Among the tumours and other space-occupying lesions of the central nervous system there are some congenital conditions with obvious pathological birthmarks on the skin, retina and other organs. These lesions, which have been studied pathologically and clinically during the last 80 years, perhaps can be grouped under the general term of phakomatoses of van der Hoeve (phakos = birthmark). No doubt some pathologists would prefer other denominations, like hamartomas or hamartoblastomas because they consider the term phakomatoses inadequate. However, they do agree about the overlapping of the different diseases included in this large group with cutaneous manifestations and involvement of peripheral and central nervous systems.

An interesting feature of many of these conditions is that they appear as borderline cases between congenital malformations and tumours. Norman considered that some of these anomalies belong to the category of hamartomas or congenital malformations with a potentiality for growth. The general term of hamartoblastomatosis was preferred by Zülch to the one of phakomatoses and this author also referred to the classical concept of Bielschowsky considering these lesions as developmental disorders with a tendency to blastomatosis ("Entwicklungsstörungen mit blastomatosem Einschlag").

Material

In our series of 2,200 brain tumours and other expansive intracranial lesions and 275 cases of different types of spinal-cord compression that we have operated on in Madrid during the last 16 years, we have had several examples of the so-called phakomatoses.

We shall present very briefly the main features of 12 patients with very obvious cutaneous and peripheral abnormal birthmarks together with other neurological symptoms who have been submitted to neurosurgical procedures.

Although there is some confusion in the literature about the different types and the numbers of the so-called phakomatoses we shall consider only three main groups of practical and neurosurgical interest: (i) neurofibromatosis (von Recklinghausen’s disease); (ii) tuberose sclerosis (Bourneville’s disease); and (iii) the wide group of angiomatosis which includes the encephalofacial angiomatosis of Sturge-Weber, the retinocerebellar angiomatosis of von Hippel-Lindau and other more rare types of cutaneous and nervous angiomatosis.

Neurofibromatosis
(von Recklinghausen’s Disease)

The clinical and pathological manifestations of von Recklinghausen’s neurofibromatosis are well known. Besides the typical cutaneous pigmentation and the multiple peripheral and subcutaneous tumours, there may be associated malformations of the central nervous system. But more interesting from our point of view is the occasional presence in these patients of intracranial or spinal tumours. Neurofibromas, meningiomas and different types of gliomas have been described.

Two of our patients with von Reckling-
hauscn's disease (19 and 32 years old) presented signs of spinal-cord compression and at the operations, carried out by our co-worker Dr. Boixados, multiple intradural neurofibromas were removed from the cervical region in 1 and from the dorsal region in the other. Postoperative results were good in both cases, but 1 patient presented a recurrence of symptoms 4 years later and another large neurofibroma was removed from the same cervical region.

In 2 other patients (28 and 35 years old) with the typical manifestations of von Recklinghausen's disease and verified peripheral neurofibromas there appeared symptoms of an increase of intracranial pressure. A frontal meningioma was removed in 1 of these patients and in the other only a decompression was performed after the air studies showed a basal tumour in the region of the 3rd ventricle.

The association of von Recklinghausen's disease with gliomas of the optic nerves and chiasm also was observed in 2 of our patients with histologically verified optic gliomas and the typical cutaneous pigmentations.

But our most interesting example of this group concerns a case of gliona of the 4th ventricle which already has been reported in detail. A woman 45 years of age had a clear von Recklinghausen's disease of hereditary basis, as the cutaneous and peripheral manifestations (Fig. 1) also were very marked in another sister 30 years old. The biopsy of one of the subcutaneous tumours of the patient demonstrated a typical neurofibroma. Besides there were symptoms of vertigo, headaches, vomiting and difficulty in walking and standing. Papilloedema, nystagmus, tremor and profound disturbances in the gait were the most outstanding signs. The possibility of acoustic tumours was disregarded as the result of otological examinations, and ventriculography revealed a filling defect in the 4th ventricle, besides a marked dilatation of the lateral and 3rd ventricles.

At operation a reddish, soft tumour filling the 4th ventricle and implanted in its floor was removed. The histological sections (Dr. Escalona) demonstrated an astrocytoma of fibrous type, with marked hyperplasia of the neuroglia fibers (Fig. 2).

The evolution of this case has been quite good during the year passed after the operation and she is greatly improved.

From the histological point of view there may be doubts and discussion about the classification of some of the central lesions that appear in the neurofibromatosis of von Recklinghausen. The so-called "central neurinomas" of the old literature may be considered as malformations by some pathologists or under different names of tumours by others (astrocytomas, spongioblastoma polare, schwannoma, etc.). As we have emphasized before, the lack of sharp boundaries of such lesions confers a special interest in this group and in the following group in which malformations, anomalies of development and growth of tumours sometimes are closely related within the central nervous system of those dysplastic and dysontogenetic organisms.

**Tuberose Sclerosis**
(Bourneville's Disease)

There is no need to recall the great diversity of lesions in this condition affecting the skin, brain and other organs, such as kidneys,
heart, lungs, etc., in which anomalies and tumours can be found.

We have in our neurosurgical series 2 patients, 14 and 16 years old, with the typical adenoma sebaceum of Pringle in the face (Fig. 3) and also with subungual fibromata of the fingers or toes.

Both patients presented a history of infantile convulsions and 1 of them a moderate degree of mental retardation. During the last year of their clinical histories the 2 patients complained of symptoms of increased intracranial pressure. There was papilloedema in both cases, with secondary optic atrophy in 1, and two typical retinal phakomas in the other. No focal signs could be disclosed. In the electroencephalographic studies there appeared slow diffuse activity with delta waves during the hyperventilation test.

Roentgenograms of the skull demonstrated signs of increased intracranial pressure, erosion of the sella and some small and diffuse calcifications in both cases. Ventriculography showed hydrocephalic dilatation of the ventricles with a large ventricular mass in the frontal horn of 1 of the patients (Fig. 4) and obliteration of the 3rd ventricle in both of them. In 1 patient we could identify several nodules projecting into the lateral ventricles following the typical description of the so-called “candle gutterings.”

Only a decompression was performed in 1 of these cases with a relief of the intracranial pressure during 1 year of postoperative survival. In the other patient a large vascular tumour was removed from the lateral ven-
tricle showing several sites of implantation on the ependymal wall.

The histological sections of the intraventricular tumour (Dr. Escalona) demonstrated a subependymal astrocytoma-astroblastoma with giant cells (Figs. 5 and 6).

Russell and Rubinstein recently have emphasized the similarity between some retinal phakomas of tuberose sclerosis and the subependymal giant-celled astrocytomas which may appear to be associated with this condition or in an isolated manner on other occasions. According to Russell and Rubinstein these tumours usually occupy the walls of the lateral ventricles over the basal ganglia, are frequently calcified and differ from other cerebral astrocytomas in their benign course. These authors suggested their origin in the nests of monster astrocytes so characteristic of tuberose sclerosis. There may be intermediate stages between the well-defined neoplasms and the “heterotopias” of the sclerotic patches or tubera that are typical in the cortical gyri of such condition and that contain groups of large abnormal astrocytic and neuronal cells.

Angiomatosis

Within this large group of cutaneous and cerebral angiomatosis the best known clinical syndrome is the encephalofacial angiomatosis of Sturge-Weber. We shall refer very briefly to our 2 personal observations of this condition; both patients were operated on to relieve their epileptic manifestations.

The vascular malformation of Sturge-Weber usually affects the skin of the face with the typical port-wine naevus and the leptomeninges of most of the surface of one cerebral hemisphere or of its posterior parietal and occipital regions. The main cerebral symptoms and signs of this disease, such as epilepsy, mental retardation, disorders of personality, gyriform calcifications visible in the plain roentgenograms and infantile hemiplegia in some patients, seem to be secondary to the diminished cortical blood flow and the anoxia and obliteration of the vascular bed with consequent atrophy, destruction of nerve cells and calcium deposits.4

Our patients with Sturge-Weber’s disease were 2 girls, 11 years old, the first with the typical facial naevus and the second with an infantile hemiplegia. Epilepsy appeared in both cases during the first months of life and continued with frequent and severe attacks in spite of anticonvulsive medication. Both patients presented some degree of mental retardation and disorders of personality that were more marked in the second one. The characteristic gyriform calcifications were localized in the occipital region in the first case and in a more diffuse pattern over the parietal region of the second patient. In the electroencephalogram there was, besides a generalized slow activity, a depression of the rhythms over the affected area of the first case and a focal slow activity over the parietal region of the second. A marked cranial and cerebral hemiatrophy was present in the second patient as shown by the neuroradiological studies.

A wide occipital lobectomy was performed in the first patient 10 years ago, and a complete hemispherectomy (Fig. 7) in the second one 6 years ago with very good symptomatic results on the epileptic convulsions and a marked improvement of behaviour and mental adjustment.

The specimens of these 2 cases histologically (Dr. Morales and Dr. Ceballos) showed the typical picture of leptomeningeal

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Fig. 4. Intraventricular glioma of tuberose sclerosis demonstrated by ventriculography.
angiomatosis with abnormal vascularity and irregular deposits of calcium in the deep layers of the cortex and also in the white matter that seemed to be caused by circulatory disturbances. The neurons and glia cells were only secondarily affected in the calcified areas, but showed no other changes.

There is no doubt that radical surgery with extensive lobectomies or hemispherectomies can be very useful in the control of convulsions caused by Sturge-Weber’s disease. Norlén, Alexander and Norman, and Falconer and Rushworth recently have reviewed the results obtained from the surgical treatment of this condition.

The combination of retinal or facial angiomatosis with other vascular lesions in different levels of the central nervous system is also well known. We have not in our series recognized examples of retinal angiomatosis and cerebellar hemangioma (von Hippel-Lindau’s disease).

We studied recently a 23-year-old patient with a facial angioma (Fig. 8) and a short history of increase of intracranial pressure during the last 6 months. Ten years before he had a transient episode of loss of consciousness followed by symptoms of meningeal irritation during several days and presumably caused by a subarachnoid hemorrhage. On examination we found marked papilloedema and pupillary and oculomotor signs of the Parinaud syndrome that pointed definitely to a lesion of the midbrain.

No significant changes were demonstrated in other examinations (electroencephalography, plain radiographical studies, etc.), but carotid angiography revealed a large and deep arteriovenous aneurysm in the mesencephalic region (Fig. 9) that was fed by different large arteries of the posterior cerebral group and drained through very large veins of Galen.

In view of the unfavourable situation of

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**Fig. 5 (left).** Astrocytoma-astroblastoma of lateral ventricle in tuberose sclerosis. General view of tumor showing presence of giant neuroglial cells. Hematoxylin and eosin, X160.

**Fig. 6 (right).** Same tumour as in Fig. 5 with silver staining demonstrating large bipolar cells. del Rio-Hortega’s silver carbonate stain, X400.
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FIG. 7. Roentgenogram of removed cerebral hemisphere of Sturge-Weber’s disease with typical gyriform calcifications over parietal region.

this vascular lesion a supraoptic ventriculostomy was carried out as a palliative measure to relieve the increased intracranial pressure secondary to the large hydrocephalus produced by compression of the aqueduct. The patient improved temporarily but died suddenly several months afterwards probably because of the rupture of the vascular malformation.

We have considered this case as an example of the so-called angiomatosis of Bonnet-Dechaume-Blanc.6 Apparently these French authors described the association of facial, retinal and diencephalomesencephalic angiomatosis, although there were previous pathological and clinical reports. Paillas et al.7 have reviewed this clinical syndrome, and have collected altogether 28 examples from the literature, including a personal observation. However, only 10 cases were studied at autopsy or by cerebral angiography and the predominant localization of the intracranial vascular lesion appeared around the thalamic or mesencephalic region.

Summary

Twelve obvious cases of the so-called phakomatoses with striking abnormal birthmarks and other peripheral and central manifestations that required a neurosurgical procedure were collected from our series of 2,200 expansive intracranial lesions and 275 spinal-cord compressions operated upon.

Of 7 patients with Von Recklinghausen’s disease there were 2 with spinal neurofibromas, 2 with gliomas of the optic nerve and chiasm, 1 with a frontal meningioma, 1 with an astrocytoma of the 4th ventricle and 1 with a deep-seated unverified tumour.

Two patients with tuberous sclerosis presented an increase of intracranial pressure produced by intraventricular tumours. One of them was verified and appeared as a subependymal giant-celled astrocytoma-astroblastoma.

The interest in some of these gliomas is emphasized because of their association

FIG. 8. Facial angiomata associated with mesencephalic arteriovenous aneurysm.

FIG. 9. Carotid angiography of patient in Fig. 8 demonstrating large arteriovenous aneurysm of mesencephalic region.

FIG. 9. Carotid angiography of patient in Fig. 8 demonstrating large arteriovenous aneurysm of mesencephalic region.
with malformations and the possibility of intermediate stages between such anomalies of development and definite growth of tumour.

In the group of cutaneous and central angiomas we have had 2 patients with Sturge-Weber’s disease who were treated successfully by occipital lobectomy and hemispherectomy for the relief of severe convulsions.

A rare example of facial angioma associated with arteriovenous aneurysm of the midbrain, demonstrated by angiography and producing an increase of intracranial pressure, also was observed in our series and was included in the group of the so-called angiomatosis of Bonnet-Dechaume-Blanc.

Addendum

After this paper was completed we had an interesting example of bilateral acoustic neurinomas in a girl 19 years of age with some peripheral neurofibromata demonstrated by biopsy. Both neurinomas were removed radically and successfully in a one-stage operation.

Another patient, 46 years old, with a striking peripheral von Recklinghausen’s disease had a temporoparietal astroblastoma with extensive necrosis and died several months after operation.

References