Hemispherectomy for intractable seizures: long-term results in 17 patients followed for up to 38 years

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Seven patients who underwent hemispherectomy for intractable epilepsy between 1950 and 1971 were reviewed to evaluate outcome for seizure control and the development of late complications. Sixteen had complete resection and in one the frontal pole was preserved. The follow-up period was 19 to 38 years (mean 28 years). One patient was lost to follow-up review 10 years after surgery. Three patients had died but none of the deaths were related to the surgery or to epilepsy. Ten patients had no postoperative complications, and three developed late complications: two had elevated intracranial pressure with enlargement of the remaining lateral ventricle after 13 and 16 years, and one had recurrent bleeding into the cerebrospinal fluid after 6 years. All were treated surgically and have since remained well. Eight patients (47%) had no seizures after surgery and eight (47%) were almost seizure-free. It is concluded that classical hemispherectomy is an effective operation for control of some types of epilepsy. The late complications, which occurred in 17% of the cases in this series, can be successfully treated. This series presents the longest follow-up results after hemispherectomy reported to date.

KEY WORDS • hemispherectomy • epilepsy • infantile hemiplegia • cerebral palsy

The operation of hemispherectomy, which is in essence cerebral hemidecortication, was introduced in the 1920's by Dandy and L'Hermitte in an attempt to improve treatment of gliomas of the nondominant cerebral hemisphere. However, the results, even with such a radical procedure, proved not to be curative. Williams and Scott cite McKenzie's 1938 work as the first application of the procedure to the management of intractable seizures in infantile hemiplegia. It was not until 1950, when Krynauw reported 12 cases with excellent short-term results for control of seizures and behavioral disturbances, that interest in the procedure for intractable epilepsy in patients with unilaterally damaged hemispheres was really stimulated. Many reports have subsequently confirmed the efficacy of the operation in this regard. Some patients demonstrated a period of insidious deterioration ending in death. Autopsy findings included superficial hemosiderosis of the brain and spinal cord, enlargement of the remaining lateral ventricle, and the presence of a membrane similar to that found in a chronic subdural hematoma lining the cavity and the walls of the remaining ventricular system. These complications were reported to occur as soon as 1 year and as late as 20 years after surgery. The incidence of late hemorrhagic complications was reported to be between 18% and 35%, and the mortality rate was high. For example, Wilson reported 50 cases of cerebral hemispherectomy with a mortality rate for the series of 32%.

In order that such an effective operation should not be abandoned, modifications to the technique were developed by Adams and Beardsworth, Rasmussen, and others; these have been reported to reduce the incidence of late complications while preserving the efficacy of the operation for seizure control. Others have recommended corpus callosum section as an alternative surgical treatment for seizures in cases of infantile hemiplegia. Although this operation has less risk of long-term complications, it is considerably less successful at completely abolishing seizures. Stimulated by these reports, we reviewed the cases of 17 patients who underwent hemispherectomy at the...
University of Minnesota between 1950 and 1971. All of these patients had the "classic" unmodified operation. A shorter-term review of eight of these cases has been reported previously.7,8

Clinical Material and Methods

Patient Population

Between March, 1950, and April, 1971, 17 patients with medically intractable epilepsy underwent hemispherectomy at the University of Minnesota Hospitals. Details of the patients are given in Table 1. Eleven were male and six female. Age at surgery varied from 3 years to 38 years (mean 18 years). There were nine right-sided and eight left-sided procedures.

The etiology of the seizure disorder (Table 1) was birth trauma in seven cases; two patients had intrauterine occlusion of the middle cerebral artery. Five patients suffered an episode of cerebral inflammation in early childhood, one had Sturge-Weber syndrome, and one exhibited a large hemispheric arteriovenous malformation (AVM). The age at which seizures began ranged from 1 week to 26 years (mean 3.9 years). The first patient in the series (Case 1) had undergone glioma resection 12 years previously and subsequently suffered persistent seizures; no evidence of recurrent or residual tumor was found at the time of hemispherectomy. Three other patients had previously undergone craniotomy. One of these (Case 10) had a craniotomy and exploration of a large hemispheric AVM without resection in 1948. Two temporal lobe resections were performed on Case 13 in 1954 and 1957, and two cortical resections on Case 14 in 1958 and 1959; in neither of these patients did the seizure condition improve after these operations.

Preoperative Evaluation

Preoperative evaluation included cerebral angiography, pneumoencephalography, and electroencephalography. A representative air study obtained in Case 7 is shown in Fig. 1. The right lateral ventricle is dilated, compatible with cerebral atrophy on that side.

Operative Technique

The operative technique was similar in each case. A large craniotomy flap was turned. The middle cerebral and anterior cerebral arteries were ligated after ensuring that the opposite anterior cerebral artery was competent. The posterior cerebral artery was ligated about 1 cm from its origin. The veins entering the dural venous sinuses were then divided and the corpus callosum sectioned. The lateral ventricle was entered and the sylvian terminals visualized and incised so that the caudate nucleus was separated from the thalamus. The dissection was taken down to the internal capsule to emerge at the incisura (Fig. 2). A wedge of tentorium was often removed, exposing an area of the cerebellum, thereby enlarging the incisura to facilitate drainage from the cavity. The choroid plexus was routinely coagulated and destroyed. The extent of the hemispherectomy varied a little from case to case regarding the quantity of basal ganglia removed; however, in one patient (Case 16) the frontal pole was preserved. The entire cortex was removed including insula, hippocampus, amygdala, and inferior orbital gyri. Figures 3, 4, and 5 illustrate the operation and typical specimens.

Results

To obtain information for this report, the charts for each case were reviewed. A typical postoperative computerized tomography (CT) scan is shown in Fig. 6. The patients themselves or their nearest relatives were contacted by telephone. It was possible to contact the patient or relatives in 14 of the 17 cases. Relatives of two of the patients who had died (Cases 5 and 9) could not be reached. One patient (Case 1) was lost to follow-up review 10 years after surgery; at that time, he was
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FIG. 1. Pneumoencephalogram, anteroposterior projection, in Case 7 showing dilatation of the right lateral ventricle consistent with cortical atrophy on that side.

FIG. 2. Drawing showing the extent of resection of brain tissue in Case 6 (cross-hatched area). The thalamus is preserved.

FIG. 3. Photograph showing the operative field in Case 15, with the right hemisphere exposed. Evidence of scarring is seen at the posterior end of the sylvian fissure.

FIG. 4. Photograph showing the lateral aspect of the excised hemisphere from Case 4. There is evidence of frontal scarring. The dark areas are due to intraoperative hemorrhage.

FIG. 5. Photograph showing the medial aspect of the excised hemisphere from Case 4.

FIG. 6. Axial computerized tomography scan of Case 7, obtained 37 years after surgery, showing the right-sided hemispherectomy cavity. There is modest dilatation of the left lateral ventricle. Cranial asymmetry is evident.
alive and well and reported no further seizures. The longest follow-up period was 38 years and the shortest for a patient known to still be living was 19 years (mean 28 years, median 32 years) (Table 2).

Mortality

At follow-up review, three patients had died (Table 2), but none of these deaths was related to the surgery. One (Case 5) died of diphtheria 13 months following surgery, another (Case 6) died of chronic renal failure due to diabetes 36 years postoperatively, and the third (Case 9) died 24 years after surgery from necrotizing encephalitis of the remaining hemisphere, presumed to be herpetic although inclusion bodies were not identified in the brain at autopsy.

Early Complications

Ten patients had no complications due to the surgery (Table 2). There were three instances of early complications. One patient (Case 4) developed an axillary artery thrombosis in his nonparietal arm related to an arterial line placed at the time of surgery. This resulted in weakness of the arm which has persisted to this day. Two patients had bone flap infections, one of which (Case 16) was successfully managed by debridement and secondary closure of the wound. The other (Case 10) required removal of the bone flap. A subsequent tantalum cranioplasty eventually became infected, necessitating removal and leaving her with a cranial defect.

Late Complications

There were late complications in three cases. One patient (Case 14) developed recurrent bleeding into the cerebrospinal fluid (CSF) 6 years after surgery. A complaint of severe headaches and repeatedly bloody lumbar CSF samples led to an angiogram being performed, which demonstrated a subdural hematoma on the left (the side opposite to the previous surgery). Drainage of this provided very little improvement. Ventriculography suggested no communication between the right-sided cavity and the remaining ventricles, and the craniotomy flap on the right was reopened. The cavity was found to be lined with a thick membrane and was filled with straw-colored fluid. There were also areas of vascular fibrinous proliferation along the falx. In an attempt to obliterate the cavity, the convexity dura was infolded and sutured down on itself along the falx and to the membrane medially. Histological examination of the membrane revealed highly collagenous granulation tissue. The tissue was dense and poorly cellular in some areas and looser and more cellular in others. There were rare hemosiderin-laden macrophages. Since this procedure, the patient has experienced no further problems.

Three patients developed increased intracranial pressure (ICP) with enlargement of the lateral ventricle. Case 9 was investigated for deteriorating neurological status in 1973, 16 years after surgery, and ventriculography showed partial obstruction at the aqueduct of Sylvius. She responded well to insertion of a ventricular-atrial shunt. She subsequently had two shunt revisions and died 8 years later (in 1981) of encephalitis. At autopsy, there was a large cavity on the right lined by a thick membrane. Leptomeninges were fibrotic and there was hemosiderin staining at the base of the brain. Evidence of gliosis was found in the medulla,pons,thalamus, and head of the caudate nucleus. The aqueduct and fourth ventricle were obliterated. The left cerebral hemisphere was swollen, with evidence of ten-
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torial herniation, and the temporal lobe was soft and discolored. Microscopically, there was extensive necrotizing encephalitis of the temporal lobe.

Another patient (Case 12), operated on at the age of 13 years, had evidence of elevated ICP in 1972, 13 years after left hemispherectomy. He had sustained a minor head injury in a motor-vehicle accident 3 years previously. Ventriculography demonstrated an enlarged lateral ventricle, no communication with the left-sided cavity, and obstruction at the aqueduct. At the time of the shunt insertion, a left frontal burr hole was made and a biopsy taken of the parietal and visceral membranes that were noted to line the cavity. The former showed “dense, poorly cellular connective tissue” and the latter a “greater amount of hemosiderin pigment scattered throughout the membrane.” The patient has had no further problems and has required no shunt revisions.

The third patient with elevated ICP (Case 13) sustained a severe head injury at work 21 years after a left hemispherectomy. He was unconscious for 3 days and made a slow recovery, with somnolence being a prominent feature. A CT scan revealed enlargement of the right lateral ventricle. A ventriculoperitoneal shunt produced dramatic clinical improvement. Since then, he has required one shunt revision but otherwise there have been no further problems. It seems likely that the head injury was the major precipitating factor for the enlarged ventricle and the clinical picture.

Motor Function

None of the patients experienced an increase in their preoperative hemiparesis due to the surgery. All patients remained fully ambulatory for the duration of their follow-up period.

Language Evaluation

Initially, intracarotid Amytal (amobarbital) tests were not carried out on the patients undergoing left-sided resection, but later in the series five patients were tested. Testing in one patient (Case 12) was unsuccessful. Of the four patients successfully tested, three were shown to have right-sided hemisphere dominance for language and one had mixed dominance. This patient (Case 10) had dysphasia postoperatively and continues to have expressive and receptive difficulties. The pathology in this case was a large left hemisphere AVM.

The first patient in the series was dysphasic following resection of a glioma 12 years prior to his hemispherectomy, and the deficit was not increased after the hemispherectomy. None of the other patients have had language problems postoperatively.

Seizure Control

Table 2 shows the preoperative and postoperative monthly seizure frequency. Prior to surgery, seizure frequency varied between one every 2 months to over 200/month. Most patients had at least ten seizures/month. Following surgery, eight patients have had no seizures; six of these were still taking antiepileptic medications at the time of follow-up review. One patient (Case 5) continued to have frequent seizures after surgery until she died 13 months later of diphtheria. Another (Case 11) had a single seizure 10 days after surgery and has had none since. A third patient (Case 13) had one seizure immediately after a severe head injury sustained 21 years after surgery; apart from this, he has had none. Two patients have had a total of two seizures since surgery and two reported having a “few” seizures, representing less than one per year. One patient (Case 9) had a seizure 16 years after surgery when she presented with hydrocephalus. At the time of latest review, 13 of 16 patients were still receiving antiepileptic medication.

Employment Status

Ten patients have become employable since surgery, usually in a sheltered setting (Table 2). Six patients have led independent lives and six have lived protected existences with their families. Three have been semi-independent, living in community homes with other disabled people.

Discussion

Seizure Control

The results of hemispherectomy for seizure control are so good that the operation has been called the best procedure available for treating epilepsy. For example, Wilson reported that, of 50 patients operated on by McKissock, epilepsy was completely or substantially relieved in 82%. Rasmussen described 29 cases with a follow-up period of 11 years; of these, 48% were seizure-free after surgery and a further 37% had a marked reduction in seizure frequency. The results reported here show a similar experience. A good result was obtained in all but one of 17 patients (94%). Eight patients (47%) have been totally free of seizures since surgery and eight (47%) almost seizure-free. Two of this latter group have had only one seizure each in 30 years of follow-up monitoring, one soon after surgery and one precipitated by a severe head injury. Only one patient continued to have frequent seizures before dying of diphtheria 13 months postoperatively.

Case Selection

A previously damaged hemisphere is a prerequisite for undertaking the procedure. Most patients have had an infantile cerebral hemiatrophy; in 75% of these the damage occurred in utero or perinatally and in 25% in early childhood. The insult may be hemorrhage, thrombosis, traumatic softening, or infectious encephalitis. Occasionally, the operation has been undertaken for congenital disorders such as Sturge-Weber syndrome and hemimegalencephaly as well as for chronic idiopathic progressive unilateral hemisphere inflammation (Rasmussen syndrome). Spastic hemiparesis is invariably present and often homonymous hemianopsia. If hemianopsia is not present prior to surgery, the resection will produce a completely homonymous field defect but otherwise the neurological deficit should not be increased.

If the damaged hemisphere is the left and the insult
has occurred in the first years of life, language function may be expected to have transferred to the right hemisphere. Thus, in three of four cases in our series in which an intracarotid sodium Amytal test was successfully performed, language was represented on the right; in only one patient (Case 10), where the pathology was a vascular malformation and where the surgery was performed at 26 years of age, was some language preserved on the left. Apart from this patient, no others in the series were rendered dysphasic by the surgery. Wilson reported that six patients, five of whom had left-sided resections, developed dysphasia postoperatively and in half of these the deficit was permanent.

Late Hemorrhagic Complications

Late hemorrhagic complications have been reported to occur as early as 1 year and as delayed as 20 years after surgery. The clinical picture is one of neurological deterioration, mental slowing, somnolence, tremor, ataxia, and evidence of elevated ICP. There may be repeated headaches and meningismus in instances where there is intermittent bleeding into the CSF.

The typical pathological features of late hemorrhagic complications have been described in detail by Oppenheimer and coworkers. A hemorrhagic membrane lining the hemispherectomy cavity is described. It lines the dura and the remaining basal ganglia and communicates with the third ventricle through the foramen of Monro. Second, the ventricular system is lined with granular ependymitis consisting of a proliferative layer of fibroglia covering the ependyma with a layer of subependymal gliosis. This obstructs the aqueduct or exit foramina of the fourth ventricle. Third, in the subdural space there is superficial siderosis causing brown staining of the brain stem, cerebellum, and spinal cord.

Essentially, the cavity appears to behave in the same way as a large subdural hematoma except that, unlike a subdural cavity, it communicates with the ventricles and CSF through a patent foramen of Monro. The mechanism for development of late complications is therefore presumed to be that the vascular membrane bleeds, either spontaneously or as a result of minor trauma, and blood passes through the patent foramen of Monro into the remaining ventricles. Deposition of blood on the ependyma produces the typical granular ependymitis and eventually gliosis, which then obstructs the aqueduct or exit foramina of the fourth ventricle and results in increased ICP with enlargement of the remaining ventricular system. Pial deposition produces superficial hemosiderosis which is particularly harmful to the cerebellum, brain stem, and eighth cranial nerves.

The incidence of late hemorrhagic complications has been reported to be between 18% and 35% and has been noted to carry a high mortality rate. Thus, death occurred in 10 of 15 cases with intracranial hemorrhage and in two of three cases with hydrocephalus reported by Wilson.

Surgical Procedure

In the classic operation, as originally described by Krynowa, the hemisphere cortex was removed in four segments working from within the lateral ventricle. The middle cerebral artery was taken lateral to the anterior perforated substance and the choroid plexus was coagulated. The thalamus as well as the head and tail of the caudate nucleus were preserved. Other surgeons advocate removal of all or part of the caudate nucleus and claim equally good results. The foramen of Monro was left patent. Essentially, this was the procedure performed in all patients in our series, apart from one in whom the frontal pole was preserved.

In an attempt to reduce the incidence of late complications, two principal modifications to the operative technique have been advocated, each taking a different approach. Rasmussen, et al., apparently influenced by the mechanics of the development of these complications and noting that they did not occur with subtotal hemisphere resections, argued that lack of support by the absent hemisphere resulted in the remaining brain being susceptible to repeated jolting and hence intermittent bleeding. Their solution was preservation of the frontal and occipital poles to ensure support of the remaining brain while cutting the white matter connections with the other side to produce an anatomically incomplete but functionally complete hemispherectomy. They called this a "functional" hemispherectomy. No attempt was made to occlude the foramen of Monro. At the time this technique was reported, there were no late complications, but the follow-up period was relatively brief.

Adams took a different line, impressed more by the pathological findings. Since the complications arise mainly from the passage of blood into the circulating CSF, he maintained that there should be two objectives. The first is to prevent formation of hematoma in the cavity, and the second is to deny access of any blood to the ventricles. Thus, he recommended meticulous hemostasis at the time of the operation to reduce the likelihood of hematoma formation, then reduction of the volume of the subdural space and the exposed surface area of dura by suturing the convexity dura down to the falx, tentorium, and dura lining the floor of the anterior and middle cranial fossae, thereby creating a large extradural space (this latter innovation was, in fact, first proposed by Wilson). Third, the cavity is insulated from the ventricles by obstructing the foramen of Monro with a plug of muscle and ensuring the integrity of the septum pellucidum. Consequently, the choroid plexus should be destroyed to discourage CSF formation in the now closed cavity. Results so far are encouraging, with no deaths and complete cessation of seizures in 70% of cases. No hemorrhagic complications have been noted, but as yet the reported follow-up period is only 7 years.

Several authors have emphasized that the late hemorrhagic complications of hemispherectomy, once developed, should be remediable and need not produce a relentless decline in condition. Falconer and Wilson successfully treated four patients with late hemorrhagic complications by surgical evacuation of the hematoma and lavage of the cavity. Wilson subsequently enunciated the principles of treatment: removal.
of products of hemorrhage and correction of secondary hydrocephalus with shunting.

Three patients in our series had evidence of late complications, representing 18% of the cases. One of these (Case 14) had repeated bleeding into the CSF and evidence of recent hemorrhage into the cavity 6 years after the hemispherectomy. Another (Case 9) had obstructive ventricular enlargement treated with a shunt 16 years after hemispherectomy. At autopsy 8 years later, there was evidence of cerebral hemosiderosis, although it was not the cause of death. She had remained well following placement of a shunt soon after elevated ICP was diagnosed. The third patient (Case 12) had obstructive hydrocephalus 13 years postoperatively and has remained well since placement of a ventriculoperitoneal shunt. The elevated ICP and ventricular enlargement in another patient (Case 13) was likely a consequence of a subsequent severe head injury, although the fact that he had a hemispherectomy may have predisposed him to develop hydrocephalus. All were treated promptly for their complications and suffered no further neurological deterioration.

Conclusions

We believe that the incidence and severity of late hemorrhagic complications after hemispherectomy may have been overestimated and that the classic operation, without modifications, is an effective and relatively safe one. Meticulous attention to hemostasis at the time of surgery, as emphasized by Adams,1 and drainage of the cavity for several days to ensure minimal collection of blood products within it, as practiced in our neurosurgical unit now, may minimize the risk of hemorrhagic complications. Prompt shunting of hydrocephalus when it develops should also pre-empt deterioration.

Cases suitable for hemispherectomy are less abundant than they were 40 years ago due to advances in obstetrical care, but we believe that in suitable cases the operation can be recommended enthusiastically with the expectation of good results for seizure control. Furthermore, in the event of the development of late complications, suitable surgical measures are available to prevent any deterioration.

References

23. Paillas JE, Vigroux R: Considerations sur les hemispherectomies; a propos de 9 observations. Neurochirurgie 2:441-446, 1956


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