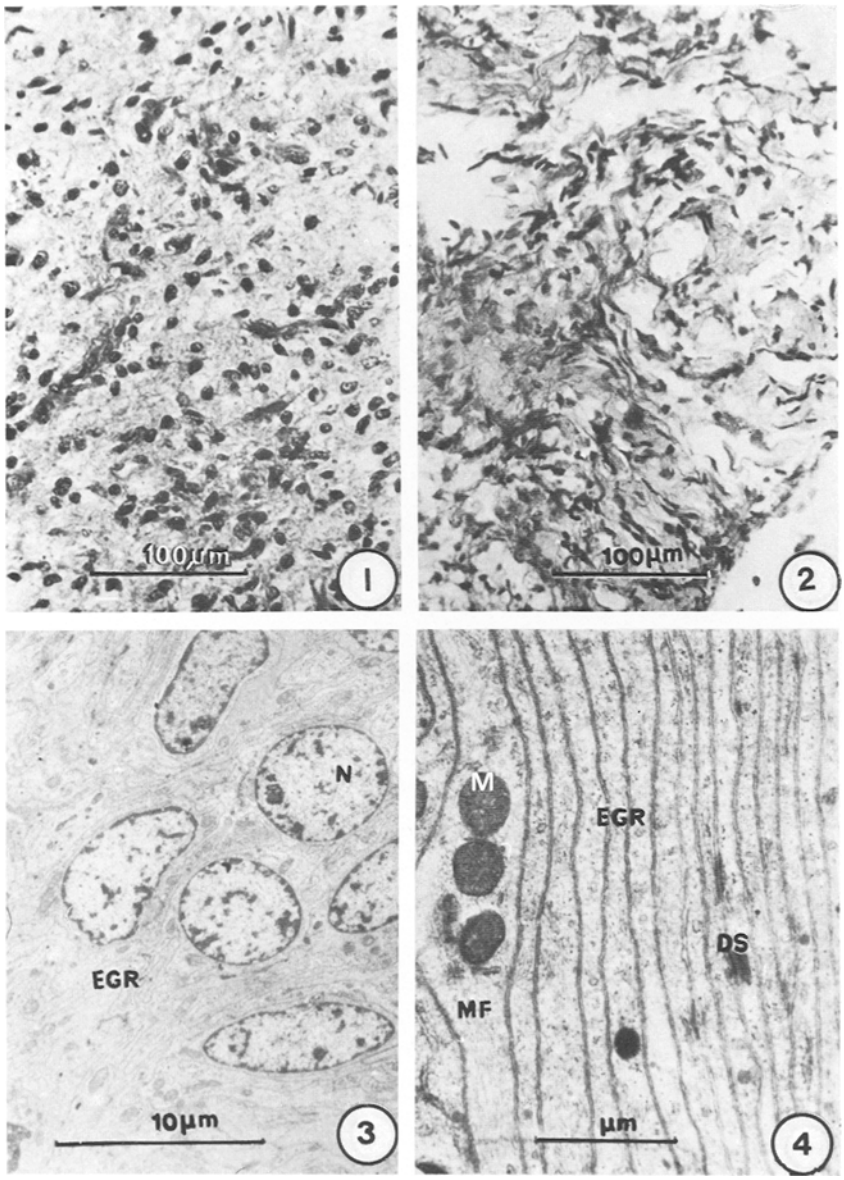
After electron microscopic studies, it is obvious that these tumors (23 meningiomas were observed) are not homogeneous. Some of them are endotheliomatous, others fibroblastic; the difference is sometimes clear-cut on light microscopy (Figs. 1 and 2). At a low or medium magnifications on the electron microscope all tumors appear to have different histological organisation; high magnification shows that the cells have a homogeneous ultrastructure, regardless of their origin.

1. Histological Organization (Apparent With Low and Medium Magnification)

We encountered many different patterns of cellular organization. These usually occupied the whole sample but were occasionally only a few hundred micrometers in diameter. Several of these patterns were found in the same meningioma (Table 1). Graduations between purely epithelial and purely fibrous arrangement are described below, in seven stages.

a) Type 1: Purely Epithelial Pattern (Figs. 3 and 4). With a low magnification, the ovoid or rounded nuclei do not seem to be bounded by plasma membranes. However, we discovered that these cells are characterized by a very complicated outer shape. Lamellary extensions 1 to 2 μm thick from surrounding cells intermingle with the perikaryon, which is 10 to 15 μm in diameter, thus producing a folded effect. All of these complicated folds are very tight, and between them there is only the minimum intercellular space observed in an epithelium (roughly 200 Å). Desmosomes spanning these folds link each cell with the next, a well defined epithelial characteristic.

b) Type 2: Purely Epithelial Pattern (Fig. 5). Here the cells are clearly visible individually; their outline is sinuous but their general shape is more or less



DS Desmosome, *EGR* Cell invagination, *MF* Microfilaments, *M* Mitochondria, *N* Nucleus

Fig. 1. Light microscopy: an endotheliomatous or syncithial meningioma (× 250)

Fig. 2. Light microscopy: a fibroblastic meningioma (× 250)

Fig. 3. Type 1: epithelial cells with rounded nucleus and interdigitating cytoplasmic limits (× 3,500)

Fig. 4. Detail of the same field: A mass of processes containing microfilaments linked by desmosomes (× 20,000)

Table 1

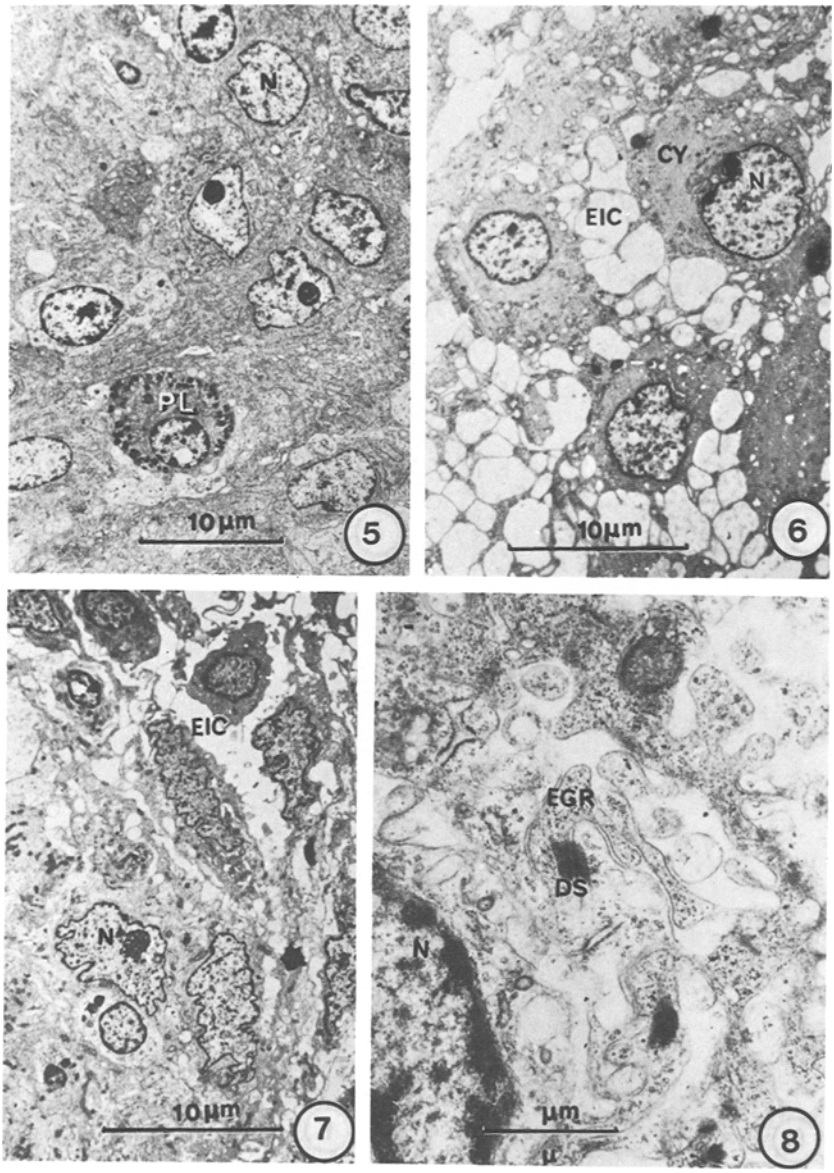
Meningiomas	Epithelial				Fibroblastic		Transitional
	1st type	2nd type	3rd type	4th type	5th type	6th type	7th type
1	+	++	−	−	−	−	+
2	+	+	−	+	−	−	+
3	++	++	−	−	−	−	+
4	−	−	++	+	−	−	−
5	−	−	−	+	++	+	−
6	++	+	−	+	−	−	+
7	+	++	−	−	−	−	+
8	−	−	++	+	−	−	−
9	++	+	−	−	−	−	−
10	−	−	−	+	+	++	
11	+	+	−	+	−	−	−
12	−	−	−	+	+	+	−
13	+	++	−	+	−	−	+
14	−	−	−	+	+	+	−
15	−	−	−	−	++	+	−
16	−	−	−	−	++	+	−
17	++	+	−	+	−	−	+
18	++	+	−	+	−	−	−
19	+	−	−	++	−	−	−
20	−	−	−	+	+	++	−
21	−	−	−	+	+	+	
22	+	++	−	+	−	−	+
23	−	−	−	+	+	+	−

polygonal. They are roughly 15 μm. The extensions present in the preceding type are generally no longer observable. As in Type I, the cells of type 2 are also joined by numerous desmosomes.

c) Type 3: Purely Epithelial Pattern (Fig. 6). These cells are uniform in size (15 μm), are either rounded or polyedral, and are separated by widened spaces (3 or 4 μm) filled with flaky matter and irregularly crossed by filiform cytoplasmic streams. They are linked together by desmosomes which are localized on the cytoplasmic processes, thus reshaping the appearance of the intercellular bridges of the Malpighian system. However, the accuracy of these observations can be questioned because of the possibility of fixation artefact. If an artefact is present, it is only observable in these particular cellular zones.

d) Type 4: Uncertain Epithelial Pattern (Figs. 7 and 8). The cells are elongated, the outline of their nuclei is more indented, and in particular the intercellular spaces are considerably widened (from 5 to 10 μm). They are traversed by irregularly shaped cytoplasmic streams (as in type 3) but are bounded by fewer desmosomal junctions than in the previous types.

e) Type 5: Fibroblastic Pattern (Figs. 9 and 10). The elongated cells (from 30 to 50 μm) have spindle shaped nuclei. The intercellular spaces are much



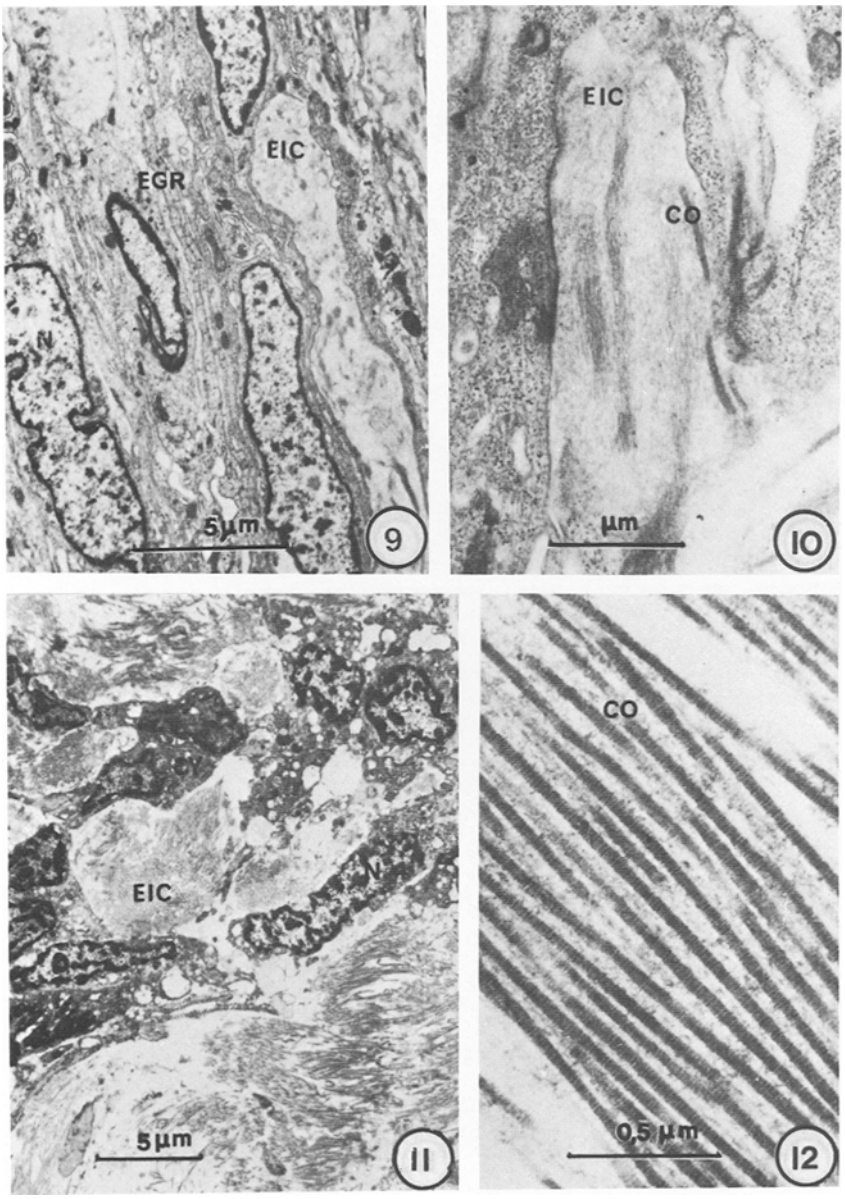
CY Cytoplasm, *DS* Desmosome, *EGR* Interdigitating cytoplasm limit, *EIC* Intercellular space, *N* Nucleus, *PL* Polyedric cells

Fig. 5. Type 2: Polyedral cells, clear cells and a plasma cell (×2,500)

Fig. 6. Type 3: Epithelial cells separated by large areas and bounded by fine cytoplasmic processes (×3,000)

Fig. 7. Type 4: Elongated epithelial cells with more or less indented nuclei and separated by large areas (×3,500)

Fig. 8. At high magnification, desmosomes and invagination of lateral cell surface (×20,000)



CO Collagen, *EGR* Cell invaginations, *EIC* Intercellular spaces, *N* Nucleus

Fig. 9. Type 5: Spindle shaped fibroblastic cells with inter-cellular spaces as in Fig. 8 (×5,500)

Fig. 10. The same type: Intercellular spaces with tropocollagen and collagen fibers (20,000)

Fig. 11. Type 6: Elongated fibroblastic-like cells and intercellular spaces with prominent collagen (×3,500)

Fig. 12. Detail of the preceeding field. Abnormal cross banding of mature collagen (period of 1,200 Å) (×55,000)

larger, occupying at least the same area as the cells. They contain collagen fibers but disorganized tropocollagenous fibers predominate. No desmosomes can be seen.

f) Type 6: Fibroblastic Pattern (Figs. 11 and 12). Fibroblast-like cells can be seen: spindle cells without connection, floating in very abundant intersitial tissue rich in collagen.

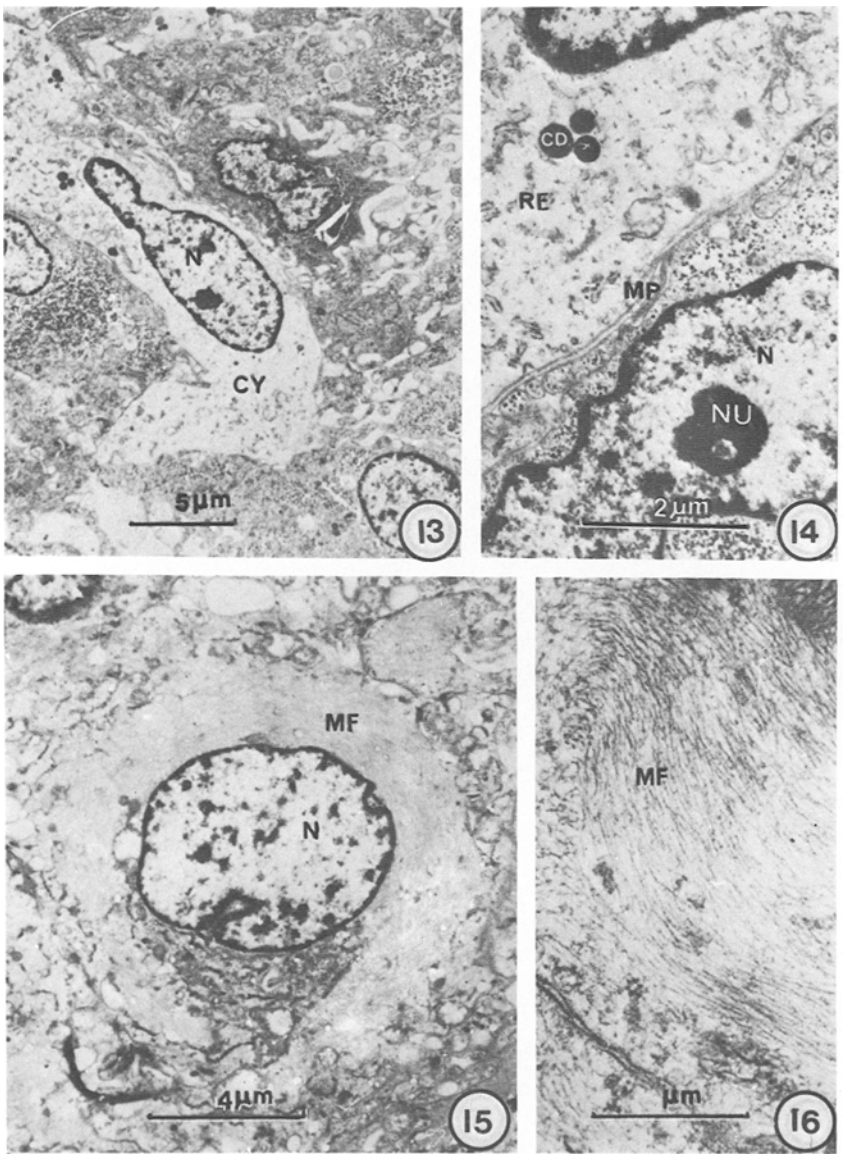
g) Type 7: Scattered Cells With Transitional Features (Figs. 13 and 14). We have previously described homogeneous cellular patterns using a gradation or a comparison of similar characteristics. The stranded cells of type 7 are clear and scattered among cells of endotheliomatous type. It is worth studying them as a special case since they exhibit epithelial features (well defined cell boundary and interdigitating extensions) but have no desmosomes.

2. Detailed Fine Structure (High Magnification)

The tumor cells contain the usual organelles. We have paid particular attention to the microfilaments, desmosomes and the cilia. These characteristic features of epithelial cells vary in the cellular categories we have studied. Other organelles seem to be numerically constant in all cellular types.

a) Epithelial Characteristics. In endotheliomatous meningioma, all the cells contain some microfilaments, and some are completely filled with them (Fig. 15). These microfilaments which are from 40 Å thick and several micrometers long, are clumped focally into bundles (Fig. 16). We found them in every area of the cytoplasm, the cell body, and processes (when present) regardless of how thin they are. The increased in microfilaments is sometimes so marked that they push away all the other organelles toward a small part of the cytoplasm. Many microfilaments are found in the first three patterns described, there are less in the fourth. Conversely, in the last two types (6 and 7) fibroblast-like cells do not contain microfilaments (Figs. 17 and 18) except in sections very near the plasma membrane where they are tropocollagen fibers. Clear cells encountered in endotheliomatous meningiomas have few cytoplasmic microfilaments (Figs. 21 and 22). High mignification is required to distinguish them, they are less numerous and not clumped in bundles.

The Desmosomes (Fig. 23). The first three types contain many desmosomes but there are less in the fourth. These desmosomal junctions may be found on the lateral boundaries and processes of the cells. They are small (0.5 μm) and almost always poor in microfilaments, which run parallel to the plasma membrane. They do not exhibit any singular fine structure, and do not appear in fibroblastic types where the cells are not in contact. The clear cells which adhere to other epithelial cells bear interdigitating cytoplasmic extensions, but lack desmosomes completely (Fig. 21).



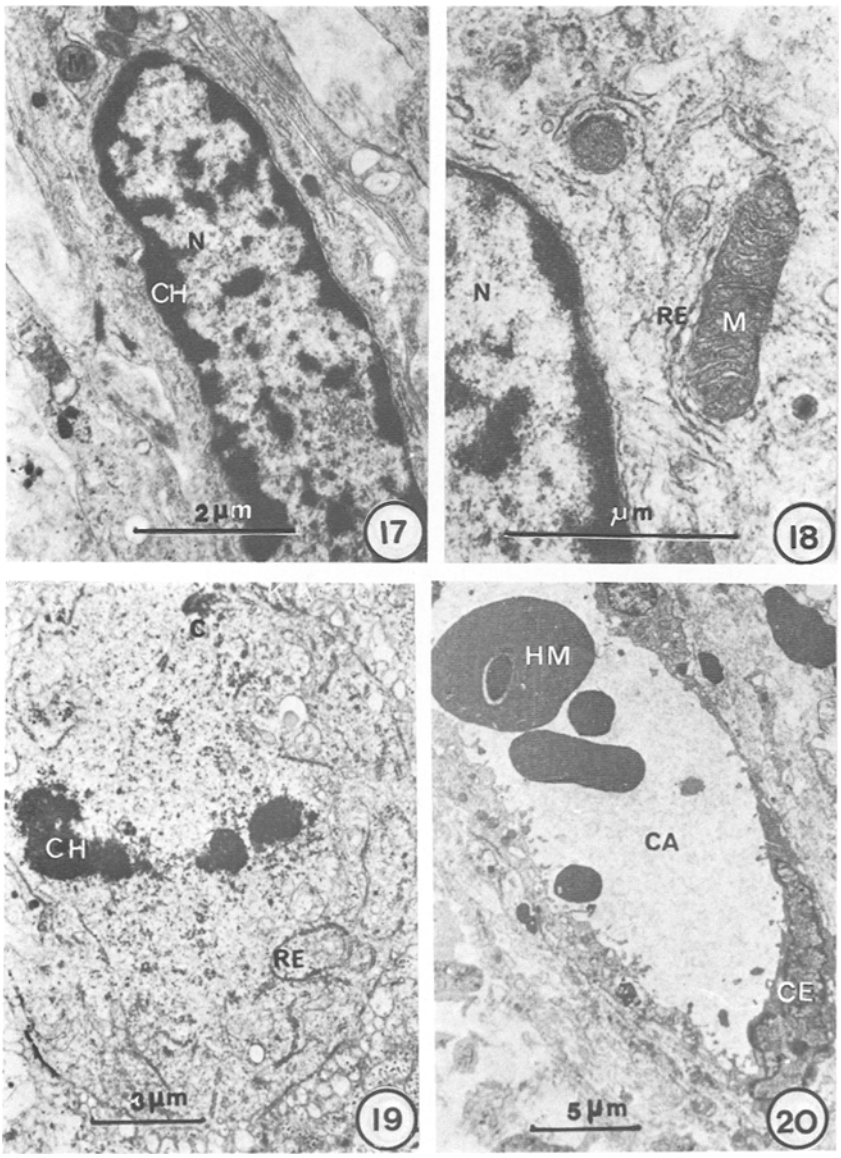
CD Dense bodies, *CY* Cytoplasm, *MF* Microfilaments, *MP* Plasmic membrane, *N* Nucleus, *NU* Nucleolus, *RE* Endoplasmic reticulum

Fig. 13. Type 7: Clear cells in endotheliomatous meningioma (× 3,500)

Fig. 14. Detail of cellular junction with invaginations of plasma membranes of adjacent cells (× 12,000)

Fig. 15. A mass of microfilaments in a cell of endotheliomatous meningioma (× 7,000)

Fig. 16. At high magnification, bundles of microfilaments in the same cell (× 50,000)



CH Chromatin, *M* Mitochondria, *N* Nucleus, *RE* Endoplasmic reticulum, *C* Centriole, *HM* Erythrocyte, *CA* Canal, *CE* Endothelial cell

Fig. 17. A cell of a fibroblastic meningioma lacking microfilaments (× 12,000)

Fig. 18. Detail of the same cell with mitochondria and endoplasmic reticulum (× 40,000)

Fig. 19. A mitotic figure: some metaphasic chromosomes and a centriole (× 6,000)

Fig. 20. A section of a typical capillary without abnormalities (× 3,000)

The Cilia (Figs. 24 and 25). These small organelles, found in the depth of the cytoplasm, are seen in the first four histological groups (endotheliomatous) but are not very numerous (on a section, one cell per hundred possesses a cilium). They may be normal, each cilium containing two central microtubules surrounded by nine triple ones, or atypical, in which case it is the number of microtubules which is abnormal. Basal bodies and striated rootlets can be seen in each cilium. We have not found cilia in the fibroblast-like cells or the clear cells.

b) Fibroblastic Characteristics. The form of the cells (typically spindle-shaped with processes) found in type 4, is a fibroblastic characteristic. Loose connective areas with collagen characterize the fifth and six types. Some of the atypical collagen fibers formed have a periodicity of 1,200 Å, instead of the 640 Å characteristic of normal fibers. It is possible that the intracytoplasmic fibrillary structure of these cells may represent tropocollagen macromolecules. Characteristics of epithelial differentiation are absent.

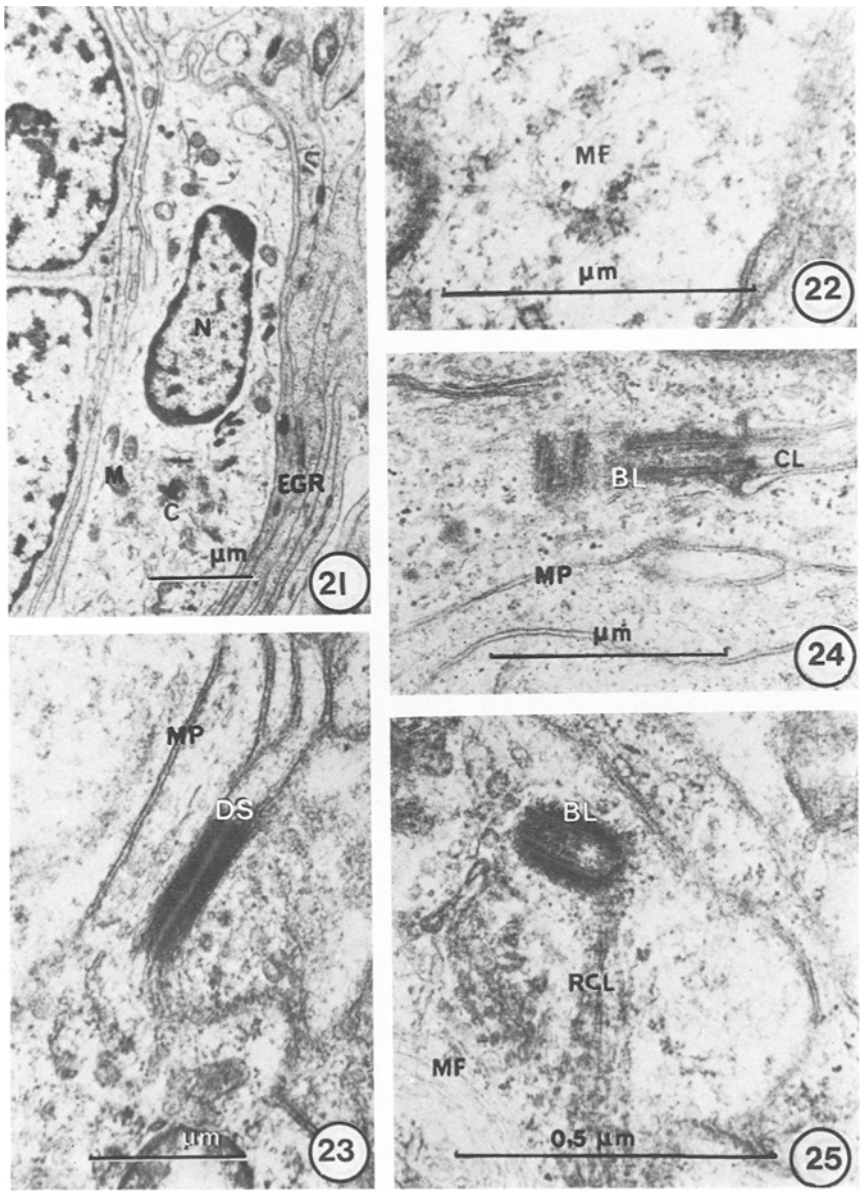
c) Other Organelles. Most of the organelles of all the cells are normal. The mitochondria, which may be reduced in number, are of normal size (roughly 1 μm) and thread-like or rounded (Fig. 18). There does not seem to be any difference between the cells of endotheliomatous meningiomata and those of the fibroblastic meningiomas in the number and the shape of the mitochondria. The Golgi apparatus, with the usual flattened saccules surrounded by minute vesicules, are also reduced in numbers (Fig. 26). No difference is seen between the different types. The endoplasmic reticulum and the ribosomes adhering to the outer surface of this limiting membrane are also few in number (Fig. 18). Fibroblast-like cells seem to contain more than other cells, clear cells have almost none. Glycogen-granules are frequently seen in epithelial-like cells (Fig. 27) and their paucity characterizes fibroblastic cells. Glycogen-granules where present are normal (200 Å) and often grouped in rosette-like aggregates.

Dense bodies from 500 Å to 1,000 Å in diameter, limited by a membrane occur in all the cells, perhaps in greater number in the endothelial cells. These bodies are probably lysosomes (Fig. 28).

The centrioles are normal and never multiple.

d) Possible Abnormalities. The meningiomas show few abnormal organelles. Some mitochondria (among many hundred observed) are atypical showing paucity of the cristae and the occurence of a central dense inclusion, which is more or less tubular (Fig. 29). Cristalloid-like inclusions can be found in the cytoplasm but only in small numbers. In reality these are bundles of microfilaments, often fitted into a notch in the nuclear envelope (Fig. 30).

In the nuclei some complex bodies can be seen (Fig. 31). Monstrous cells are rare and in some instances their numerous processes (Fig. 32) tightened with collagen aggregates suggest macrophage-like features. They are, perhaps, giant cells (40 μm at least) whose nuclei contain some membranous inclusions suggesting the beginning of cell death (Fig. 33).



BL Basal body, *C* Centriole, *CL* Longitudinal section of centriole, *DS* Desmosome, *EGR* Intercellular spaces, *MF* Microfilaments, *MP* Plasmic membrane, *N* Nucleus, *RCL* Rootlets

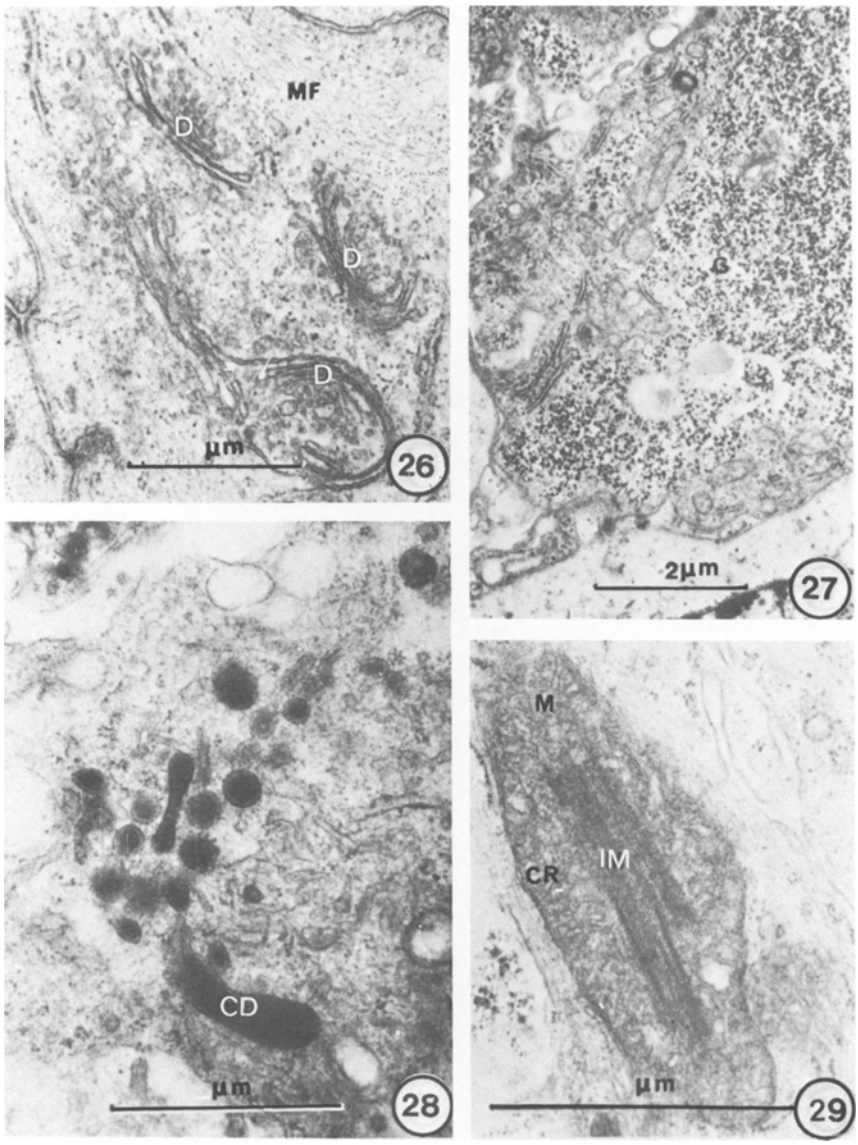
Fig. 21. A clear cell (× 8,000)

Fig. 22. At high magnification: in the same cell, some microfilaments (× 50,000)

Fig. 23. Desmosomal junctions of endotheliomatous meningioma (× 50,000)

Fig. 24. Longitudinal section of a cilium in a endotheliomatous meningioma (× 40,000)

Fig. 25. Section of a basal body and striated rootlets in the same meningioma (× 50,000)



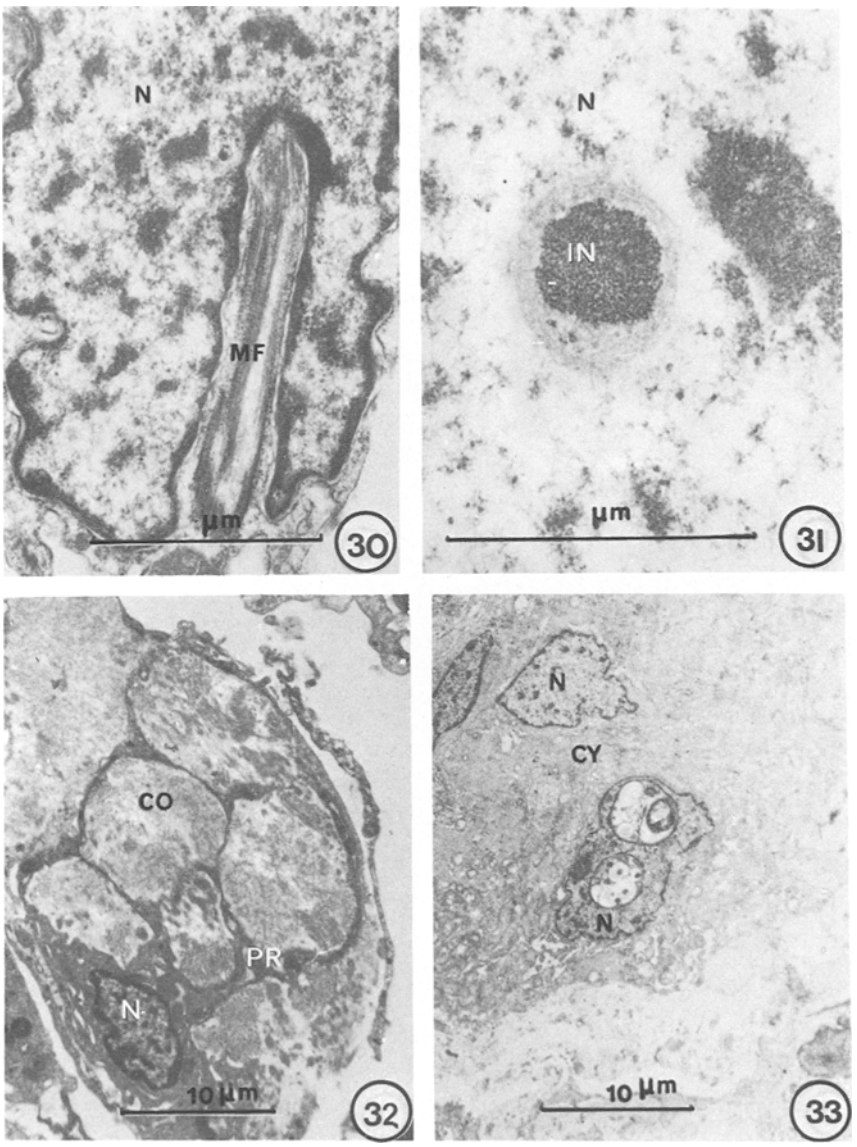
CD Dense bodies, *CR* Cristae, *D* Golgi apparatus, *G* Glycogen, *IM* Inclusion, *M* Matrix, *MF* Microfilaments

Fig. 26. Flattened saccules of Golgi apparatus (× 30,000)

Fig. 27. Granules of glycogen in an endotheliomatous meningioma (× 12,000)

Fig. 28. Dense bodies (Lysosomes) in an endotheliomatous meningioma (× 40,000)

Fig. 29. Abnormal mitochondrion (× 50,000)



CO Collagen, *CY* Cytoplasm, *IN* Nuclear inclusion, *MF* Microfilaments, *N* Nucleus, *PR* Processes

Fig. 30. Bundles of microfilaments clumped in an invagination of the nuclear envelope (×40,000)

Fig. 31. Nuclear inclusion (×50,000)

Fig. 32. A monstrous cell with several processes (×2,500)

Fig. 33. Multinucleated giant cells with nuclear inclusions (×2,500)

e) Mitosis (Fig. 19). Few mitotic figures can be observed (between one per 1,000 or one per 10,000). They look typical and under the electron microscope no modification of the microtubules, shape or density of the chromatin or the nuclear envelope can be seen.

f) Vascularisation (Fig. 20). The capillaries of the meningiomas do not seem to be modified significantly.

Discussion

We have addressed ourselves to the problem of whether the multiplicity of types of meningioma observed in the light microscope is significant. A preoccupation with nosology is linked to the histogenesis of these tumors. They have also been suggestions that the tumours may become malignant.

Light Microscopic Data

Using light microscopy, the following classifications have been suggested:

– Basing his studies upon structure, Del Rio Hortega (1934) separated diffuse nodular and lamellar meningoexotheliomas. Globus (1937) took embryological data into consideration and classified meningiomas into leptomeningiomas and dura mater fibroblastoma. Bailey and Bucy (1931) acknowledged nine types of meningiomas: mesenchymatous, meningotheliomatous, angioblastic, psammomatous, bony, fibroblastic, fatty, melanoblastic and sarcomatous types. Cushing and Eisenhardt (1938) counted up to 20 sub-groups, which Courville (1945) simplified and reduced to five groups: syncytial, fibrous, transitional, angioblastic and sarcomatous types. Lapresle et al. (1952) retained only three types: syncytial, fibroblastic and mixed. These authors considered that the angioblastic variety must be classified among the hemangioblastomata and that the sarcomatous variety may possibly become malignant.

– Russel (1959) agreed with the five types proposed by Courville. Light microscopy enabled her to distinguish three types:

Syncytial or endotheliomatous
Fibroblastic
Transitional or mixed.

These various studies also showed that these different types could coexist in the same tumor and that the presence of secondary structures (bony, pigmentary, lipid) could be superimposed. It was not possible to distinguish the angioblystic variety from the hemangioblastoma nor to solve the problem raised by the malignant sarcomatous variety.

Ultrastructural Data

Through the electron microscope, certain authors (Raimondi et al., 1962; Koinov et al., 1964) described two kinds of meningioma; one made up of endothelial-like cells with all their distinctive characteristics (desmosomes, microfilaments), the other whose structure is fibroblastic (spindle-shaped cells not connected to each other and with intercellular spaces containing collagen fibers). Other authors (Leventhal, 1959; Gonatas et al., 1963) came to the conclusion that there was a single group of meningiomas in which the two types of cells, endotheliomatous and fibroblastic, co-exist.

The majority (Kepes, 1961; Napolitano et al., 1964) suggest that there is only one cell type which is able to take either an endothelial or a fibroblastic appearance and which may show both forms within the same meningioma. The presence of cells of intermediate type provides an argument in favor of this kind of polymorphism (Guseck, 1962).

From our observations, we can support previous assertions that several types of histological arrangement can be seen together in any one meningioma, from the purely epithelial type to the purely fibroblastic type. We find all possible intermediary forms between epithelial cells and the fibroblastic cells (Table 1). It is surprising that we find transitional forms between epithelial and fibroblastic cells, however, there are findings supporting the uniqueness of the tumor cells of the meningioma. The first of these is the occurence of transitional types and the variability of histological organisation. Cultures of meningiomas quickly become fibroblastic whatever their initial arrangement (Costero et al., 1955). The mixed embryological origin of the leptomeninges may also be important (Escourolle and Poirier, 1971). It has been known for a long time that the leptomeninges will only form in the presence of the neural crest (Harvey et al., 1926); hence the term "ectomesenchymatous" used to describe this tissue. Moreover, the cells of the normal leptomeninge are of several types (mesothelial cells, cells of the perineural layer (Klika, 1968)).

Electron micrographs of meningiomas demonstrate a changeable picture ranging from purely epithelial to purely fibroblastic types, depending of the variable differentiation of a single cell. As to the possibility of these tumors becoming malignant, we did not find any ultrastructural abnormality (mitotic features) to provide an indication of this change, however (Fabiani et al., 1977) have described atypical mitoses in so called malignant meningiomas. Lastly, the monstrous cells previously described could be macrophages and might result from fusion of mononuclear phagocytes by a similar process to that seen in granulomas (Chambers, 1978).

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