CEREBRAL VASCULAR INSUFFICIENCY AS A CAUSE OF REAPPEARANCE OF NEUROLOGICAL SYMPTOMS LONG AFTER REMOVAL OF A MENINGIOMA

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Recurrence of old manifestations or the appearance of new symptoms after extirpation of intracranial meningiomas unfortunately occur frequently. It is a bitter fact that only 50 to 60 per cent of patients harboring a meningioma—"one of the most benign and surgically accessible intracranial tumours"—could be restored to their previous occupations after operation.17

Apart from the neurological manifestations that are revealed immediately upon the patient's recovery from the anesthetic, the operative undertaking may give rise to symptoms that do not become apparent until or even after convalescence. These manifestations generally appear within 1 year of the operation and usually are attributed to the process of healing: gliosis and scar formation. Epilepsy is a prominent symptom. The many patients kept under control by anticonvulsive measures represent the first and major group of those presenting recurrent or new manifestations after extirpation of their meningiomas.

The second group includes patients with actual recurrence of their tumor. The incidence of recurrence after surgical extirpation of intracranial meningiomas varies according to many factors, the most prominent of which probably are the histological variety and the site of the growth. Cushing9 had to reoperate 93 times on 43 patients in his series of 295 meningiomas for recurrence—a total case incidence of 15 per cent.

Dickel,10 reviewing 486 cases of meningiomas from Tönnis' collection, found a recurrence rate of 3.6 per cent in hemispherical as compared with 9.9 per cent in basal meningiomas—an over-all incidence of 7.9 per cent. Though clinical manifestations of neoplastic recurrence may appear at any time from a few months to 17 years after operation,9 in the majority of cases they were evident within the first 3 postoperative years.

The third group of patients, returning with symptoms long after their meningiomas were removed, represent the target for our concern in the present paper. These are patients who were readmitted, often 10 or more years after the healing processes of their operations had become quiescent, and in whom thorough neurological investigations, including angio- graphy, air encephalography and electroencephalography, failed to reveal any evidence of neoplastic recurrence. It is true that the number of patients falling under this group is small, but they represent such a clinical entity as to warrant special consideration.

Following is a brief report of the 5 cases in this last group.

CASE REPORTS

Case 1. A 44-year-old physician had undergone craniotomy for removal of a right frontal parasagittal meningioma in 1953. There was immediate postoperative left complete hemiplegia, but this improved rapidly to residual spastic monoplegia of the left leg. Occasional twitches of muscles in the left lower limb were observed during the first 3 postoperative years, and then disappeared.

Seven years after operation, at the age of 51 years, the patient began to have Jacksonian fits localized to the left leg. At the same time he noted a sensation of deep-seated pain in the same limb,
"as if his bones were being sewn up," accompanied by numbness. A few months later, the Jacksonian fits became more typical with involvement of the whole left side of the body. Three months before readmission, he noticed gradual increase in the paresis of his left leg and weakness of his left arm.

On readmission, 8 years after operation, the patient had two to three fits daily in spite of anticonvulsive medication. Blood pressure was 140/90 mm. Hg. Positive neurological findings were paresis and hyperreflexia of the left leg and left complete hyposthesia more pronounced in the leg and amounting to anesthesia in the back of the foot. Thorough investigation, including air encephalography, yielded no trace of recurrent tumor. Until contact with the patient was lost. 2 years later, his condition showed no alteration.

Case 2. A 26-year-old fireman was operated upon in 1936 for a left parietal parasagittal meningioma, the principal manifestations of which were a sense of numbness in the right hand together with the occurrence of sensory Jacksonian fits involving that hand. On his discharge, 17 days after operation, his only neurological ailment was hyposthesia of the right hand. Two years later, he sustained a light trauma to the forehead. Three weeks after the accident, slight weakness of the left arm and leg were noticed. This condition remained stationary for 7 years.

Nine years after operation, the patient began to have difficulty of speech in the form of motor aphasia and to notice an increase in the severity of the paresis in his left extremities. He became ataxic, saliva started to drool out of his mouth and he could no longer control his urinary bladder.

On readmission, 11 years after operation, the patient was 37 years old. Positive findings on examination were: complete right spastic hemiplegia, more pronounced in the arm; sensory ataxia, with a tendency to fall to the left; motor aphasia; and incontinence of urine. Blood pressure was 105/65 mm. Hg. Neurological investigations, including air encephalography, pointed to the absence of any space-occupying lesion. The condition of the patient was unchanged 3 years later.

Case 3. A 30-year-old woman underwent successful removal of a left parietal parasagittal meningioma in 1919. She suffered preoperatively from right hemiplegia and hemianesthesia, with right-sided fits and diminution of visual acuity in both eyes. Both the paresis and sensory disturbances were improved markedly after operation. The epileptic fits, however, persisted during the first 10 postoperative years, and then vanished completely during the following 10 years.

The patient began her new complaints at the age of 50, that is, 20 years after operation. Reappearance of the old right-sided fits was the first symptom, followed 2 years later by headache, further diminution of vision, weakness of urinary control and lastly increased paresis in her left arm and leg: "that was every day worse." Blood pressure was 125/100 mm. Hg. She had right hemiparesis and impairment of deep sensations in both left extremities. Neurological investigations, including electroencephalography, air encephalography and carotid angiography, proved the absence of neoplastic recurrence.

Case 4. A 40-year-old man, complaining mainly of right-sided Jacksonian fits, was operated upon successfully in 1943 for the removal of a left parietal parasagittal meningioma. A mild right hemiparesis, that however did not prevent him from carrying on his previous job, was the only postoperative sequela.

Eight years after operation, at the age of 48 years, he began to complain of headaches, attacks of petit mal, twitches of the muscles in his right arm, and an increase in the rigidity of his right extremities. Blood pressure was 110/85 mm. Hg. Positive findings were spastic hemiparesis of the right side and hyposthesia of the right arm (this last finding was not present on his discharge from hospital after operation). Neurological investigations, including electroencephalography, air encephalography and carotid angiography, provided no evidence for the presence of an intracranial tumor.

A control investigation carried out 6 years later, i.e. 14 years after operation, including electroencephalography and carotid angiography, gave negative evidence of intracranial neoplasia.

Case 5. A 40-year-old man underwent craniotomy in 1946 for removal of a frontal falx meningioma that grew mainly towards the right cerebral hemisphere. His preoperative neurological manifestations consisted mainly of headaches, diminution of vision in both eyes and a slight (only objective) left hemiparesis. The operation was not followed by any neurological deficit; on the contrary, there was marked diminution of the spasticity and hyperreflexia of the right side.

The patient started to suffer from attacks of angina pectoris 9 years after operation.

Twelve years after operation, at the age of 52 years, the new train of neurological symptoms started. It began with local fits of the left arm, which were soon followed by difficulty in walking and mild motor aphasic disturbances. Blood pressure was 130/80 mm. Hg. The only positive neurological finding was hyperreflexia of the right side of the body. Electroencephalography, air encephalography and carotid angiography gave no evidence of an intracranial tumor. Moreover, the encephalogram (Fig. 1) pointed to a process
of atrophy in the immediate neighborhood of the operation.

Table 1 presents the salient features of each of the 5 cases described.

**ETIOLOGICAL CONSIDERATIONS**

Faced with focal neurological manifestations referred to the operative area in a patient who has undergone excision of a meningioma, one is entitled to ascribe these to (i) reappearance of the tumor, (ii) injurious effect of the operation or (iii) occurrence of some new disease in or near the neighborhood of the operation. If the presence of a recurrent neoplasm is excluded, we are left to choose between the second and third possi-

### TABLE 1

*Summary of 5 cases of late post-meningioma syndrome*

<table>
<thead>
<tr>
<th>Case</th>
<th>Site of Tumor</th>
<th>Age at Op. (Years)</th>
<th>Persistent Postop. Sequelae</th>
<th>Age at Onset of Late Symptoms</th>
<th>Quiescent Interval (Years)</th>
<th>Chronology of Late Symptoms</th>
<th>Blood Pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Right frontal parasagittal</td>
<td>44</td>
<td>Spastic monoplegia lt. leg</td>
<td>51</td>
<td>7</td>
<td>Lt. Jackson, fits. Increased weakness lt. leg. Weakness lt. arm. Lt. hypoesthesia</td>
<td>140/90</td>
</tr>
<tr>
<td>2</td>
<td>Left parietal parasagittal</td>
<td>26</td>
<td>Hypoesthesia rt. hand</td>
<td>35</td>
<td>9</td>
<td>Motor aphasia. Weakness lt. arm &amp; leg. Sensory ataxia. Dimin. urin. control</td>
<td>105/65</td>
</tr>
<tr>
<td>4</td>
<td>Left parietal parasagittal</td>
<td>40</td>
<td>Mild lt. hemiparesis</td>
<td>48</td>
<td>8</td>
<td>Headache. Petit mal. Muscle twitches rt. arm. Increased rigidity rt. extremities</td>
<td>110/85</td>
</tr>
<tr>
<td>5</td>
<td>Right frontal falx</td>
<td>40</td>
<td>? Lt. hemiparesis (objective)</td>
<td>52</td>
<td>12</td>
<td>Fits lt. arm. Difficulty walking. Motor aphasia</td>
<td>130/80</td>
</tr>
</tbody>
</table>

**Fig. 1. Case 5.** Patient had onset of focal neurological manifestations 12 years after successful extirpation of a (rt.) frontal falx meningioma. (A, B) Air encephalogram demonstrating atrophic dilation of right lateral ventricle, most pronounced in immediate vicinity of the old operation. (See Fig. 1 C.)
abilities. It is difficult to imagine how an operative scar, healed and quiescent for years, could affect neighboring brain tissue to such a degree as to produce relatively severe neurological disorders. It is equally hard to conceive of the existence of a new pathological process that by chance happened to involve the old operative site. If neither of the two possibilities offers a satisfactory explanation, perhaps their combination may lead to a solution. The area already "potentially" devitalized by surgical attack, is more precarious than any other part of the brain to a "new" generalized cerebral pathology. If we remember that one of the main consequences of any major operation is interference with the blood supply of neighboring tissues (through ligation, traumatic thrombosis or compression of vascular channels), an interference which need not result in necrosis or gangrene, but may be compensated for (through collateral circulation) and thus remain "potential"; and if we remember that the most common "new" pathological process that affects human tissues as years pass by is arteriosclerosis, then a true inference could be reached.

It is our opinion that development of progressive vascular insufficiency of the aging process, i.e., "arteriosclerosis," will rob enough blood from the already potentially devascularized cerebral tissue in the immediate vicinity of the old operative scar to precipitate ischemia and secondary parenchymal (neuronal) damage.

Before the "late post-meningioma syndrome" is described further, a discussion of certain clinical and pathological points is necessary to obtain an "all-round" picture concerning the pathogenesis of the condition.

Oclusion of Cerebral Arteries and Arterioles during Operations for Brain Tumors. Surgical excision of a brain tumor entails the occlusion, through clipping and diathermic coagulation, of a good number of arteries and arterioles. That such occlusion deprives some part of the healthy brain tissue left behind in the immediate neighborhood of the operative field of its blood supply, is proved by the frequent postmortem finding, in patients operated upon recently, of areas of patchy necrosis (softening) along or near the edge of the excised part. It is certain that beside these areas of apparent softening, more extensive areas exist, the blood supply of which is either partly occluded or is efficiently carried out through an adequate collateral circulation. In both conditions, a state of "latent vascular insufficiency" exists.

If we remember that more vascular elements are clipped and cauterized during operations on meningiomas than on any other intracranial neoplasm, it is clear that a wider area of potential vascular insufficiency will result. Moreover, the grey matter of the cerebral cortex is more sensitive to anemia and anoxia than other areas of the brain. It is the vascular elements of the cerebral cortex that sustain the main brunt of an operative attack on a meningioma. Lastly, if the neighboring cerebral cortex happens to be the motor or sensory area, as was the case in our 5 patients, it is evident how occlusion of a small artery could lead to, immediate or late, profound neurological disturbances.

Cerebral Vascular Insufficiency of the Aging Process. A consideration of this wide problem is beyond the scope of the present paper. However, certain points bearing on the subject of our present discussion will be expressed briefly.

Cerebral vascular insufficiency is a term used by Corday et al. for the explanation of "some types of localized cerebral encephalopathy." The term is now used more
widely.\textsuperscript{2,7,14} We found it more adequate for our purpose.

Atherosclerotic changes are found to involve the cerebral arteries at an early age. Moosy,\textsuperscript{12} who studied the cerebral vascular system in 122 bodies of different ages, found no evidence of cerebral atherosclerosis in cadavers below the age of 20 years. From the third decade onward all bodies examined showed some degree of atherosclerosis. “Though the range of variation in quantitative severity was quite great within the fourth through the tenth decades, it was not necessarily correlated with chronological age.”

The stems of the main arteries, i.e., internal carotid and vertebral, are the most frequently and heavily affected. Arteries of the cerebral convexity are the least affected.\textsuperscript{11,13,16}

The effect of these vascular pathological changes is not only to reduce the total amount of blood supplied to the tissues, but also to slow down the vascular flow, thus doubling the injurious effect on the sensitive ganglion cells. It is this slowing down of the cerebral circulation, so well demonstrated in serial angiography,\textsuperscript{18} that represents the chief danger to an already established collateral circulation. The damming up of the blood flow to cortical ganglion cells supplied only through long small collateral vessels, often will be enough to disturb the balance and precipitate ischemia. Visintini and Macchi\textsuperscript{19} after stating that “Anastomotic circulation forms with greater difficulty in elderly subjects and in patients with atherosclerosis; this being more true for collateral circulation . . .,” added further that “ . . . in zones formerly supplied by the occluded vessel and subsequently by the collateral circulation, the circulatory rate is always slower.” Brobeil and Lowes\textsuperscript{4} found that the cerebral arteriosclerotic process prevented the proper function of the collateral circulation in the brain.

“Atherosclerosis” as Determining Factor in Development of Ischemia in Tissues Already Partly Devascularized. It is an every-day observation that young patients tolerate vascular occlusions much more smoothly than elderly ones. While major arterial ligation (common and internal carotid, axillary, femoral, etc.) carries a low morbidity and mortality in the young-age groups, the corresponding figures are much higher the older the patient.

At the same time, an organ with its principal blood supply impeded through a traumatic or pathological process may survive such an insult (through collateral supply), but succumb later on as the vascular insufficiency of the aging process sets in (to occlude the collateral vessels). A leg with obstruction of the femoral artery during youth by thromboangiitis obliterans, may start to show manifestations of ischemia many years later as atherosclerosis begins to involve the collateral supply.\textsuperscript{4} An interesting case of ligation of the left internal carotid artery that was followed 35 years later by onset of right hemiplegia and hemianesthesia will be reported briefly.

A 22-year-old soldier in the French frontier sustained in 1918 a penetrating bullet injury through the left side of his neck. The entrance was on the posterior aspect just to the left of the midline and the outlet overlay the left carotid triangle anteriorly. The missile injured both the spinal cord and the left internal carotid artery. Left hemiparesis and hemihyposthesia resulted from the spinal injury, while an operation to ligate the left internal carotid artery in the neck was carried out as soon as the patient reached the hospital.

Thirty-five years later, at the age of 57 years, there was onset of gradual weakness, hypotesia and unsteadiness of the right side of the body. These new manifestations overwhelming a patient already suffering from left hemiparesis, gradually led the poor victim to complete incapacity. Left carotid angiography (Fig. 2) demonstrated the smooth dome-shaped proximal segment of the completely ligated left internal carotid artery, while right carotid angiography succeeded in filling the anterior and middle cerebral arteries on both sides.

Cerebral Circulation and Low Blood Pressure. It is not a coincidence that 2 of our patients were hypotensive, while the other 3 had systolic tensions rather below those calculated for their age.

One of the important factors necessary for
a normal blood supply to the brain is sufficient blood tension. "The blood circulation follows the blood pressure as a dog follows its master." The importance of maintaining an adequate blood tension for the management of all grades of cerebral ischemia is emphasized by many authors. Alman and Fazekas' found that a drop in blood pressure beyond a certain level caused the appearance of abrupt severe symptoms in patients with cerebral atherosclerosis. Shanbrom and Levy found that a fall of blood pressure averaging 43 mm. Hg systolic and 19 mm. Hg diastolic would cause focal neurological manifestations in patients with carotid or vertebral thrombosis. Corday and Rothenberg stated that in the presence of systolic hypotension or reduced cardiac output, the collateral circulation of the brain fails to supply the requirements of the cerebral tissue in which arterial flow has been compromised. Brain concluded that transitory attacks of ischemic nature in association with cerebral atheroma are probably dependent on temporary falls in blood pressure.

It is clear that a low blood pressure if associated with a progressive vascular insufficiency will constitute a most deleterious combination for a functioning collateral circulation.

**DISCUSSION**

An analysis of our 5 cases, leading to consideration of the salient characteristics of the "late post-meningioma syndrome," is as follows.

**Type and Site of Tumor.** All 5 tumors were hemispherical meningiomas: 3 parietal and 2 frontal. Four were parasagittal and 1 was a meningioma of the falx. There were 3 left-sided and 2 right-sided growths.

**Sex.** Four patients were males, and 1 was a female.

**Age at Onset.** With 1 exception, the age of the patients at onset of the "new" manifestations varied between 48 and 52 years. Case 2 was only 35 years old when he started to complain for the second time.

**"Quiescent" Interval.** The interval between the operative attack and the appearance of the first "new" symptoms varied between 7 and 20 years. This interval was not a symptom-free period, since the operation had left some, though minimal, neurological deficit. The interval comes to an end when new manifestations begin to be superimposed on the "basic" postoperative residual symptoms.

**Clinical Manifestations.** Following a gradual onset, the clinical course either remains stationary or proceeds very slowly. Jacksonian fits were the first new clinical symptoms in 3 cases. Headache associated with attacks of petit mal was the mode of onset in 1 patient, while motor aphasia preceded other complaints in the patient 35 years old.

Signs of an upper motor neuronal lesion stood in the foreground of the clinical picture in all 5 cases. Though 3 tumors had a parietal localization, frank sensory disturbances in the form of hemihypoesthesia were manifest only in a single case, a frontal meningioma! Sensory ataxia was a late appearance in 1 case.

**Blood Pressure Readings.** Two patients were definitely hypotensive (Cases 2 and 4). One patient had a quite low blood pressure (Case 3) while the remaining 2 patients had systolic blood pressure readings definitely below those expected for their corresponding ages (Cases 1 and 5). The significance of such low readings has been expressed heretofore. Moreover, the pulse pressure was as low as 25 mm. Hg in 2 patients (Cases 3 and 5). In no case was the pulse pressure higher than 50 mm. Hg. The significance of these latter findings could easily be predicted when we
remember that the pulse pressure represents the main force that drives the blood through the vascular system, including all the delicate collateral circulation.

EVALUATION OF THE "LATE POST-MENINGIOMA SYNDROME"

Many years after excision of a meningioma, a patient is liable to the development of recurrent or new focal neurological manifestations related to the site of the old operation. This clinical entity, which we have referred to as “the late post-meningioma syndrome,” is caused neither by a neoplastic recurrence nor by the effect of the operative attack. We have put forward evidence to point out that the syndrome probably is the result of the advent of progressive vascular insufficiency of the aging process working through diminishing and slowing down of the blood flow through the collateral vessels supplying the already devascularized areas in the immediate neighborhood of the operation. The additive action of a low blood pressure in further jeopardizing the attenuated blood flow may also have a determining role.

The condition seems to have a special predilection to follow the excision of tumors related to the Rolandi fissure, especially to its posterior lip. However, it is certain that the syndrome can follow the removal of meningiomas at other sites; it is only the “vividly symptomatic” nature of both motor and sensory cortices that aids in bringing more patients with frontal and parietal parasagittal meningiomas into view. Moreover, it is conceivable that a similar clinical picture can follow excision of other intracranial tumors in patients with long-life expectancy.

As far as could be deduced from a material composed of only 5 cases, the condition is found more commonly in men than in women (4:1). The critical age for the development of the syndrome is 50 years (±2 years), but symptoms may start as early as the age of 35 years.

Based as it is on a probable progressive vascular insufficiency, it is no wonder that the first reaction of the cortical ganglion cells to anoxia would be irritation to be followed later on by paralysis. Jacksonian fits usually herald the clinical picture, followed rather rapidly by paralytic manifestations. Aphasia, unilateral sensory ataxia, weakness of urinary control and hypoesthesia are possible late disturbances. Obviously the clinical picture will differ when the condition follows the removal of meningiomas in other localities.

When confronted with a patient in his late forties or early fifties, who had removal of a parasagittal meningioma 10 or 20 years earlier, complaining of new epileptic fits followed by paralytic manifestations and who is found to have a low or rather low blood pressure, the diagnosis of the late post-meningioma syndrome is very probable. A signal of warning, however, is to be added: the syndrome should never be diagnosed before a full neurological investigation, including electroencephalography, air encephalography and carotid angiography, is carried out to exclude recurrent neoplasia.

In addition to rehabilitative measures, the treatment should be directed towards improving the cerebral vascular tone and blood flow. Special attention should be paid to maintenance of an adequate blood pressure.

Finally, the same pathological process might be responsible for some of the so-called “late post-traumatic complications,” generally attributed to post-traumatic “atrophy” or “porencephaly.”

SUMMARY

Focal neurological manifestations, not caused by the operation or by neoplastic recurrence, might begin many years after successful removal of a meningioma. Cerebral vascular insufficiency of the aging process and the local devascularization resulting from the old operation, together with the additive action of a low blood pressure probably combine in bringing about the condition.

This late post-meningioma syndrome tends to follow the removal of parasagittal
meningiomas related to the Rolandic fissure in men approaching or just passing the age of 50.

Five cases are reported and discussed.

REFERENCES


