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K.-JOACHIM ZÜLCH and J.-DOMINGO TOLEDO y UGARTE

TUMORS OF THE NERVOUS TISSUE

LIST OF DIAGNOSES AND DISCUSSION OF CASES

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K.-JOACHIM ZÜLCH (*) and J.-DOMINGO TOLEDO y UGARTE (**)

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PREFACE.

Prior to the discussion of isolated cases there are some introductory remarks, which seem necessary to us.

Pathology of tumors of the nervous system is not any more an occult science, a special field of a few centers of investigation. There are two main reasons for this statement:

1) The existence of a sufficient description of the different types of tumors of the nervous system.

2) The big development of neurosurgery, which provides with specimens of this kind the general Departments of Pathology, which are no more limited to the cases of p.m. examination, as they were some time ago so that they perform this field of pathological work in every days routine work.

The pathologist, on the other side, must furnish a diagnose which enables the neurosurgeon to a prognose and to an adequate treatment. Therefore, we need a classification of tumors of the nervous system which can be understood and employed in the same way by both, pathologist and neurosurgeon or clinician. This would be not only a source of better understandig in clinical work, but also of welfare for the patient, and this is our most important task.

There are two essential conditions for a useful classification:

1) A sufficient description of the morphological features of each type of tumor, demonstrated by methods usually employed in a general Laboratory of Pathology.

This description must deal about the most common morphological appearance of each type of tumor, but also with its possible variations in site and morphological aspects.

2) The main task of the pathologist in the practice is to help the clinician and the surgeon. A morphological classification of tumors of the nervous system must correspond to a clinical entity, and must furnish an information about the prognose of the disease.

(*) Neurological Clinic, Städtischen Krankenanstalten, Köln – Merheim, Germany.
(**) "Santo Hospital Civil del Generalissimo Franco", Bilbao, Spain.

There are three main lines in the Bibliography on this topic for establishing a classification of tumors of the nervous system:

1) An histogenetic classification, as performed by Spanish and French schools.

2) A classification with a special clinical scope, based on morphological appearances, and stressing the importance of anaplasia in different types of tumors, with consideration of a " grading " of some of them.

3) A classification which considers morphological, histogenetic and clinical aspects, as it was stated by Bailey and Cushing (1926 and following) and which has been accepted with slight modifications by many authors.

The UICC (Unio Internationalis Contra Cancrum) organized in Cologne (1961) a Symposium for achieving a generally valid classification in an attempt to find a common language, which could be understood by everybody, and which would represent a good startpoint for further research work on this field.

The classification adopted supposes an evolution of the classification of Bailey and Cushing, and of Zülch, with some stress on the topography of the different types of tumors. (Table 1). The tumor Atlas of the UICC contains examples of each kind of these tumors within a work including all kind of human tumors.

Zülch and Wechsler are preparing a more comprehensive Atlas, based on this classification, with an extensive iconography of usual and less usual pattern of tumors of the nervous system, and with text in six languages (english, french, german, spanish, russian and japanese) which could become a very useful tool for this work of classification.

There is another interesting point stressed by Kernohan: the biological " grading " of tumors of the nervous system for a more accurate prognose.

Zülch has adopted this idea with a slight but very interesting modification. He accepts the four grades, but states that *not every tumor has all four grades* but only *two or three*, may be even only *one grade*.

He states—as well as Kernohan and other authors—a correlation between histological type and life expectancy (Tables 2 and 3).

Tumors of grade one may show a survival time of 5 years and more, even a radical cure.

Grade two shows a period of three to five years free of symptoms.

Grade three, one to three years.

Grade four under six months until fifteen months.

Irradiation is not effective in the two first groups but should be recommended in the groups three and four.

All this statements have only a limited value within the rules of statistic dispersion. Also, the decision of classification within one grade and the next one depends rather often on the subjective appretiation of the pathologist. Nevertheless, it should be only a problem of deciding between grade I or II, or II and III, but never between I or III, or I or IV.

TABLE I.

Tumors of nerve tissues and associated structures.

I. NERVE CELLS.

1) Ganglioneuroma
Gangliocytoma
Ganglioglioma
2) Ganglioneuroblastoma
Malignant gaglioneuroma
Malignant ganglioglioma
3) Sympathicogonioma
4) Sympathicoblastoma
Neuroblastoma

II. NEUROEPITHELIUM.

5) Epithelial ependymoma
6) Papillary ependymoma
7) Cellular ependymoma
8) Malignant ependymoma
Ependymoblastoma
9) Papilloma of choroid plexus
Plexuspapilloma
10) Olfactory neuroepithelioma

III. EYE.

11) Medulloepithelioma of ciliary epithelium
Diktyoma
12) Neuroepithelioma with true rosettes
Retinoblastoma with true rosettes
13) Neuroepithelioma without true rosettes
Retinoblastoma without true rosettes
14) Malignant melanoma

IV. GLIA.

15) Fibrillary astrocytoma
16) Protoplasmatic Astrocytoma Gemistocytic astrocytoma
17) Astrocytoma of the nose Nasal glioma
18) Oligodendroglioma
isomorphous
polymorphous
19) Multiform glioblastoma
20) Spongioblastoma
Polar spongioblastoma
isomorphous
polymorphous
21) Medulloblastoma

V. PERIPHERAL AND CRANIAL NERVES.

22) Neurinoma
Neurilemmoma
Schwannoma
23) Neurofibroma
24) Malignant neurinoma
Malignant neurilemmoma
Malignant schwannoma

VI. MENINGES.

25) Epithelioid meningioma
Meningotheliomatous meningioma
Endotheliomathous meningioma
26) Fibroblastic meningioma
Fibromatous meningioma
27) Psammomatous meningioma

VII. VASCULAR STRUCTURES OF CENTRAL NERVOUS SYSTEM.

28) Hemangioma of cerebellum. Von Hippel–Lindau's disease. Hemangioblastoma

VIII. PARAGANGLIA.

29) Non-chromaffin paraganglioma
Carotic body tumor
Glomus caroticum tumor
Chemodectoma

IX. PINEAL GLAND

30) Pinealoma
anisomorphous
polymorphous

X. HYPOPHYSIS.

31) Diffuse chromophobe adenoma
32) Sinusoidal chromophobe adenoma
33) Papillary chromophobe adenoma
34) Oxyphilic adenoma
35) Papillary oxyphilic adenoma
36) Basophil adenoma
37) Craniopharyngioma
Adamantinoma of the craniopharyngeal duct
38) Chromophobe carcinoma.

TABLE II.

Modified grading for tumors of the brain and related structures.

TUMORS	Grade I benign	Grade II semibenign	Grade III semimalignant	Grade IV malignant
GANGLIOCYTOMA				
isomorphous	+	+		
polymorphous			+	
EPENDYMOMA				
isomorphous	+	+		
polymorphous			+	
PLEXUSPAPILLOMA				
isomorphous	+			
polymorphous			+	
ASTROCYTOMA				
isomorphous		+		
polymorphous			+	
OLIGODENDROGLIOMA				
isomorphous		+		
polymorphous			+	
GLIOBLASTOMA				+
SPONGIOBLASTOMA				
isomorphous	+			
polymorphous			+	
MEDULLOBLASTOMA				+
PINEALOMA				
isomorphous	+			
anisomorphous		+		
polymorphous			+	
NEURINOMA				
amitotic	+			
polymitotic			+	
MENINGIOMA				
amitotic/oligomitotic	+			
polymitotic			+	
ANGIOBLASTOMA (Lindau)	+			
SARCOMA				+
PITUITARY ADENOMA				
isomorphous	+			
polymorphous		+		
CRANIOPHARYNGYOMA	+			

This " grading " would give to us a further basis for increasing our experience on this field of biology of tumors of the nervous system, and will enable us to compare results, specially in cases treated with new method (Cobalt-therapy, intraarterial perfusion etc.).

We find most important to individualize sufficiently each type of tumor, so that we can state anatomo-clinic entities which deserve the practice of medicine.

TABLE III.

Classification of brain tumors and their different degrees of malignancy.

DEGREE OF MALIGNANCY	PROGNOSIS AFTER " TOTAL " REMOVAL	TUMORS	
		EXTRACEREBRAL	INTRACEREBRAL
GRADE I BENIGN	Cure or at least survival time of 5 and more years.	Neurinomas Meningiomas Pituitary adenomas Craniopharyngiomas	Gangliocytomas (temporo-basal) Ependymomas of the ventricles Plexuspapillomas Spongioblastomas, isomorphous Angioblastomas (Lindau) Pinealomas, isomorphous
GRADE II SEMIBENIGN	Postoperative survival time: 3 to 5 years.	Pituitary adenomas, polymorphous.	Gangliocytomas (other localizations) Ependymomas (cerebral) Astrocytomas, isomorphous Oligodendrogliomas, isomorphous Pinealoma, anisomorphous
GRADE III SEMI–MALIGNANT	Postoperative survival time: 3 to 3 years.	Neurinomas, polymitotic. Meningiomas, polymitotic.	Gangliocytomas, polymorphous Ependymomas, polymorphous Plexuspapillomas, polymorphous Oligodendrogliomas, polymorphous Spongioblastomas, polymorphous Pinealomas, polymorphous
GRADE IV MALIGNANT	Postoperative survival time: 6–15 months.	Sarcomas	Glioblastomas Medulloblastomas Primary sarcomas

Other academic questions are more a subject of investigation, which can have some day a traduction in this practice, but which are nowadays a field for special research centers.

Most important achievements on morphology of the glia and pathology of glial tumors have been reached by means of silver methods on frozen sections. They are most important for demonstration of special structures. Nevertheless, we propose the systematic use of paraffin sections for general Laboratories of Pathology dealing with surgical specimens, since they warrant an easy and safe manipulation of small piece of tissue, or of not consistent

material, and on the other side, there are sufficient methods on paraffin sections, even of silver methods, which enable us to an accurate diagnose. Only if there is sufficient material and time to spare, then it could be recommended to perform frozen sections and special methods of silver or gold impregnations for demonstration of special structurs.

For the diagnose, we consider, in each kind of tumor, from the histologic point of view:

a) Cellularity.

b) Size and shape of the cells. Signs of anaplasia.

c) Special structures characteristic to each kind of tumors. Relation to blood vessels.

d) Vascular pattern by means of a silver impregnation on paraffin section (Gomori), and eventually, pattern of reticular fibers.

1) *and 2*) (*Institute of Pathology. Bilbao*), *R. P., male. 3 yr.*

Clinical history. – Three years old boy with an abdominal tumor of progressive growth during two months. Big mass at the left kidney region. Anemia (3.000.000 red blood cells). Eosinophilia (10%) B.S.R. 35/66. After one week, 4.000.000 red blood cells and 2% eosinophils.

Urography. – Big tumor displacing considerably the left kidney.

Treatment: Cobalttherapy (2.000 r.) and subsequently Genoxal before surgical operation.

Operative findings. – Large tumor including the upper pole of the left kidney, with many enlarged lymph glands.

Clinical diagnosis: Wilm's tumor.

Case nº 1 and 2, I.P.B., B. 680.685.

There are two slides of the same case. The operative specimen weighed 780 g. including both kidney and a big tumorous mass with a lobulated surface, which induced the surgeon to think, he was dealing with lymph nodes. The tumor was not localized within the kidney, but attached to its hilus, and after separating them, the kidney proved to weight only 90 g. as it corresponds to a child. The mass was rather firm in its consistency and showed a fasciculated, intermingling structure on the cut surface. In some areas there are zones of red colour and fleshy appearance.

Microscopically there were no characteristic changes at the parenchyme of the kidney. The tumor, itself, shows two quite different patterns mixed at random in its whole extension and impossible to differentiate one from another without the aid of the microscope.

The first of them corresponds to some polygonal fields demarcated by very slender connective septa, which support capillary vessels of very thin endothelial walls. Within these fields we see a tumor tissue very rich in cells with scanty cytoplasm and rather small, dark nuclei. Among them are some big, hyperchromatic nuclei, and mitosis, even with multipolar appearances,

are present. In the middle of some of this small fields there are amorphous amounts of calcium. A fairly rare feature of this part of the tumor is the existence of some ganglioid-lookings cells, with large, rather pale nuclei, only one nucleolus per nucleus, and a considerable amount of cytoplasm. Sometimes there are two nuclei within a cell but no more than two. In spite of this appearance, we were not able to demonstrate neurofibrils nor Nissl substance within their cytoplasm.

In some areas, we see an interstitial hemorrhage of variable intensity within these structures.

The second main pattern of the tumor corresponded to a proliferation of fascicles of Schwann's cells, which include some groups of well differentiated nerve cells of the type of vegetative ganglia. The staining with cresyle violet shows Nissl substance within their cytoplasm and the impregnation with silver methods shows the existence of neurofibrils within the cytoplasm and of true nerve fibers within the tubes constituted by the Schwann cells. Only few of these tubes were with a myeline sheath.

We find in this second pattern of the tumor the most common appearance of well-differentiated gangliocytomas of the peripheral nerve system. In our experience, it is the first case with this coincidence of well differentiated parts together with highly anaplastic fields, with some isolated cells which resemble not yet differentiated neuroblasts.

Differential diagnose should be considered against a well differentiated gangliocytoma and against a malignant sympatoblastoma. The existence of both patterns in our case should provide our diagnose as a:

Malignant ganglioneuroblastoma
Grade IV.
Irradiation recommended.

In this case, as in every other case of tumors of nervous tissue, localized outside the craneal cavity, a something better prognose is to be expected, because of the possibility of eradication of the whole organ, site of the tumor. Nevertheless, we use the same biological "grading" we should have used for a tumor with the same grade of anaplasia, localized within the craneal cavity.

Follow up. – Heart stop during operation. Recuperation with hearth massage, calcium chloride and Alupent intraventricular. No recuperation of consciousness: decerebration and death, ten hours after operation.

3) (*Max–Planck–Institut. Cologne*), *D. H., male. 9 yr.*

Clinical history. – Since three and a half weeks ago, strong headaches, and something later vomiting without relation to food ingestion, with rapid loss of weight. He leaved the school because of the headaches. Four days ago, admittance into the Medical Clinic.

Clinical diagnosis. – Tumor of the posterior fossa. The patient was transferred to the neurosurgical clinic for further study of the case and surgical intervention, if indicated.

Surgical macroscopic diagnosis. – Growth of about 5 cm. of diameter, situated in the fourth ventricle, and apparently implantated on its roof and in the cerebellar vermis, extending itself backward to the cerebellar tonsil, considerably enlarged and compressed into the foramen magnum. This compression was doubtless the cause of the forced head position to the left, as an effort of the little patient to improve the tonsil impression.

A sure, macroscopic, differential diagnosis is not possible. The very short clinical history suggests a medulloblastoma. The macroscopic appearance corresponds to an ependymoma.

Case nº. 3), M.P.I.C., E. 6497.

Tumor with a rich density of isomorphous cells, with rather scanty eosinophylic cytoplasm and oval shaped nuclei. Mitoses have not been seen. There are two characteristic patterns in this tumor:

1) The presence of true tubes and rosettes, surrounded by a single layer of cells of cubic appearance. There are pseudoependymal tubes, characteristic of this tumor.

2) A radiated disposition of tumor cells around capillary vessels of single wall, with moderate thickening of its reticuline, with fibrillary differentiation of the basal part of the cytoplasm, more evident in the Heidenhein's haematoxyline stain. In the HE stain this basal part of the cytoplasm has a clear eosinophilic appearance, in form of perivascular clear zones, characteristic for this kind of brain tumor. There is also a loosening of the cellular structure in the parts of the tumors more distant to the vessels, showing in this way a characteristic pattern of " gliovascular systems ". In these loosened parts we see also a net of glial fibers.

We have here a benign tumor—cellular isomorphism and lack of mitosis —which could correspond exactly with the description of Masson for the " ependimoglyomes ", and it does not represent the most characteristic form of the group, in which we include this case, the ependymomas.

There is none special difficulty for differential diagnose. The localization in the 4th ventricule suggests already the diagnose. Lack of mitosis and presence of true tubes and rosettes are clearcut criteria for the differentiation from a Medulloblastoma.

Diagnosis. – Epithelial Ependymoma.

Grading. – I.

Irradiation. – Not recommended.

Follow up. – The little patient tolerated well the operation, and liquor flow through the aqueduct and 4th ventricle because quite normal. Without recidive one year after operation.

4) (*Max-Planck-Institut. Cologne*), *H. M., male. 31 yr.*

Clinical history. – Ten months ago, dizziness with spontaneous recovery. Five months ago, clinical treatment because of hypertension and headaches. Two months ago, visual disturbances with blurred vision. Ophthalmoscopic examination: papillar stasis.

Radiologic diagnosis. – Ventriculography: suspicion of tumor of cerebellar vermis.

Macroscopic surgical diagnosis. – Tumor of orange size, with many vessels covering the surface, situated at the romboid fossa, at the region of the calamus scriptorius. Some papillary figures were seen after a thorough examination. A complete excision of the tumor was impossible at the zone of the medulla oblongata.

Chorioid plexus papilloma.

Case nº. 4), M.P.I.C., E. 5906.

We are dealing here with a tumor with an exquisite, homogeneous papillary structure, with slender connective-vascular cores which support a single row of cuboidal cells, with medium sized eosinophylic cytoplasm and round or oval shaped isomorphous nuclei; only exceptionally isolated mitosis have been found. We don't find any goblet cells.

The localization of the tumor and its structure make unnecessary a differential diagnosis. It is however interesting to point out the age of the patient, 31 years. Commonly these fairly rare tumors (about 0,50 % in the statistic of Zülch) appear within the first decade of life.

Diagnosis. – Chorioid plexus papilloma.

Grade. – I.

Irradiation. – Not recommended.

5) *(I. P. B.), J.L.M., male. 2 yr.*

Clinical history. – Two months ago, a white reflex was observed at the right iris, confirmed on ophthalmoscopic examination, which discovers a white, roud bulk at the temporal periphery, with plenty of exudate in the vitreus. Ocular pressure is 18,5 mm Hg. in both eyes (normal). The left eye is quite normal.

Clinical diagnosis. – Retinoblastoma.

Case nº. 5), I.P.B., B. 1130/66.

The whole posterior wall of the eye cavity shows a complete disappearance of the normal retina, which is substituted by a tumorous tissue very rich in cells with dark, round nuclei and scanty cytoplasm. There are not very numerous capillary vessels with a single reticulin layer. The tumour cells show a well preserved structure around the capillary vessels, with transition to areas of necrobiosis in the parts between two different vessels in the middle region. We don't find rosettes. There is no infiltration of the sclera.

We are dealing with a malignant tumor of the eye chamber. A differential diagnose should be considered with the other variant of the same type, the retinoblastoma with true rossettes, but both of them show the same biological malignancy.

Other eye tumors, as the malignant melanoma are easily discarded because of the round nuclei and lack of pigment of the case we are dealing

about. The diktyoma or medulloepithelioma of the ciliary epithelium is a tumor very rare, localized in the anterior part of the eye chamber, with an easily recognizable relation to the cyliary body, and shows a more teratoid pattern with a greater mensenchymal component, appearance of cysts, cartilage, and several mixed structures, some of them quite similar to the retinoblastoma pattern, but not forming the whole of the tumor.

Diagnosis. – Retinoblastoma without true rosettes.

Grade. – IV.

Irradiation. – Recommended.

Follow up. – This is another instance of the dissociation of grading in cases outside the craneal box. In spite of the great dedifferentiation of this tumor, the little patient had a right eye protesis and a left eye quite normal, two years after the operation. Lack of invasion of the sclera and of the optic nerve show to be very important for a better prognosis of the case.

6) (*M. P. I. C.*), *E.G., female. 25 yr.*

Clinical history. – Generalized cerebral cramps attacks, first with loss of consciousness, afterwards without. Headaches and hemilateral manifestations.

Radiologic diagnosis. – Angiography suggests a left fronto-temporal tumor.

Surgical findings. – Left front-temporal tumor which overrides the incisura sylviana including completely the group of the a. cerebri media. Cyst in the frontal part of the tumor, which shows otherwise a rubbery consistence and lack of vessels. It was tried to excise the whole tumor in both areas, preserving the group of the a. cerebri media.

Surgical macroscopic diagnosis. – Left fronto-temporal astrocytoma.

Case nº. 6), M.P.I.C., E 6041/66.

We are dealing here with a tumor with rather poor cellularity and considerable amount of interstitial substance in form of glial fibers. Among them, in the peripheral zone, some nerve fibers can be demonstrated by means of specific methods. Tumor cells have a round, isomorphous nucleus and an inapparent cytoplasm. The nuclear chromatine is not very compact, but we see another kind of cells with a rather smaller nucleus with darker chromatine. In metallic impregnations the cells show a clear field at the place of their nuclei, suggesting their nature as oligodendrocytes. There are not very numerous capillary vessels with a single wall. Mitoses have not been observed.

Ther is no doubt about the glial nature of this cells. The main type can be classified as fibrillary astrocytes and the second one as oligodendrocytes.

Here we have the question of the differential diagnose. It is easy to differentiate in this case between a fibrillary and a protoplasmic astrocytoma. The rather poor cellular density, the rubbery consistence, the predominant component of fibrillary differentiation make easy this diagnose. The pre-

sence of some oligodendrocytes evokes the question of the " Mischglyom ", of the mixed glioma. It is not rare to find some different kind of glial cells within a tumor. Nevertheless, we can always distinguish a predominance of one type and a general pattern of the tumor which enable us to a clearcut diagnose after the old principle " ex potiori fit denominatio ".

Considering this case, with the oligodendroglioma as alternative, this last kind of tumor is very rich in closely packed cells, and we discover always in different parts, the honeycombed appearance which is considered as characteristic for this group.

In this tumor number six, none of these characteristic patterns of the oligodendroglioma have been observed.

A malignant degeneration is very easy to be discarded. We found neither a rich cellularity, nor nuclear atipias, nor mitoses, nor exhuberant vascular appearances, which are characteristic for the glioblastoma.

Diagnose. – Fibrillary astrocytoma.

Grade. – II.

Irradiation. – Not recommended.

Follow up. – Excision of the vena sylviana during operation, with impairment of the general condition of the patient, almost equivalent to the section of the group of the cerebri media. A post-operative paresis has been observed, with survival of the patient the first months after the operation. Still under control.

7) (*M. P. I. C.*), *W. J., male. 28 yr.*

Clinical history. – Since four months ago, headaches accompanied by nauseas and vomiting. Admission into the Neurosurgery six days ago. One day later, apathic, somnolent condition, which turned soon to a deep loss of consciousness, which could not be improved in any way by dehydratant therapy.

Arteriography. – Signs of a tumor in the left frontal lobe, with fine, pathologic, tumor vessels in a round zone of 5 cm. diameter. (A scintillogramm previously performed had given a positive result in this region)

In order to evacuate a fluid content of a possible cystic tumor and to produce in that way a cerebral decompression, an intratumoral puncture was performed three days after admission. The drill came into a cystic cavity, whose evacuation conditioned the sudden awakening of the patient.

This clearance of consciousness continued during three days, and at that time a surgical intervention was performed.

Surgical macroscopic diagnosis. – Growth about 7 cm. in diameter, rather poorly vascularized, which infiltrates widely the left frontal lobe.

Case nº. 7), M.P.I.C., E. 6838.

Tumor with middle cell density, with a predominant disposition of the elements around the capillary vessels which show a reduplication of their reticulin cover. In some of them, perivascular cystic cavities can be seen, but in the most cases, the cells attach cytoplasmic prolongation in the form

of sucker feet to the vessel wall. Tumor cells show a plump, eosinophilic cytoplasm, with several prolongations, some of them connected, as already mentioned, to the vessel wall. The nuclei are excentric, round or oval shaped, something irregular in shape. Mitosis have not been observed.

We are dealing here with a very well defined type of glial tumor, with big cells with several cell processes around a wall. This kind of tumor corresponds to the so-called " astroblastoma " by Bailey and Cushing (s. also Masson), but nowadays there is not a remarkable reason for separating this group from the protoplasmic astrocytomas, since its cells belong to this kind of them, and we can be glad about every name which disappears rendering more simple our schema of classification.

A differential diagnose against the fibrillary astrocytomas is not worthy to be mentioned extensively. There is not a fibrillary interstitial substance and tumor cells are rich in cytoplasm.

Lack of mitosis and of bizarre vascular pattern, as well as the loose disposition of tumor cells differentiate these structures from those of a glioblastoma. It has been recorded that malignant astrocytomas arise more frequently from this group than in the other groups of astrocytoma in case of incomplete resection, but this statistic matter of fact does not enable us to classify actually this tumor as malignant or semimalignant.

The type of cells of this tumor is quite similar to the bizarre glial cells appearing in the tuberous sclerosis, but we find here a clear tumor arrangement instead of the interstitial appearance of them in the tuberous sclerosis.

Concluding, we classify this tumor as a protoplasmatic astrocytoma, we could add the qualification of gigantocellular or gemystocitic as a subvariety, but we consider obsolete the term of " astroblastoma ", since we don't find a quite clear embryologic explanation for it, and the biological behaviour corresponds to that of a cytoplasmatic astrocytoma.

Diagnose. – Protoplasmatic (gemystocytic) astrocytoma.

Grade. – II.

Irradiation. – Not recommended.

Follow up. – One day after the operation, progressive loss of consciousness, with right midriasis, irregular breathing, fever up to 40° C. and arterial pressure up to 190 mm Hg. The E. E. G. curve suggested a left intracraneal hypertension, and one could suppose a postoperative bleeding as its cause. Reintervention the same day after percutaneous aspiration of 50 c.c. of blood in two occasions within this same day. Epidural coagulated bleeding, 2 cm. thick and tumefaction of the whole left frontal lobe and surrounding structures. This picture was followed by death of the patient in the early morning of the next day.

8) (I. P. B.), V.C., male. 37 yr.

Clinical history. – After one year, focal crises of the right limbs with subsequent progressive right hemiparesis, of crural predominance, accompanied by subjective impairmen of sensibility on this side. Lately headaches. No family nor personal antecedents.

Exploration. – Right spastic hemiparesia with crural predominance and sensibility disturbances, manifested by a right hemi-hipo-algesia. No signs of endocraneal hypertension.

Angiografic diagnosis. - Downward deviation of the peri-callosal artery in the parietal region. No filling of temporal vessels.

Clinical diagnosis. – Left parietal tumor.

Surgical macroscopic diagnosis. – Tumor of the upper area of the left parietal lobe. Glioma, possible oligodendroglioma.

Case nº. 8), I.P.B., B. 569/65.

Macroscopically we found a round tumor of some 8 cm. in diameter, soft consistence and a white colour with some dark spots after the fixation. The cut surface shows a white substance with small red, haemorrhagic spots.

Microscopically, tumor with a very rich cellularity. The nuclei are round or slightly oval shaped, isomorphous, and no mitoses have been observed. In some areas, quite distinct patterns of honeycombs appear very clearly. The vascularization shows some capillary vessels of lacunar type, with partially hialinized walls, whereas in other fields they show just a common single wall and no dilatations of their lumina. There are some small cysts and interstitial haemorrhages, but no calcifications were present.

At the marginal zone of the tumor, some rests of nerve fibers can be observed, whereas it is impossible to demonstrate them in the central part. The limit with the surrounding cerebral tissue is formed by a barrier of gemystocytic astrocytes, with a dense glial network among their cell bodies.

We are dealing, therefore with a tumor of glial nature, very rich in cells, some of them with a clear honeycombed picture, with a rather slow rate of growth, with cyst formation and with a limiting barrier of ameboid glia.

We can easily put the diagnose: Oligodendroglioma. There is no question of malignancy of the tumor, because of the isomorphism of their nuclei, lack of mitosis, and " quiescent " appearance of the blood vessels. A malignant glioblastoma can be discarded. We have discussed elsewhere the question of mixed gliomas, and within this tumor we find, indeed, some cells with an astrocytic character. Nevertheless, we find a very typical honeycombed disposition of tumor cells, and the specific impregnation for oligodendroglía (after MELLER) shows most of the tumor cells to belong to this type. The marginal, ameboid glia can be considered as a reaction of the surrounding tissue to the tumoral growth.

If we consider the clear appearance of cytoplasm in the honeycombed zones, a doubt could arise concerning the differentiation from the so-called hypernephroma, or clear cell carcinoma from the kidney. In this one we found an epithelial disposition of tumor cells in rows over slender connective-vascular cores. Somewhere, we find pseudoglandular cavities. The cells are more irregular poliedric, haemorrhages are more prominent and a fat staining show both mono—and birefringent lipoids, which are not be found at the oligodendroglioma.

A rather characteristic feature of this kind of tumors is lacking in this case: the presence of small calcifications, which can orientate the diagnose but which are not quite specific of this type of gliomas.

Diagnose. – Isomorphous oligodendroglioma.

Grade. – II.

Irradiation. – Not recommended.

Follow up. – Patient without clinical disturbances three years after the operation.

9) (*M. P. I. C.*), *F.W., female. 48 yr.*

Clinical history. – Headaches since 3-4 years. Nine months ago, attacks of parestesia of the left hand. Fourteen days before admission to the clinic, appearance of weakness at the left hand, and eight days afterwards of the left leg, too. Neurologic findings: left spastic hemiparesia.

Clinical diagnosis. – Right parietal, well-vascularized, probably malignant tumor.

Surgical macroscopic diagnosis. – Glioblastoma multiforme.

Localization at the operation. – White substance of the right parietal lobe.

Arteriographic diagnosis. – Pattern of peripheric vascular flow, about the size of a prune, with slight stasis of the regional vessels, at the right parietal zone. One sees only significant marginal opacifications. A sure precocious venous pattern is not demonstrable.

Case nº. 9), M.P.I.C., E. 3.670

We are dealing here with a very cellular tumor composed by elements which show a clear honeycombed disposition. Some of them are radially disposed around the capillary vessels, which are very numerous, and which show sometimes a reduplication of their reticuline wall. No glomerular lacunar spaces, or network structures can be observed among this vessels. In some points, we see small necrotic areas surrounded by a palisading of tumor cells. The most characteristic feature of the microscopic appearance of this case is the presence of giant cells, with hyperchromatic, lobulated or multiple (up to 20) nuclei, in a size equivalent to four or five of the smaller cells are also observed. There are many mitosis, some of them multipolar. No calcifications have been observed.

There is no doubt about the malignancy of this case, revealed by the very acentuated cellular atypias and the presence of mitosis. The silver impregnation by the methode of MELLER show by the tumor cells the characteristic appearance of oligodendrocytes, with a clear nuclear field within a darker, silver loaded cytoplasma. This nature was already suggested by the honeycombed pattern of the tumor cells. Nevertheless, it is not the common picture of an oligodendroglioma, as we are used to see, but a different one. We are dealing here with the picture of a polimorphous oligondendroglioma.

Zülch has made of this tumor a field of research in spite of the fact that their existence as a different group is not accepted by many other authors. We shall point out now the facts, that enable us to make a differential diagnose from other kind of tumors.

First of all, we shall considere the malignant glioblastoma. The giant cells could correspond to the cells which are found in the polimorphous variant of the glioblastoma. But the other cells are different, and we don't see honeycombed structures nor a positive picture on MELLER's silver stain in the glioblastoma cells. Other important feature is the vascular disposition. Vascular changes, considered as changes of the tumoral stroma, are nevertheless considered as pathognomonic for the diagnose of a glioblastoma, when they are present in its full development.

Nothing of this has been observed in this case, but a fairly rich supply with capillary vessels of normal structure.

One of us (Zülch) points ont, that probably most of cases of malignant glioblastoma with a longer survival belong probably to this group, which was not considered as a diagnostic possibility.

Another differential diagnostic possibility would be the intracerebral ependymoma, because of the irradiated perivascular arrangement of tumor cells in a similar way as they are found in the ependymoma. Nevertheless, we never find such cellular atypias in this later one, and the honeycombed pattern and the silver stain are decisive features for separating both of them.

A differential diagnose from the metastatic clear cell carcinoma from the kidney could be made in the same way as in the isomorphous oligodendroglioma.

The bizarre giant cells are similar to those which are observed in the polymorphous sarcoma but the presence of the honeycombed pattern and lack of interstitial reticuline network in the silver stain are fairly sure criteria for differentiating them.

Diagnose. – Polymorphous oligodendroglioma.

Grade. – III.

Irradiation. – Recommended.

10) (*I. P. B.*), *J–M. L., male. 61 yr.*

Clinical history. – Craneal trauma, four years ago. Since six months, headaches, nightmares, hyperhydrosis, nervosity. Three months ago, one convulsive attack, with loss of consciousness, month foam, and involuntary micturition. Since two weeks, headache with occipital predominancy, loss of equilibrium, restlessness, delirium, confusion, amnesia, hyperbulia, rigidity, stereotypia, clonus, Babinski (+), tremor.

Evolution: Progressive impairment of the patient's condition and exitus.

Clinical diagnosis. – Astroglioma multiforme.

Case 10), I.P.B., B. 1434/66.

The macroscopic examination was performed in the whole brain after death. No permission for whole autopsy. Tumor about 5 cm. in diameter, localized subcortically at the basal right frontal lobe, protruding through the cortex, fairly well limited against the surrounding tissue, but without encapsulation. Soft consistence and alternating red and yellow zones on the cut surface.

Microscopically, tumor very rich in cells, which are rather uniform in size and shape, with an astrocytic appearance in some areas. Some other bigger cells, with evident eosinophilic cytoplasm, and excentric, lobulated or irregular nuclei are also seen. Mitoses are present, but not in overwhelming number. There are necrotic areas in the middle of the tumor mass, at the fields more distant to the blood vessels, forming sometimes the picture of perivascular crowns of preservated tumor tissue, surrounded by necrotic one. The PTAH show a clear astrocytic character of many of the tumor cells, and the Alcyan Blue stain show a beginning mucoid degeneration in the scarce intercellular substance, between the tumor cells.

A bizarre vascular structure can be observed all over the tumor: reduplicated capillary vessels, profuse network formation, appearance of glomerular patterns etc. Necrotic vessels and interstitial haemorrhages can also be found.

We are dealing, therefore, with a tumor rich in cells, with evident atypias, presence of mitosis and necrosis and a very prominent vascular growth. Our diagnose is malignant glioblastoma.

From the point of view, the differentiation of this tumor from the malignant astrocytoma is becoming obsolete. For the malignant astrocytoma plaided a longer clinical history, and the recognition of clear astrocytic zones, as they are seen in an astrocytoma, with other zones of malignant appearance, or the diagnose of malignancy in the histologic examination of a case, which previously proved to have been correctly classified as benign.

Electron microscopic studies have shown, that even in glioblastomas ab initio, the appearance of gliofibrils is a constant pattern. We cannot sustain, therefore, for a longer time the theory, the glioblastoma is a quite different kind of tumors that astrocytomas, and if we consider the possibility of progressive anaplastic changes in an astrocytoma, more or less rapid, so that they would be considered as glioblastomas from the very beginning, as in this case, or as astrocytomas with malignant change into a glioblastoma, from the point of view of the diagnostic praxis, we shall find blurred limits between the two kinds of malignant glial tumors from the type of glioblastoma, so that their differentiation becomes not so important at the end stage. On the opposite, it is still important to differentiate them from other groups of malignant tumors.

The differential diagnose from the polymorphous oligodendroglioma has been already discussed. The sarcoma show an interstitial reticuline network on the silver stain, which is not present in this case.

We do not believe, there is a relation of the origin of this tumor and the craneal trauma related in the clinical history, four years before the last complains.

Diagnose. – Malignant glioblastoma.

Grade. – IV.

Irradiation. – Would have been recommended.

11) (I. P. B.), M–C. M., female. 5 yr.

Clinical history. – Eighteen days before admittance to the clinic, otalgia and convergent strabismus of the right eye. Two days later, vomiting and pain on the right side of the neck. Eight days later, diplopia and urinary disturbances. From the very beginning staggering gait.

Family and personal histories without interest. Exploratory findings: convergent strabismus of the right eye. Right facial paresis. Ataxic walking. Neck stiffness. Bilateral Babinski. Slight right disdiadocokinesia.

Clinical diagnosis. – Syndrome of endocraneal hypertension produced by a tumor of the posterior fossa.

Radiological diagnosis. – Diasquisis of the sutures.

Evolution. – Exploratory craniotomy. Death within the postoperative course.

Surgical macroscopic diagnosis. – Tumor of the Brain Stem.

Case n°. 11), I.P.B., A. 68/64.

On the macroscopic examination, bulky tumor in the pons and body of the 4th ventricle, in the form of considerable thickening of these structures, at least double as much as it would correspond to a patient of this age. The aqueduct was obstructed with internal hydrocephalus of the first three cerebral ventricles and flattening of the giri and sulci and digital impressions on the inner side of the calotte.

Histologically we find a dissociation of the elements corresponding to this brain region by fusiform cells with elongated regular nuclei. Nerve cells and nerve fibers are conserved. We have been able to demonstrate Nissl substance and neurofibrils within the nerve cells, and nerve fibers by silver stain, and their myelin sheaths by means of the Luxol blue stain. The fibrae arcuatae are clearly recognoscible. The Alcyan blue method demonstrates the presence of a considerable interstitial amount of acid muchopolysaccarides. We find only few capillary vessels with a single wall. The PTAH shows the presence of thick, something tortuous fibers, which have been described as Rosenthal fibers, from the author who described them for the first time. These formation can be found in other conditions, such as productive inflammation of brain tissue, and are supposed to be degenerated glial fibers (Rosenthal, Hortega, Zülch). They are supposed to be originated from the subependymal glia, and are almost specific for this kind of tumor,

the spongioblastoma polare, which have been described as the most benign form of brain tumor, with very slow rate of growth, and conservation of pre-existing structure. Because of that, in our case symptoms were not present until 28 days before death, and this could be explained by the almost complete conservation of normal structures of the pons, which conserved their function in spite of their interstitial dissociation. Death was not caused by failure of the functions of pons and medulla oblongata, but by endocraneal hypertension. Here we are again before a frightful example, how a very benign tumor can have a fatal evolution when it implyes vital structures, which cannot be operated off, within the watertight box constitued by the craneal walls.

This tumor is common in children, and has been former described as " hyperplasia of the brain stem ", corresponding to the middle line.

Our diagnose is spongioblastoma polare. This entity has been discussed as such, and there are some authors, who see only a variety of the astrocytoma, conditioned by the disposition of the preexisting nerve structures. We believe, it can be separated from the astrocytoma group because of its biological, very benign behaviour, the site of presentation, their structure, and the presence of Rosenthal fibers.

We could consider the gangliocytoma from the point of view of differential diagnostic, but the nerve cells and fibers, which we found in these cases are quite differentiated and normal in their structure and arrangement, having only been infiltrated by elongated, isomorphous tumor cells. In the gangliocytoma we find different stages of differentiation of nerve cells, the pattern of nerve fibers is more scarce and irregular, and no Rosenthal fibers can be found.

A differentiation from the astrocytoma has already been discussed.

Diagnose. – Spongioblastoma polare.

Grade. – I.

Irradiation. – Would not have been recommended.

12) (*I. P. B.*), *J-M. P., male. 3 yr.*

Clinical history. – One year and a half before admittance, start of predominantly right visual disturbances. Diagnosis of primary optic atrophy. After eight months, progressive right paresia. Posteriorly, headaches and loss of vision in both eyes. No personal nor familial antecedents of interest.

Exploratory findings: Bilateral amaurosis with primary optic atrophy in both eye grounds. Right spastic hemiparesia, without sensibility disturbances.

Conventional radiologic diagnosis. – Diasquisis of sutures. Wide erosions around the optic foramina, and of the anterior and posterior clinoid processes of the sella turcica.

Ventriculografic diagnosis. – Symmetrical hydrocephalus internus, with upward deviation of the anterior part of the third ventricle.

Surgical macroscopic diagnosis. – Tumor of the chiasma opticum extending to both optic nerves and radicals.

Case nº. 12., I.P.B., B. 491/64.

Tumor with zones of middle and zones of dense cellularity. In some parts, the subdivision in fields from the optic radicals is still recognizable. The tumor cells are disposed in interlacing fascicles, and show oval, regular nuclei in size and shape, and some mitosis. There are some mucinous cysts. The PTAH stain shows some Rosenthal–fibers. The vascularly pattern is formed by a great deal of capillary vessels of some irregular distribution.

This case was examined first by one of us alone (Toledo, 1964). He had some difficulty in the classification, because the apparent paradoxe of the general histological features of the tissue, which corresponded to a glioma of the middle line in children—age was an important argument in the consideration —, that is to say, a spongioblastoma polare, on one side, and on the other side, to the cytological pattern, which corresponded to a proliferative tumor of glial nature. At that time, he considered the possibility of a differential diagnose with a malignant glioblastoma of the fusocellular sub-type. He thought, it could be a malignant spongioblastoma, although he did not know at that time about its existence.

During the discussion of cases with prof. Zülch he knew about this very rare possibility of finding this polymitotic, malignant spongioblastoma polare, which has been described very seldom.

Diagnose. – Spongioblastoma polare, polymorphous.

Grade. – III.

Irradiation. – Recommended.

Follow up. – Death two months after operation.

13) (I. P. B.), M-C. De., female. 12 yr.

Clinical history. – Vomiting since a year ago, intensified during last four days, accompanied with headaches. Right eye deviation. Difficulty in speach articulation. Stuporous condition. Slight temperature (0,3º – 0,4º C).

Slight neck stiffness. Babinski (+). Normal eyeground. Lazy patellar reflexes.

Urine examination: No glucose, no acetone, no albumine. Hemorrhagic CRL.

Impairment of general condition. Blood pressure, 12/7 – 14/8. In the final period, anisocoria with left midriasis and right miosis.

Clinical diagnosis. – Cerebral hemorrhage? Tumor?

Case nº. 13), I.P.B., B. 304/66.

The macroscopic examination showed an encephalus with a total weight of 1.440 g. with evident flattening of giri and sulci in both hemispheres.

Pressure deformation on both cerebellar hemispheres more accentuated on the right one.

On the surface of section cerebral structures without any alteration; on the section of the cerebellum, the 4th ventricle appears very enlarged and occupied by a red mass of jelly consistence, not adherent to the inferior wall and growing from the upper posterior one, at the level of the cerebellar vermis. It has a something irregular spherical shape, with a diameter of 4 cm.

It was allowed to perform only the head autopsy.

Microscopically we found a very cellular tumor which infiltrates more or less the different cerebellar lames, and which shows signs of interstitial haemorrhage in its intraventricular part.

Tumor cells are rather small, with not distinguishable cytoplasm and oval, carotshaped nuclei. Mitoses are very scarce. We have had to look almost anxiously in several different slides for finding a single one. This tumors cells are sometimes disposed in rows, sometimes in fascicles, sometimes without a recognizable disposition. At its periphery they show small proliferating buds, which infiltrate the white matter of the cerebellum. We find also some nerve cells included in the peripheral mass of the tumor. At the cerebellar cortex we see a substitution of the cerebellar granules by tumor cells, which are something bigger in size, and oval in shape, compared with the smaller size and round shape of cerebellar granules. After having infiltrated the molecular layer, the tumor cells begin to extend themselves over the subaracnoideal space.

We are dealing here with a very cellular tumor of aggressive behaviour against the surrounding tissues, in spite of the small number of mitoses. No differentiations of type of rosettes, tubes, or perivascular clear areas have been observed. These last features would have played for an ependymoma, which is the kind of tumor, that could be considered at this localization in a young patient. Instead of it, we are dealing with a medulloblastoma, a very malignant tumor of the posterior fossa in young age. The cellular type, its disposition, and the infiltrative pattern, extending itself along the subaracnoideal space are very characteristic. Not common for the medulloblastoma is the presence of an intratumoral haemorrhage, and it is exceptional the very small number of mitoses seen in this case.

There are many theories about the true nature or histogenetic origines of this tumor. The name suggest the origine from the primitive multipotent cell of the nervous system. Some authors claim for its nature as tumors of embryonic nerve cells, as they have been able to demonstrate neurofibrils in some cases by means of special silver stains. At the last time, Gullotta has insisted upon the mesodermic structures demonstrable in these tumours and he believes, they are not tumors of the nervous tissue but true sarcomas.

From the practical point of view, it is important to stress, that, independently of their histogenetic origine, and without taking a definitive position on this item, we want to stress that we are dealing here with a very clear-cut anatomo-clinic entity, as well in its age and site of appearance, as in its morphologic patterns, and that for practical purposes, this investigations should not modify the existence of this group as such, even if we admit, as in the

case of the spongioblastoma, that we use a term which does not any more correspond to the true histogenetic nature of the tumor, but which is worthy to be conserved, because its use is already accepted by most of pathologist, and to try to change it would lead to a great amount of confusion.

Diagnose. – Medulloblastoma.

Grade. – IV.

Irradiation. – Would have been recommended.

14) (M. P. I. C.), W.S., female. 42 yr.

Clinical history. – Three years ago, deafness of the right ear with inability to hear through the phone, and sometime later, absolute deafness. Since that time, dizziness, vomiting and instability, with a diagnosis of hepatic or intestinal disease with corresponding treatment. After the ophthalmoscopic diagnosis of bilateral stasis papillae with more than 5 diopters, the patient was transferred to the Neurologic Department, under suspicion of brain tumor. An arteriography of the carotid and vertebralis was performed, with extravasation of the most part of the contrast fluid and serious worsening of the patient's condition; recovery after two days, but patient lies somnolent and apathic, with an almost unintelligible speech.

Surgical macroscopic diagnosis. – Acoustic neurinoma of the right side.

Case nº. 14), M.P.I.C., E. 5573.

Tumor with a recognizable capsule in some parts of its periphery, formed by elongated cells with cigarette-shaped nuclei, with an interlacing-fasciculated pattern. Sometimes we find a beginning palisading of the nuclei but these features are not very prominent, and we do not find the so-called rosettes of Verocay. This part of the tumor, we are now describing is rather compact. With strong enlargement, we do not observe cellular atypias or mitoses.

Another areas of the tumor show clear cells, with an almost empty cytoplasm, and small, excentrical nuclei. There are fairly extense interstitial haemorrhages, which can be correlated in some cases to the bleeding vessel. The vascular pattern is something irregular: we find some enlarged capillary vessels with thickened, hyalinized wall.

The silver stain shows a dense network of argentofile slender fibers. Zülch had demonstrated some morphological differences from these fibers of this type of tumor against reticuline fibers. Wechsler has demonstrated by means of the electronmicrocope its identity with cellular basement membranes.

Our diagnose of this tumor is: neurinoma. Antoni has described two different types A and B, according to the predominance of the more compact, fasciculated form (A) or the vacuolated-cell appearance (B). We could classify this tumor within the group B, but it is to be said, that no biological nor clinical difference has been observed between both groups.

A differential diagnose could be considerated in the vacuolar cells, which could resemble those from the oligodendroglioma. There is a safe rule for differentiating clear cells from an oligodendroglioma from those from a neurinoma or even from an astrocytoma. In the oligodendroglioma, the honeycombed structure of its cells shows closed spaces, and the nuclei have an appreciable size and lie in the middle of the clear field. In the case of the neurinoma and the astrocytoma, the nuclei are something smaller, lie often excentrically within the clear fields or in the crossing point of two lines. Besides of that, we are able, with special stains, to demonstrate the presence of mono—and birefringent lipoids in the neurinoma, and of mucoid substances in the astrocytoma.

We could consider this case as a type Antoni B. After a total removal of the tumor one can expect a complete healing of the patient.

Diagnose. – Neurinoma.

Grade. – I.

Irradiation. – Not recommended.

15) (I. P. B.), M–T. R., female. 53 yr.

Clinical history. – Since eight years, slowly progressive chiasmatic syndrome, and, in the last two years, endocraneal hypertension. At the beginning of this condition, an operation was adviced and not accepted by the patient. At the moment of the actual examination, the endocraneal hypertension is considerable and the patient lies in coma.

Radiologic diagnosis. – Enlargement of the sella turcica with erosion of the clinoid processes.

Clinical diagnosis. – Tumor of the suprasellar region.

Angiographic diagnosis. – The same.

Surgical macroscopic diagnosis. – Meningioma of the tuberculum sellae.

Case nº. 15), I.P.B., B. 228/66.

Macroscopically we see several pieces of tissue from operation, the biggest one with diameters of 3,5 × 2,5 × 2 cm. Total weight, 35 g. White-pinkish colour and, on the section, surface subdivided in small nodes.

Microscopically we find a tumor tissue fairly rich in poligonal cells disposed in a laminated pattern, sometimes forming concentrical whorls. Mitoses have not been observed. The stroma is formed by slender connective septa which divide uncompletely the tumor in smaller alveoli or field of cells. The silver stain shows no penetration of reticuline fibers into these tumor fields. The vascularization corresponds to single capillary vessels. There are isolated spherular calcifications.

There is a rather easy diagnose, an endotheliomatous meningioma. Some authors have described as many as fourteen different types of meningioma, but we think, it is to complicate too much the classification.

Actually only three subdivisions are accepted: the endotheliomatous (or epitheloid, or meningiomatous) meningioma, the fibroblastic (or fibromatous) meningioma, and the psammomatous meningioma.

We are dealing here with the first subdivision type. The second one is characterized by the presence of collagenous and reticulin fibers all over the tumor, and the third one, by the presence of a great deal of spherular calcification. In happens in older women, most in the thoracic spinal cord.

A differential diagnose with other kind of tumors is not worthy to be considered.

More interesting is in this case the clinical behaviour, with a slow growth, eight years long, as a proof of its benign biological condition. Because of the refusal of the patient, the operation was performed too late and in a very poor condition.

Diagnose. – Meningiomatous meningioma.

Grade. – I.

Irradiation. – Not recommended.

Follow up. – Operation in comatous state. Patient in a very poor condition. Death after eight days with endocraneal hypertension and hypothalamic insufficiency.

16) (I. P. B.), J.Z., male. 39 yr.

Clinical history. – Started eleven years ago, with recurrent focal Jacksonian epileptic crisis of the right leg, which later included the arm. After six years, convulsive epileptic crisis, which leaves a right hemiplegia, headaches and a stuporous condition.

No other antecedents. Exploratory findings: Right flaccid hemiplegia with slight stuporous condition. No stasis papillae.

Clinical diagnosis. – Tumor of the left centro-parietal area.

Angiographic diagnosis. – Downward deviation of the a. pericallosa, slight filling of tumor vessels. No arterio-venous fistules.

Surgical macroscopic diagnosis. – Well circumscribed tumor of the high fronto-parietal area, with necrotic-hemorrhagic appearances inside.

Pathology. – Initially diagnosed as a benign ganglioglioma, later as an astrocytoma, and finally as a glioblastoma multiforme.
Satisfactory evolution during five years. After this time progressive focal crisis with appearance of an exocraneal tumor, and appearance of a progressive hemiparesia.

Clinical diagnosis. – Glioma recurrent with invasion of brain covers.

Surgical macroscopic diagnosis. – Parasagittal tumor, attached to the dura invasive to the brain to the skull and to the epicraneum. Posible malignant meningioma.

Case nº. 16), I.P.B., B. 1.682/67.

Macroscopically we find two pieces of operation tissue. The first one with an irregular form, (5 × 3 × 2 cm.) with a capsule. Surface of section with a white, fibrous tissue. The second one (4,5 × 2,5 × 2,5 cm), has a

membrane formation at one of its ends. On the section, white, fibrous tissue with softer gelb-reddish tissue.

On the microscope we are able to differentiate four different patterns of tissue in different zones:

a) Zones very rich in cells with scanty cytoplasm, and hyperchromatic nuclei, with considerable variations in size and shape. There are some giant forms. Mitoses are present, some of them multipolar. On the silver stain, we find a very dense network of reticulin fibers. Vascularization in form of not very numerous capillary vessels.

b) Similar to the form one, but with collagenous fibers mixed with tumor cells of the characteristics already described.

c) Zone of predominant fibrosis with very scanty cell contain.

d) Zones of necrosis.

There is no doubt, we are dealing with a malignant tumor with giant, monstruous cells, and the first impression could be that of a malignant glioblastoma. The collagenous fibers in some parts of the tumor lead already to the suspicion of a mesenchymal origin, and the silver stain is definitive, showing a dense network of reticuline around the tumor cells, which has been never found in the glioblastoma. On the other side, these tumors show, as already described, a very exuberant vascular pattern, whereas here we only find scanty, single capillary vessels.

The attachment of the tumor to the duramater could suggest a meningeal origine, but we do not have here the image of the polymitotic meningioma, resembling much closer a meningiomatous structure, but a very polymorphous mesenchymal tumor, most probably originated from the dura matter and belonging to the group of the intracraneal sarcomas.

Based on his experience, Zülch has proposed following types of intracraneal sarcomas:

a) Circunscribed sarcoma of the blood vessels (so-called monstrocellular sarcoma) (79 cases.).

b) Fibrosarcoma of the duramater. (30 cases).

c) Diffuse sarcomatosis of the meninges (9 cases).

d) Retothelial sarcoma (6 cases).

e) Sarcoma of the cerebellum (5 cases).

f) Adventitial sarcomas (diffuse) (4 cases).

This case would correspond to the group *b*), but with prominent monstrocellular features.

It is interesting the history of eleven years, and the former changing histological diagnosis, which we have not been able to confirm.

Diagnose. – Polymorpho-cellular sarcoma of probable dural origin.

Grade. – III to IV.

Irradiation. – Recommended.

Follow up. – Treatment completed with Cobaltherapy and intra-arterial perfusion. Multiple epicraneal recidives and perifocal metastases. Still alive ten months after the operation.

17) and 18), (I. P. B.), A.U., female. 38 yr.

Clinical history. – Admittance through the Casualty Department. Since six days ago, headaches and anorexia. She says, she had loss of vision that morning for a while.

Casualty diagnosis. – Histerism? Under observation.

At the Medical Unit, it was impossible to perform an anamnesis because of the psychic condition of the patient. She complained of headaches and manifested agitation, disorientation in time and space, delirant appearance and hallucinations. Alcoholic antecedents.

Starved, agitated patient, who does not answer to the questions. Head: No pain on percussion. Isocoric, normo-reactive pupillae, conjunctivae somewhat pale. Septic mouth. Without other findings. Blood pressure oscilating between 10/7 and 21/14. Pulse frequency between 90–100. Temperature 37,3° C. Blood and urine examinations, normal.

Diagnosis of the medical unit. – Acute Psycosis. Pneumonia. Tuberculous meningitis.

Psychiatric examination. – Poor physical condition. Probable organic cerebral cause (Intoxication, brain edema). Abnormal personality with a psyco-genetic reaction, where alcohol plays an important role.

Psychiatric diagnosis. – Psyco-genetic reaction with possible impairment through alcohol abuse, on a probable organic cerebral basis.

Cases nº. 17 and 18), I.P.B., B. 1.118/67.

Brain with a total weight of 1,180 g., which was examined after formalin fixation. No body autopsy. At the right temporal lobe, black colour at the subaracnoidal space. No changes in the brain surface, neither prominence nor depression. At the other parts of the brain surface, small dark brown spots up to 0,5 cm. in diameter. Around the subarachnoidal vessels there is a darker, almost black colour on the section, no changes in the internal brain structure.

Microscopically, we find a proliferation of reticuline fibers and of number of cells within the subaracnoidal space. This cells have their cytoplasma filled with fine or coarse granules of a brown pigment. Cells were sometimes elongated, sometimes stellate in shape, and disposed predominantly around the vessels, or in a looser arrangement all over the subaracnoidal space. This pigmented cells disappear at the transition between subaracnoidal and Virchow Robin's space.

Iron stain proved to be negative, excluding the possibility of being an old subaracnoidal haemorrhage. In this last case, the macroscopic colour would have been brown, but not brown-black, even after fixation, since we have not seen recent haemorrhages, which could appear in this colour after formalin fixation.

The only suspected possibility for this pigment was to be melanine, and we performed the silver stain for this pigment after Rio-Hortega, which correspond to the slide nº. 18), and which proved to be positive.

We are dealing, therefore, about a condition with a diffuse storage of melanic pigment all over the subaracnoidal space. The first possibility was to think on a metastatic lesion, but there was no nodular appearance in the brain tissue, nor the physical exploration in life of the patient had shown any suspicions pigmented lesion either in the skin nor in the eyes.

We thought, therefore, it should be a primary cerebral lesion, which is very rare, but which has been described as a " diffuse meningeal melanosis ". Without extending ourself too long on relations between melanin forming cells and nervous tissue, we want to stress, that melanoblasts have been described in normal meninges, and therefore is not to wonder this possibility of giving origine to tumor-like conditions.

Although we have not seen any changes at the blood vessels, this condition is supposed to cause disturbances in the blood supply to the brain, which could explain a part, at least, of the clinical picture.

Diagnose. – Diffuse subaracnoidal melanosis.

Grade. – II.

Irradiation. – Would not have been recommended.

19) (M. P. I. C.), M.K., female. 53 yr.

Clinical history. – Progressive history of endocraneal hypertension with a left cerebellar syndrome. Besides, transitory attacks of incomplete homonime right hemianopsia, which suggest compression of the left occipital lobe adjacent to the left cerebellar hemisphere.

Clinical diagnosis. – Tumor of the upper part of the left cerebellar hemisphere.

Surgical macroscopic diagnosis. – Cystic tumor of the left cerebellar hemisphere.

Case nº. 19), M.P.I.C., E. 6465.

Microscopically, we find a tumor with middle cell density. The nuclei are round or oval, sometimes elongated, isomorphous, with dark chromatine and absence of mitoses. The cytoplasm is eosinophilic, well recognoscible. The tumor cells are disposed around capillary lumina with a different grade of dilatation, taking sometimes a lacunar appearance, containing blood. Sometimes the cytoplasm has a foamy appearance, looking as a pseudo-xantomatous cell. Sometimes there are greater dilatations of the lumina, forming middle-sized cysts. A metachromatic stain shows mastocytes among the tumor cells. The silver stain demonstrates a dense network of reticular fibers surrounding each vessel. The cerebelar cortex can be recognized at a coin of the slide, with an infiltrative pattern of the tumor against the surrounding nervous tissues.

Here we have a case of a vascular tumor which appears within the nervous tissue, almost always in the cerebellum. Its capillary nature the presence of cysts, and the argirofilic fibers render very easy the diagnose. There are no other conditions which could be confused with this one, if we are aware of it.

Diagnose. – Hemangioblastoma (Lindau).

Grade. – I.

Irradiation. – Not recommended.

20) (*I. P. B.*), *G.S., male. 17 yr.*

Clinical history. – One year ago, noted a painless progressively growing at the right cervical area, over the sterno-cleido-mastoid muscle. Surgical exeresis, apparently complete. Pathologic diagnosis: Reticulum-cell-sarcoma. Radiotherapy administered. After four months, progressive local recurrence. Excission biopsy performed.

Case nº. 20), I.P.B., B. 1298/66.

Tumor with a great cellular density and infiltration of the surrounding striated muscle. In some fields is possible to recognize an alveolar pattern; in other parts we find pseudo-tubular appearances. We can find also a loosening of the tumor cells, showing pseudo-papillar structures around the vessels. The silver stain confirm the alveolar arrangement of the tumor cells.

The examination of the tumor cells with a high magnification show sometimes a scanty cytoplasm, sometimes more abundant, with a prolyhedrycal shape and a clear appearance. The nuclei are round or oval, with a medium dark chromatine and evident nucleoli. Mitoses are easy to be found.

We are dealing with a tumorous condition of the neck, with a rich cellularity and an advanced grade of differentiation. One of us thought at the beginning on an epithelial tumor originated possibly at the thyroid gland. Nevertheless, the relation tumor-cells stroma did not look as in an epithelial tumor and the scintillogramm showed no alteration of the thyroid gland. The clinical examination did not reveal another epithelial organ as possible source of this tumor.

The cellular appearance could be that of a reticulosarcoma, but the arrangement of the reticular fibers and the pseudo-tubular structures, as well as the alveolar, epitheloid patterns did not look as those of a reticulum-cell sarcoma.

This case was discussed in a meeting of the Spanish Society of Pathology, where it was labelled as a malignant chemodectoma originated at the carotic body. Both of us sustained also this opinion, during our discussion of cases, previous to the Congress. There are very few cases of malignancy recorded within this group, and this renders this case very interesting.

Diagnose. – Malignant chemodectoma.

Grade. - III to IV.

Irradiation. – Recommended.

Follow up. – Radiotherapy administration. After three months, progressive appearance of small cutaneous nodes around the operatory scar in the neck, followed by other nodes in the toracic, abdominal and crual skin, having the size of a cherry on the thighs. Progressive radiculalgias six months after operation. Tumoral cachexia. Numberless pinhead size nodes all over the chest skin only perceptible to palpation. Death one year after operation. No p. m. examination.

21) (*I. P. B.*), *J.B., male. 54 yr.*

Clinical history. - Eight months ago, visual disturbances with left predominance. Progressive visual impairment in form of bitemporal hemianopsia.

On inspection, hypopituitaric aspect, bitemporal hemianopsia, with predominance in the right eye and pallor in both pupillae.

Conventional radiologic diagnosis. – Erosion of the sella turcica with disappearance of the posterior clinoid processes.

Clinical diagnosis. – Tumor of the sellar region. Probable cromophobe adenoma.

Pneumoencephalographic diagnosis. – Up. – and backward deviation of the suprachiasmatic cistern.

Surgical macroscopic diagnosis. – Adenoma of the sellar region.

Case nº. 21), I.P.B., B. 834/66.

Tumor tissue with slender connective septa which support a system of capillary vessels, covered by a single epithelial layer of cells of scanty cytoplasm and oval or round nuclei, with an uniform size and shape. No atypias nor mitoses have been seen. In some places the epithelial layer becomes multiple, forming solid trabecular structures. On other places we see a papillary pattern, which becomes more evident on the transverse section.

The silver stain shows reticular fibers around the capillary vessels. Trichrom stains do not show a clear acidophilic nor basophilic reaction of the cellular cytoplasm.

The most plausible diagnose would be that of chromophobe adenoma of the hypohysis. There are three main types of it: the diffuse, the sinusoidal and the papillary form, being this third form, which corresponds to our case, the rarest one.

As a differential diagnose we could consider the papillary ependymoma. Antoni (1950) has described a type of tumor, localized in the chiasmatic area, which corresponds to this type, and which he classifies as an ependymoma. We see just the mixo-papillary form of the ependymomas in the region of the cauda equina, where they have been also described as neuroepitheliomas, but should not consider as such this other kind of tumors, which do not correspond exactly with any of the well known types of ependymoma.

Diagnose. - Papillary chromophobe adenoma of the hypophysis.

Grade. - I.

Irradiation. - Not recommended.

Follow up. - Very satisfactory evolution, with disappearance of the visual disturbances.

22) (I. P. B.), C.G., male. 62 yr.

Clinical history. - Four months ago, frontal headaches, postural dizziness, nausea and vomiting. Posteriorly, permanent instability on walking. In the last month, development of a syndrome of endocraneal hypertension with stasis papillae. No personal nor familial antecedent of interest.

Exploratory findings. - Syndrome of endocraneal hypertension, bradipsychia, and complex parkinsonian appearances with astasia-abasia.

Clinical diagnosis. - Endocraneal hypertension following deep tumor or cerebellar metastase.

Angiografic diagnosis. - (left carotid a.) Slight hydrocephalic curve of the a. cerebri anterior.

A ventriculography was planned, but patient died suddenly of respiratory arrest.

Case nº. 22), I.P.B., A. 129/64.

Tumor tissue with a papillary arrangement of epithelial cells around connective cores with capillary vessels. The epithelial tumor cells form sometimes a single layer, sometimes there are several cell layers. With high magnification we see polyhedral cells with scanty cytoplasm and oval nuclei, irregular in size and shape, with prominent nucleoli. Mitoses can be observed. There is a clear, homogeneous, eosinophilic substance among this papillary structures. The limit against the nervous tissue is formed by multiple layers of tumor cells which finish suddenly on a zone with a moderate astrocytic reaction. The whole tumor node is isolated within the nervous tissue of the cerebellum, without connection to the ventricular system.

The papillary pattern could suggest a chorioid plexus papilloma, but the connective cores are more irregular, the epithelial cover is very irregular, and the cytologic pattern is very atypical for being considered as a chorioid papilloma, whose cellular isomorphism and regular arrangement have been stressed elsewhere (Case nº. 4). We do not find here a connection with the 4th ventricle.

Our diagnose has been, metastatic tumor. We were able to perform a complete p. m. examination of this case, but no primary tumor could be discovered. The papillary structure could suggest a thyroid gland carcinoma, but nothing was seen on the macroscopic sections. Bronchial, kidney and breast carcinoma are the kind of tumors which metastatize most frequently in the brain, but we were not able to demonstrate a primary tumor in any of these structures. So we have to consider it as a metastatic tumor of unknown origin, the only one of our statistic (Bilbao).

Diagnose. – Metastatic carcinoma of the cerebellum of unknown origin.

Grade. – III.

Irradiation. – Would have been recommended.

23) (I. P. B.), J.G., male. 53 yr.

Clinical history. – Twelve years ago, resection of an hypernephroma of the right side. Appearances of very slowly progressive right hypacusia with phonesis on both side. One year before examination, nauseas with occasional vomiting, dizziness and occasional instability in walking. Posteriorly, occasional headaches.

Neurologic examination. – No signs of endocraneal hypertension. Slight vestibular disturbances, with bilateral cochlear hypofunction.

He is examined after seven months, with impairment of the neurologic appearances, disturbances in walking and beginning of stasis papillae, accompanied by diplopia, without other focal symptomes.

Clinical diagnosis. – Possible cerebellar metastase of an hypernefroma.

Ventriculographic diagnosis. – Hydrocephalus internus with aqueduct block in the upper third.

Surgical macroscopic diagnosis. – Metastatic tumor of the uppermedial area of the left cerebellar hemisphere.

Case nº. 23), I.P.B., B. 1156/67.

We are dealing here with a tumor of compact structure with a pseudo-endocrine arrangement of its cells in a trabecular form, with some occasional figures of pseudoglandular lumina.

The tumor cells show very prominent, polyhedral cell boundaries, and a clear, almost inapparent cytoplasm, with swimming, oval, excentrically placed nuclei of an irregular size. Mitoses can be observed occasionally, but they are not very frequent. The fat stain shows mono—and birefringent lipoids within the cytoplasm of the tumor cells.

The stroma is composed by slender connective septa carrying capillary vessels, in a transition to wider septa, predominantly hyalinized or fibrous, with macrophagic cells, whose cytoplasm is filled with granulations of a brown pigment with a positive iron reaction. The silver stain shows a dense reticular frame within the consective septa, which stress the pseudo-endocrine arrangement of the epithelial cells.

This is a very well known picture to a general pathologist for being confused with any other one. We have here a cerebellar metastase of a clear-cell carcinoma of the kidney, the so-called hypernephroma.

Most interesting in this case is the fact, that the patient was submitted to a kidney resection 12 years before this second one, and the pathological diagnose was a clear-cell carcinoma of the kidney. All the meantime the patient was free of symptoms. As we have already said, the kidney is one of

the most common places of origin of brain metastases and as long periods as 20 years after resection of the primary tumor have been recorded in the bibliography.

From the point of view of the differential diagnose, the honey combed architecture of the oligodendroglioma could be considered. Nevertheless, the demonstration of fat within the tumor cells, the presence of tubular structures, the trabecular arrangement between the connective-vascular frame, and its demonstration by means of the silver stain are easy criteria for the clear-cell carcinoma.

Diagnose. – Cerebellar metastase from a clear-cell carcinoma of the kidney.

Grade. - III.

Irradiation. – Recommended.

Follow up. – Free of symptoms one year after removal.

List of diagnoses.

1) and 2). Ganglioneuroblastoma.
3) Ependymoma.
4) Choroid papilloma.
5) Retinoblastoma without rosettes.
6) Fibrillary astrocytoma.
7) Protoplasmatyc (gemistocytic) astrocytoma.
8) Oligodendroglioma, isomorphous.
9) Oligodendroglioma, polymorphous.
10) Multiform glioblastoma.
11) Spongioblastoma, isomorphous.
12) Spongioblastoma, polymorphous.
13) Medulloblastoma.
14) Neurinoma.
15) Endotheliomatous meningioma.
16) Sarcoma.
17) and 18). Diffuse meningeal melanosis.
19) Angioblastoma (Lindau).
20) Malignant chemodectoma.
21) Papillary chromophobe adenoma of the hypophysis.
22) Metastatic carcinoma of unknown origin.
23) Metastatic clear-cell carcinoma from the kidney.

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EXPLANATION OF PLATES

Plate I.

Case n. 1 and 2.

a) Hematoxyline–eosine. 90 ×. Ganglionic cells with one or two excentric nuclei. Fascicles of Schwann cells.

b) Hematoxyline–eosine. 90 ×. Anaplastic area of the tumor, with dense cellularity and some giant abnormal nuclei, and abnormal mitotic figures (arrow).

c) Hematoxyline–eosine. 225 ×. " Ganglioid " cell of neuroblastic appearance withing the anaplastic area of the tumor.

PLATE II.

Case n. 3.

Hematoxyline-eosine. 225 ×. Tumor tissue rich in cells, with clear perivascular zones of radiated structure (perivascular radiated crowns) and ependyme-like tubular formations.

Case n. 6.

Hematoxyline-eosine. 225 ×. Small round nuclei within a fibrillary intercellular substance. Cytoplasm of the tumor cells inapparent. Quiet vascular pattern.

PLATE III.

Case n. 7.

Hematoxyline-eosine. 225 ×. Scanty cell content, with elements rich in cytoplasma, with thick, not very long processes, and with predominant perivascular dispossition.

Case n. 8.

a) Hematoxyline-eosine. 225 ×. Tumor tissue rich in cells of honey-combed appearance, with evident cell membranes, and central lying nuclei within a clear cytoplasma.

b) Silver impregnation after Meller 225 ×. Clear nuclei surrounded by a dark cytoplasm with slender processes. Characteristic appearance of olygodendrocytes.

PLATE IV.

Case n. 9.

a) Hematoxyline-eosine. 225 ×. Tumor rich in cells with very anisomorphous nuclei, abnormal mitoses, and a honey-combed pattern of the cytoplasma.

b) Silver impregnation after Meller. 225 ×. Clear appearance of nuclei of tumor cells, characteristic for olygodendrocytes.

PLATE V.

Case n. 11.

Hematoxyline-eosine. 90 ×. The so-called " hyperplasia of the pons ". Dissociation of pre-existing nerve cells by elongated isomorphous tumor cells. Nerve fibers are partially conserved, explaining the absence of clinical symptoms during a long time.

Case n. 12.

Hematoxyline-eosine. 25 ×. Tumor rich in cells disposed in fascicles; oval isomorphic nuclei, and presence of mitoses (arrow).

PLATE VI.

Case n. 13.

Hematoxyline-eosine. 90 ×. Cerebellar cortex with granular layer infiltrated by fascicles of cells with carot, small shaped nuclei and inapparent cytoplasma. Within the molecular layer, dendritic processes of a Purkinje cell can be clearly seen.

Case n. 14. – Hematoxylina-eosine 90 ×.

a) Zone with fascicles of Schwann cells with elongated nuclei (Antoni A).

b) Zone with vacuolated cytoplasm where fat substances can be demonstrated by special methods. (Antoni B).

PLATE VII.

Case n. 15.

Hematoxyline-eosine. 225 ×. Endotheliomathous cells arranged in whorls, with a scanty connective stroma.

Case n. 16.

Hematoxyline-eosine. 225 ×. Fascicles of elongated cells with oval or polymorphous nuclei, and many mitoses.

PLATE VIII.

Case n. 17.

Hematoxyline-eosine. 90 ×. Subarachnoidal space with cells whose cytoplasma is full of melanotic pigment.

Case n. 19.

Hematoxyline-eosine. 90 ×. Tumor tissue with a system of capillary vessels of different size, with a single layer of endothelial cells.

PLATE IX.

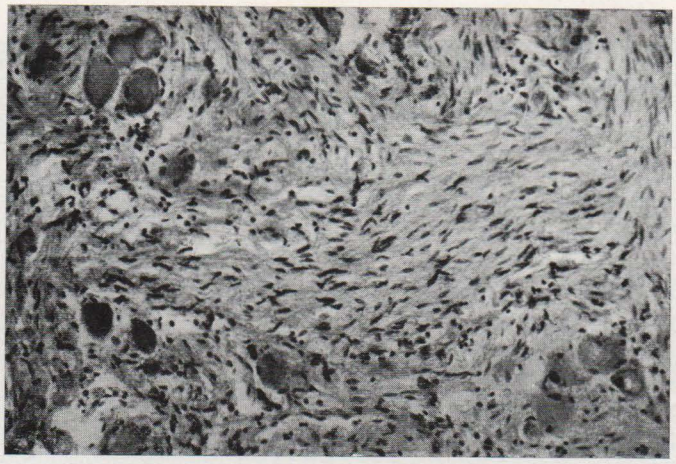
Case n. 22.

Hematoxyline-eosine. 90 ×. Tumor tissue with epithelial papillary structures with a transition to a solid area.

Case n. 23.

Hematoxyline-eosine. 90 ×. Tumor tissue with clear cells in a trabecullar or pseudoglandular arrangement, and with nuclei lying something excentrically within the cell.

Case 1 and 2.



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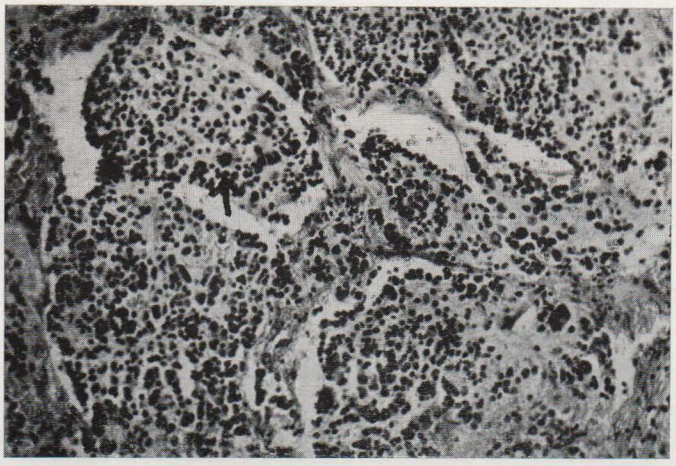

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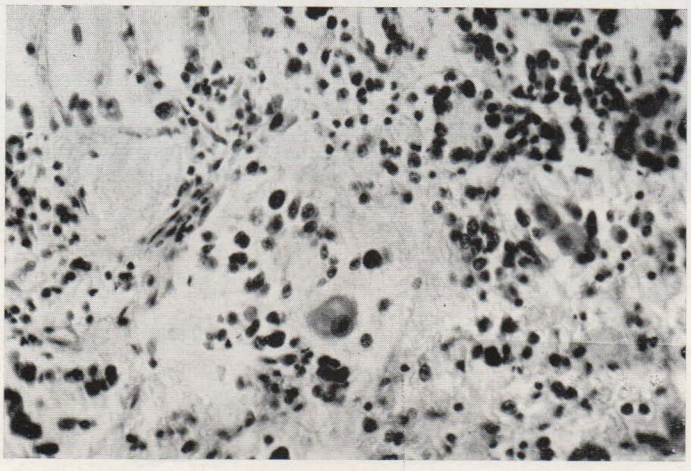

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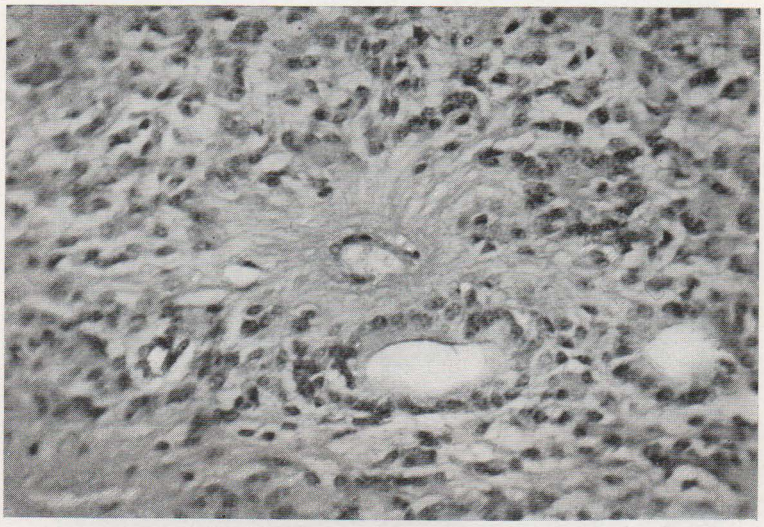

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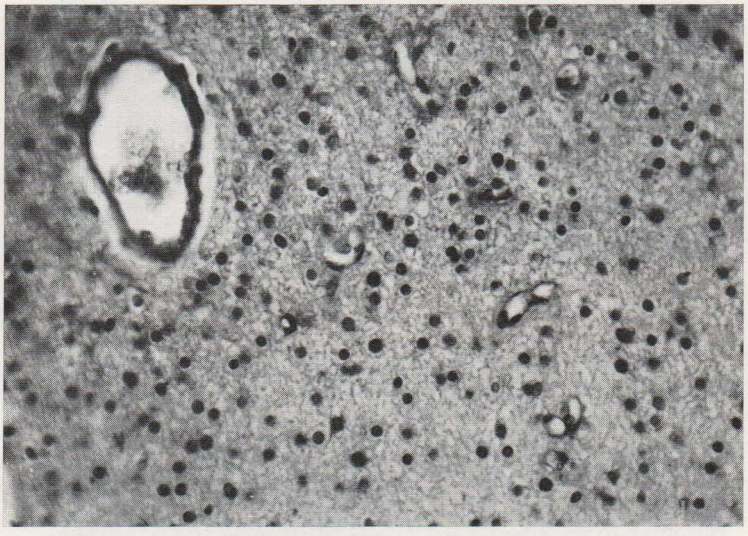

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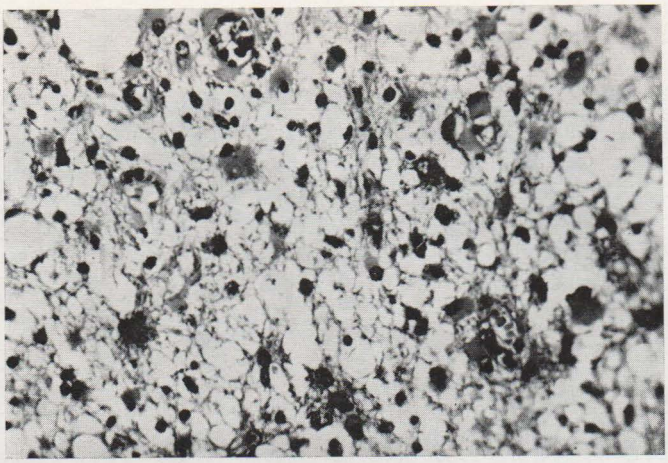
Case n. 7.



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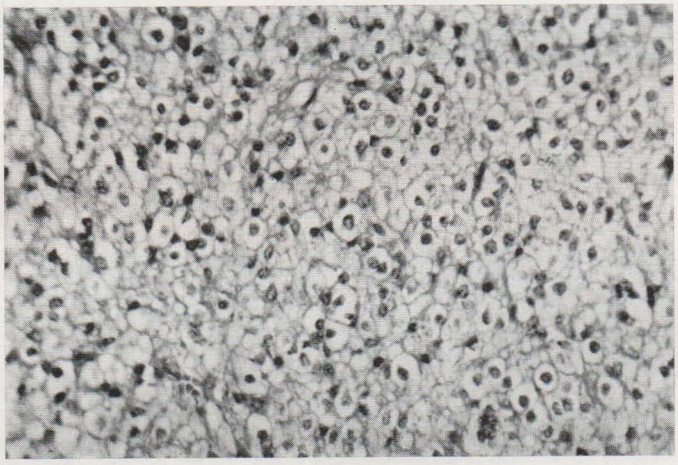

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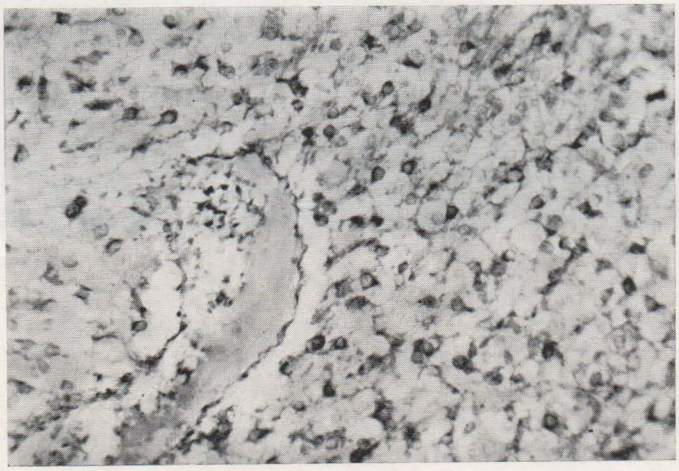

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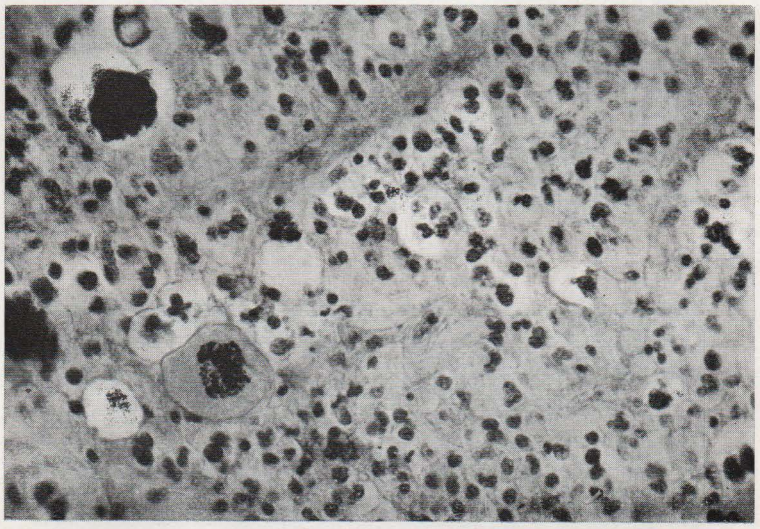

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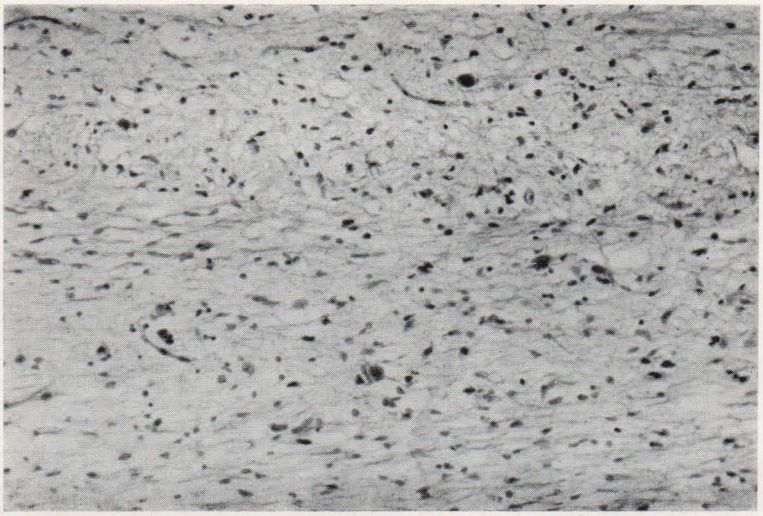

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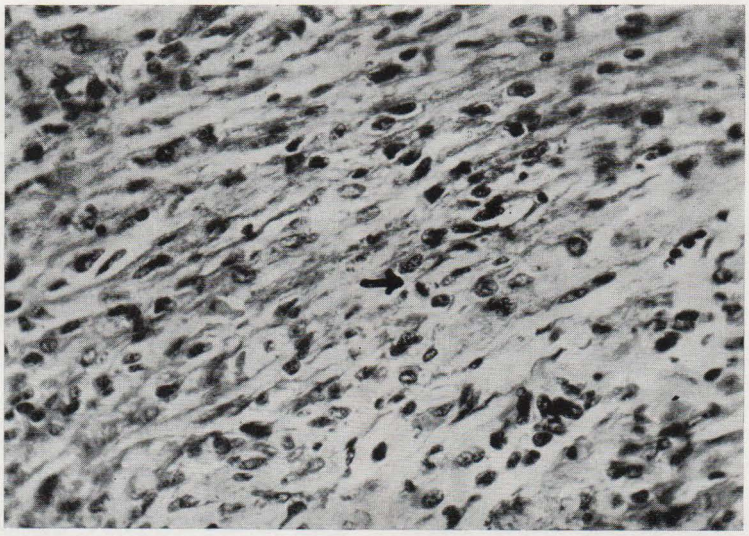

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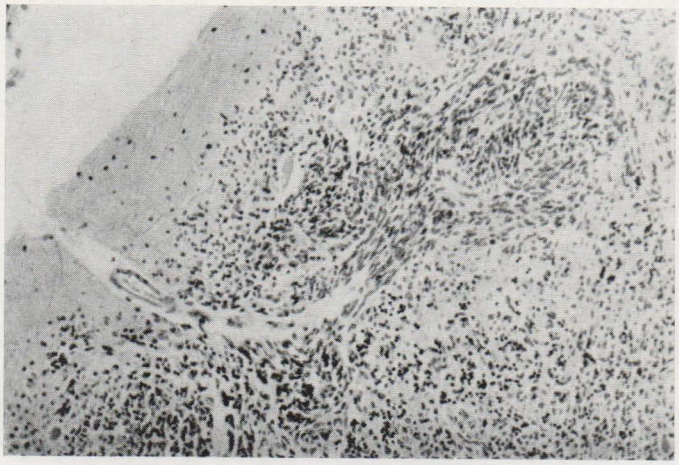

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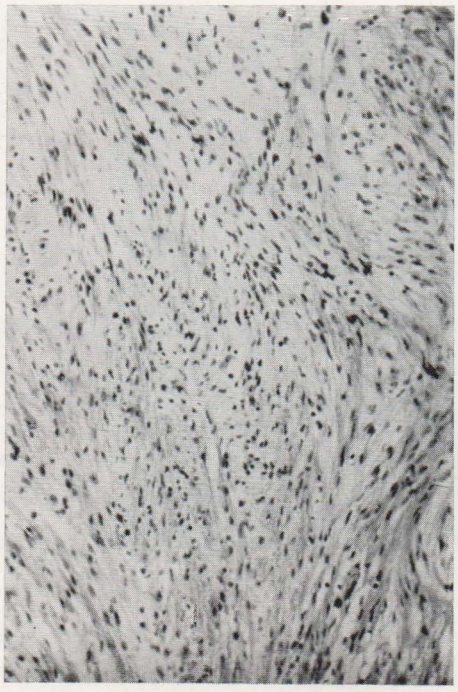

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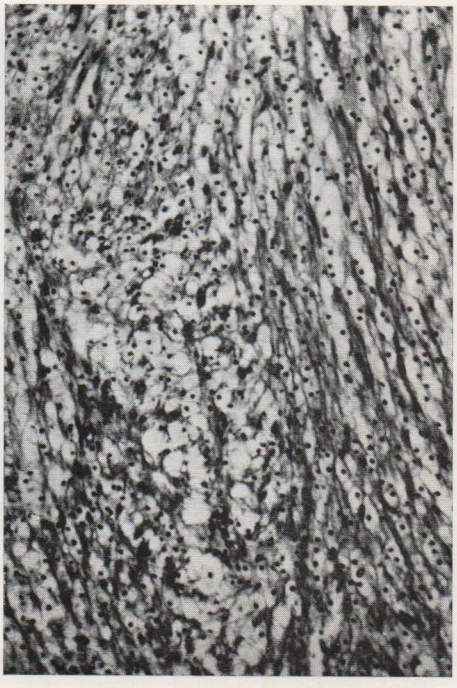

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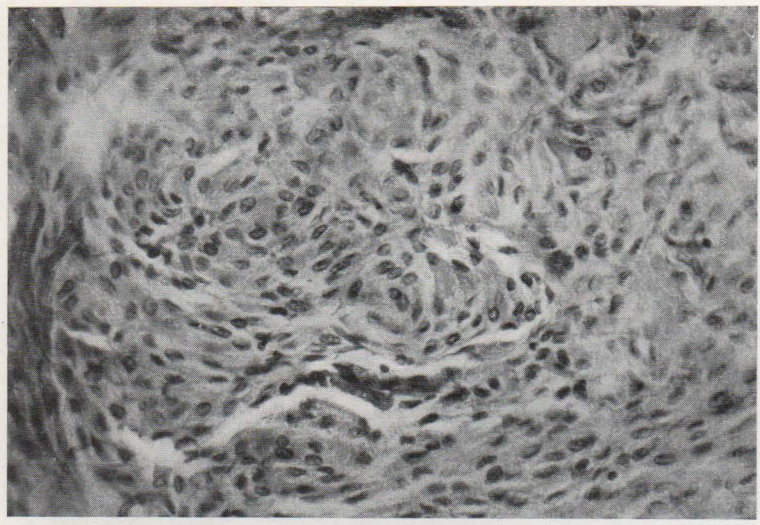

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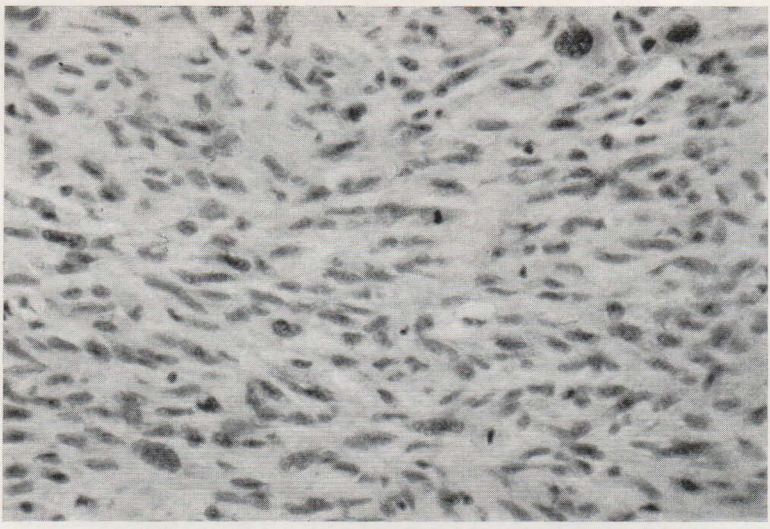

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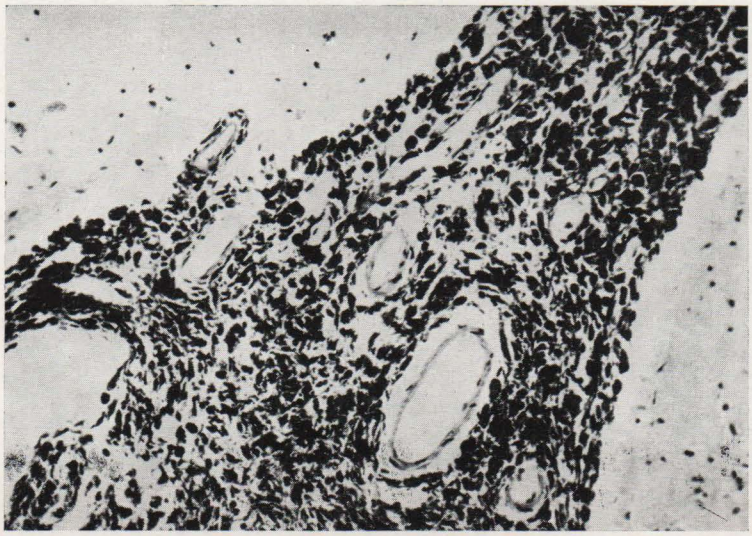

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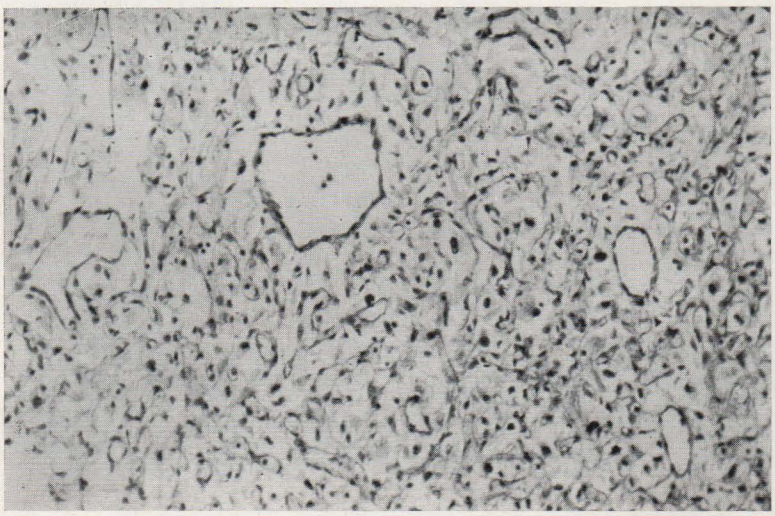

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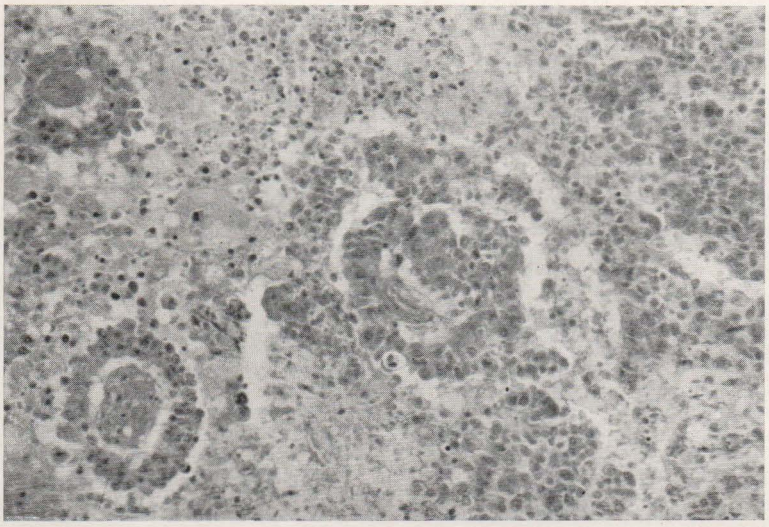

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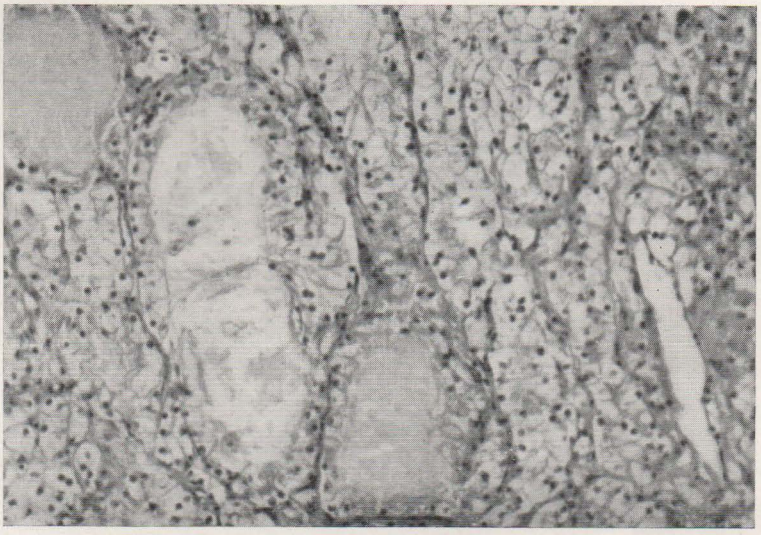

Case n. 23.

ROMA, 1970 — Dott. G. Bardi, Tipografo dell'Accademia Nazionale dei Lincei