Unilateral germinomas involving the basal ganglia and thalamus

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Clinical characteristics of six cases of germinoma involving a unilateral basal ganglion and thalamus are summarized. The incidence was estimated as 10% of all intracranial germinomas. The average age at the onset was 10.5 years. The sex incidence showed a male dominance. The clinical course was slowly progressive, and the average duration between onset and diagnosis was 2 years 5 months. Common symptoms and signs were hemiparesis in all cases, fever of unknown origin and eye symptoms in most, mental deterioration and psychiatric signs in three, and convulsions, pubertas praecox, and diabetes insipidus in two. Signs of increased intracranial pressure were found in only two cases in the later state of the disease. Early diagnosis is difficult because of nonspecific symptomatology and slow progression. Carotid angiography and pneumoencephalography showed abnormal findings compatible with basal ganglia and thalamic tumors, but not specific to germinoma. Ipsilateral cortical atrophy and ventricular dilatation might be significant findings. Radioisotope scanning was useful. Computerized tomography scans were the best method of detecting the location and nature of this tumor, and repeat scans showed response to radiation therapy.

KEY WORDS • intracranial germinoma • basal ganglia • thalamus • radiation therapy

Over the years, there have been occasional case reports of unusual localization of intracranial germinoma other than in the pineal and suprasellar (chiasmatic) regions. We are reporting six cases of germinoma arising from the basal ganglia and/or thalamus of one side, without the demonstrable coexistence of any common midline tumors.

Clinical Material

Between 1965 and 1978, 40 cases of intracranial germinoma were treated in our department. These were classified into three groups according to tumor localization. Twenty-eight were in the pineal region, and all the patients harboring them were males between 5 and 34 years of age (mean 15.2 years). Eight of the 40 patients had suprasellar germinomas; of these, three were male and five female between 6 and 15 years old (mean 10.5 years). Four male patients, between the ages of 8 and 12 years (mean 10.5 years), were treated during this time for germinoma in the basal ganglia and thalamus (Table 1).

This paper reports six cases of ectopic pinealoma in the basal ganglia and thalamus: the four patients mentioned above and two other cases treated prior to 1965. Clinical data of the cases are summarized in Table 2.

<table>
<thead>
<tr>
<th>Location</th>
<th>Cases</th>
<th>Sex</th>
<th>Age (yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pineal region</td>
<td>28</td>
<td>70</td>
<td>28</td>
</tr>
<tr>
<td>Suprasellar region</td>
<td>8</td>
<td>20</td>
<td>3</td>
</tr>
<tr>
<td>Basal ganglia &amp; thalamus</td>
<td>4</td>
<td>10</td>
<td>4</td>
</tr>
</tbody>
</table>
Table 2
Clinical summary in six cases of germinomas in the basal ganglia and thalamus

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age at Onset (yrs), Sex</th>
<th>Duration Onset to Admission</th>
<th>Signs &amp; Symptoms*</th>
<th>Location of Tumor</th>
<th>Treatment</th>
<th>Follow-Up Period &amp; Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8, M</td>
<td>3 yrs</td>
<td>rt hemiparesis, lt ptosis, mental deterioration, mutism, akinesia, fever, aphonia, &amp; pubertas praecox</td>
<td>lt thalamus</td>
<td>craniotomy &amp; biopsy; shunt; radiation (4000 rads)</td>
<td>1 yr: fair</td>
</tr>
<tr>
<td>2</td>
<td>10, M</td>
<td>1 yr 10 mos</td>
<td>lt hemiparesis, pubertas praecox, mental deterioration, polyuria, &amp; polydipsia</td>
<td>rt thalamus</td>
<td>craniotomy &amp; biopsy; radiation (5500 rads)</td>
<td>4 yrs 6 mos: excellent</td>
</tr>
<tr>
<td>3</td>
<td>10, M</td>
<td>2 yrs 10 mos</td>
<td>rt hemiparesis, mental deterioration, lt oculomotor palsy, &amp; fever</td>
<td>lt thalamus, hypothalamus</td>
<td>radiation (3400 rads)</td>
<td>1 yr 6 mos: good</td>
</tr>
<tr>
<td>4</td>
<td>12, M</td>
<td>4 yrs 6 mos</td>
<td>lt hemiparesis, polyuria, polydipsia, drowsiness, fatigue, mental deterioration, &amp; reduced visual acuity</td>
<td>rt thalamus, hypothalamus</td>
<td>craniotomy &amp; partial removal; radiation (4000 rads)</td>
<td>6 mos: dead</td>
</tr>
<tr>
<td>5</td>
<td>11, M</td>
<td>1 yr 4 mos</td>
<td>lt hemiparesis, convulsions, character change, fever, visual cut, raised ICP</td>
<td>rt thalamus</td>
<td>ventricular drainage; craniotomy &amp; partial removal; radiation (6000 rads)</td>
<td>18 yrs 6 mos: fair</td>
</tr>
<tr>
<td>6</td>
<td>12, M</td>
<td>3 yrs</td>
<td>lt hemiparesis, diplopia, character change, automatism, hearing loss, reduced visual acuity, raised ICP</td>
<td>lt thalamus, hypothalamus</td>
<td>ventricular drainage; craniotomy &amp; partial removal; radiation (3000 rads)</td>
<td>20 yrs 7 mos: fair</td>
</tr>
</tbody>
</table>

* ICP = intracranial pressure.

Case Reports

Case 1

This 8-year-old boy had been completely healthy until he received a head injury from falling into a well in 1975. He then began to have involuntary movements of his right hand. During the next year he gradually developed right hemiparesis that also affected his face. He was referred to a neurologist in 1976, who reported that a carotid angiogram and computerized tomography (CT) scan were normal. The patient underwent physical rehabilitation for the hemiparesis at a hospital. Subsequently, repeat CT was performed at another medical center in May, 1977, and no abnormality was found except cortical atrophy of the right hemisphere.

He was admitted to a hospital affiliated with Nagoya University on July 19, 1977. Neurological examination revealed spastic right hemiplegia, left oculomotor palsy, mental deterioration, dysphasia, and pubertas praecox. By November, his hemiparesis had progressed. He vomited often and had right-sided convulsions. On December 8, CT and carotid angiography disclosed a subdural hematoma over the left frontotemporal convexity, and trephinations revealed 180 ml of xanthochromic fluid with a surrounding capsule. After operation, he did well for 6 months, but in June, 1978, his hemiparesis and speech deteriorated again. He became lethargic.

On September 19, 1978, CT revealed a large, irregular, enhancing mass in the left basal ganglion and thalamus (Fig. 1A and B). Left angiography showed elevation of the middle cerebral artery. Stretching and downward displacement of the anterior choroidal and posterior cerebral arteries was visible on the lateral films. The anteroposterior projections showed widening of the space between the pericallosal and middle cerebral artery, with slight shift of the pericallosal artery across the midline, and stretching and lateral displacement of the lenticulostriate arteries. Venograms revealed elevation of the internal cerebral and thalamostriate vein with shift across the midline, and downward and backward displacement of the basal vein. The patient had macrogenitalia with profuse pubic hair, but his urinary human chorionic gonadotropin (HCG), serum follicle-stimulating hormone (FSH), and luteinizing hormone (LH) levels were within normal range. Electroencephalography (EEG) showed slow activity in the left hemisphere.

A left frontotemporal craniotomy was performed on October 27, 1978. The cortex was slightly atrophic, and a subdural fluid collection was found. The mass was biopsied through the temporal lobe and diagnosed as a pinealoma of a two-cell pattern. On November 14, whole-brain irradiation using megavoltage x-rays was begun. Repeat CT scans during and after radiation therapy were made every week. The effectiveness of radiation therapy was confirmed on serial...
Unilateral germinomas of basal ganglia and thalamus

FIG. 1. Case 1. Follow-up computerized tomography (CT) scans before (A, B), during (C–F), and after (G) radiation therapy. A: Plain scan before radiation therapy shows a large, irregular mass in the left thalamic region, which is composed of isodense to slightly high-density parts, and irregular low-density areas inside or around the mass. Hydrocephalus is prominent, and the third ventricle is shifted to the right side. B: The mass is highly enhanced by contrast medium except for the low-density areas. A semilunar low-density area is found over the left frontal lobe, which corresponds to subdural fluid that collected after removal of the hematoma. C–F: A large contrast-enhanced thalamic mass decreased in size during the course of irradiation. C: At 575 rads. D: At 1150 rads the mass became nonenhanced. E: At 2050 rads. F: At 3000 rads. G: At the termination of irradiation the mass is replaced by a smaller low-density area, and the third ventricle is restored to normal.

CT scans. The high-density area corresponding to the tumor had disappeared by the time the patient had received 1150 rads, and was replaced by a localized low-density area. The size of the lateral ventricle also decreased gradually (Fig. 1C–G). The patient improved from akinetic mutism, and was able to communicate by the time the 4000-rad course of radiation therapy had finished on December 27, 1978. Physical therapy improved his hemiparesis to the point that he could walk with minor assistance, and he was discharged on February 13, 1979.

Case 2

This 10-year old boy was reported in October, 1972, to have a change of voice, growth of pubic hair, and macrogenitalia; he was also easily fatigued. No abnormality of cerebral angiograms was reported. In April, 1973, he complained of a limping gait, was often thirsty, and had polydipsia. He was referred to a university hospital where left hemiparesis was found. Four-vessel angiography was performed, but again no abnormality was noted. On August 6, 1973, the patient was admitted to the Department of Neurosurgery at Nagoya University for further examination.

Examination on admission revealed pubertas praecox, diabetes insipidus, mental deterioration, left hemiparesis, and character changes. Electroencephalography showed a delta-wave focus over the right parietotemporal region. Radioisotope technetium-99m (99mTc) brain scan revealed a higher uptake of the isotope in the right basal ganglion (Fig. 2A). A hormone assay disclosed a high serum level of LH (90 to 120 mIU/ml), but no response to LH-releasing hormone (LH-RH). The patient's serum FSH was below normal, but other hormone values were normal. Pneumoencephalography (PEG) showed asymmetry of the lateral ventricles, the right larger than the left. The third ventricle was deformed, and had shifted slightly from right to left. Right carotid angiography at this time revealed abnormal findings compatible with basal ganglia and thalamic tumors.
FIG. 2. Case 2. Radioisotope scintigrams with technetium-99m. Higher uptake of the isotope in the right thalamic region is demonstrated in the preoperative scan (A). The area of uptake is diminished on the scan taken after radiation therapy (B).

On September 5, 1973, a right frontotemporal craniotomy was carried out, and biopsy of the tumor revealed a typical two-cell pattern pinealoma. Radiation therapy was initiated on September 18, using a linear accelerator with a field large enough to cover the whole tumor region (8 x 9 cm). At the termination of the irradiation (5500 rads), the patient's mental and character changes and diabetes insipidus had disappeared. There was a diminished area of uptake on the postoperative brain scan (Fig. 2B). Hemiparesis also improved gradually. The patient was discharged on October 30, 1973, sufficiently recovered to return to school.

Case 3

In 1975, this 10-year-old boy had noticed a slight motor weakness of his right limbs which progressed slowly. He was admitted to a hospital and a diagnosis of brain atrophy was made by PEG. His mentality deteriorated, and he became somnolent. On January 12, 1976, he was admitted to the Department of Neurosurgery at Toyohashi Hospital, where he was found to have mental deterioration, right hemiparesis, left oculomotor palsy, and loss of body temperature regulation. Cerebral angiography and CT scans were reported normal, but PEG again revealed cortical atrophy of the left hemisphere. He was discharged and followed up at the outpatient clinic.

He was readmitted on September 5, 1977, with progression of dementia and loss of consciousness. Plain CT revealed an area of slightly high density in the left putamen, with ipsilateral dilatation of the cortical sulci. On administration of contrast media, the high-density area became enhanced (Fig. 3A). Pneumoencephalography revealed left cortical atrophy and asymmetry of the lateral ventricles with elevation of the floor on the left side. Minor shift of the third ventricle was found. Cerebrospinal fluid (CSF) cytology revealed an increased cell count (48/3), especially of lymphocytes, but no tumor cells were found. From the neuroradiological findings, a slowly growing thalamic tumor was suspected. On September 20, 1977, radiation therapy was administered via the betatron to the whole skull. At the termination of irradiation (3400 rads), CT showed that the high-density area was diminished (Fig. 3B). The patient became alert, with only minor mental deterioration. His hemiparesis had improved by the time of his discharge on November 18, 1977.

Case 4

This 12-year-old boy first exhibited abnormal behavior in 1968, when his academic record in the middle school was unusually poor. By the time of his graduation in 1971, he had the worst academic record in his class, and was often obstreperous. On April 3, 1971, he was hit by a car while riding his bicycle and suffered a minor head injury. One month later, he became restless, and abnormal behavior, general fatigue, anorexia, and polydipsia were noted. He had
Unilateral germinomas of basal ganglia and thalamus

FIG. 3. Case 3. A: Enhanced computerized tomography scan shows a homogeneously enhanced mass in the left thalamic region. Ipsilateral ventricular dilatation and widening of cortical sulci are also seen. B: After whole-skull irradiation with a total of 3400 rads, the enhanced mass disappeared and was replaced by a small low-density area.

also acquired a limp, which had progressed to left hemiparesis by June. He was referred to a psychologist and admitted to the Department of Psychiatry of Nagoya University Hospital on September 29, 1971. On admission, he had severe mental changes and left hemiparesis including the face, and his sensorium deteriorated gradually. Carotid angiography and brain scans showed no abnormality, nor was PEG informative (Fig. 4A and B). The patient was transferred to the Department of Neurosurgery on December 16, 1971, when he began to vomit and have convulsive seizures with deteriorated mentation and sensorium. Emergency ventricular drainage was performed to reduce increased intracranial pressure. Carotid angiography and pneumoventriculography showed marked hydrocephalus with shift of the third ventricle to the left, and a mass in the right basal ganglion and thalamic region was suspected (Fig. 4C and D). On December 19, a right frontotemporal craniotomy was performed, and the tumor was partially removed through the lateral ventricle. The pathological diagnosis was a pinealoma of two-cell pattern, and whole-skull irradiation of 4000 rads was given. The patient's general and neurological condition gradually improved during and after radiation therapy. He was alert and able to walk with the assistance of apparatus when discharged on January 22, 1961. Today, 18 years after his release, the patient's condition is reported to be fair.

Case 6

This patient suffered from left hemiparesis which had originated in the left hand and spread to his leg and face by the time he was 12 years old (in 1955). In March, 1956, he entered a local hospital for the treatment of his slowly progressive hemiparesis. The clinical diagnosis was polioencephalitis, and physical therapy was given at the hospital's outpatient clinic. Two years later, on February 14, 1958, the patient was readmitted because he complained of headaches and vomiting, with further progression of the hemiparesis. On admission, papilledema, narrowing of the visual field, oculomotor palsy, and spastic hemiplegia were found. An EEG showed marked suppression of hemiparesis. Subsequently, he was given a course of physical rehabilitation by an orthopedist until August, 1959. Because of a change in personality, he was referred to a psychiatrist at the end of August. On October 17, 1959, he was admitted to our department for evaluation of his left hemiparesis and character change. Neuroradiological examinations and EEG were not diagnostic at this time. Ophthalmological examinations revealed a slight temporal cut of his left eye, but visual acuity and ocular fundi were normal. A CSF study showed a slightly increased cell count, but no tumor cell was identified. Protein and sugar content were within normal ranges, and he was discharged on November 5, 1959.

Because of severe headaches and vomiting followed by convulsive seizure and unconsciousness, the patient was again admitted to our department on September 17, 1960. At the time of readmission, he was semicomatose with left hemiplegia and anisocoria, the left pupil larger than the right, with absent light reaction. Carotid angiography showed marked hydrocephalus, and an emergency ventricular drainage was performed. Pneumoventriculography revealed a large mass in the right basal ganglia and thalamus obstructing the foramen of Monro, and the third ventricle was distorted and shifted to the left side.

On October 15, 1960, right frontal craniotomy was performed, and the tumor was partially removed by a transventricular approach. The pathological diagnosis was a pinealoma of two-cell pattern. Irradiation with cobalt-60 was given, in a total of 4000 rads to the whole brain and 2000 rads to the tumor. The patient's general and neurological condition gradually improved during and after radiation therapy. He was alert and able to walk with the assistance of apparatus when discharged on January 22, 1961. Today, 18 years after his release, the patient's condition is reported to be fair.

Case 5

This 11-year-old boy had complained of a weakness of his left hand after he had received a minor head injury from a bicycle accident in March, 1959. Within 2 months, the weakness gradually developed into
FIG. 4. Case 4. Cerebral angiograms (upper) and pneumoencephalograms (PEG) (lower). A: Angiography on September 29, 1971, showed no shift of the anterior cerebral artery or asymmetry of the middle cerebral arteries. B: At the same time, PEG showed slight dilatation of the right ventricle but no shift of the third ventricle. C: Angiography on December 19, 1971, after ventricular drainage, showed signs of hydrocephalus, a shift of the anterior cerebral artery, and asymmetry of the Sylvian points. The middle cerebral arteries were laterally displaced, but no tumor stain was found. D: At this time, PEG showed bilateral enlargement of the lateral ventricles and shift of the third ventricle. The floor of the right ventricle is also elevated.

the basic electric potential rhythm, but no focal abnormality was reported. Carotid angiography was not diagnostic. He was treated conservatively, and his neurological signs stabilized thereafter. However, beginning on July 15, 1958, he had weekly attacks of unconsciousness of several hours' duration. During these attacks, he showed automatism in which he wandered and wept. He also had hyperesthesia of the left half of his body, abnormal appetite behavior, unusual emotions, and tendency to place whatever was in his hand in his mouth.

The patient was transferred to the Department of Neurosurgery, and emergency ventricular drainage was performed after cerebral angiography showed marked hydrocephalus. A right frontotemporal craniotomy was performed on August 5, 1958. A deep temporal mass was partially removed with temporal lobectomy. Pathological diagnosis indicated an ectopic pinealoma. His recovery was uneventful, and he received cobalt-60 radiation therapy with a course of 3000 rads to the whole brain. Today, 20 years later, his condition is fair.
Unilateral germinomas of basal ganglia and thalamus

Discussion

A high incidence of pineal tumors among Japanese is well documented. However, the incidence of germinoma in the basal ganglia and thalamus has not been known. In four out of 40 cases (10%) in our series of intracranial germinoma, the tumor mainly involved these regions. These four patients and two additional cases are reported here. All six were male, aged between 8 and 12 years at the onset of symptoms. The age and sex incidence is very similar to that in reported cases. It is interesting that male predominance has been found in cases of pineal germinoma, while both sexes were equally affected in suprasellar lesions.

One of us (N.K.) has previously reported the clinical manifestations of germinoma in the basal ganglia. However, the pathological characteristics were not fully understood until autopsy findings were available. According to Kwak, et al., the most common site of the lesion was unilaterally in the thalamus, but the tumor invaded and spread throughout structures of the basal ganglia.

Symptomatology

In many respects, this tumor exhibits quite different symptomatology from that of other intracranial tumors. All the patients experienced a rather slowly progressive condition, and the duration between the onset and the diagnosis varied from 1 year and 4 months to 4 years. There were no signs of intracranial hypertension until late in the course (Cases 5 and 6). This is probably because the tumor is invasive in nature and rarely obstructed the ventricular system. Ipsilateral cortical atrophy and the ventricular dilatation might also be the responsible factors. The initial signs and symptoms were hemiparesis in five patients, mental deterioration and oculomotor palsy in three, and involuntary movement of one limb in two.

Convulsive seizures, diabetes insipidus, and pubertas praecox were initial findings in one of the cases. Symptoms that presented during the course of the disease were: hemiparesis in all cases, eye symptoms in five cases, fever of unknown origin in four cases, and mental disturbances and abnormal behavior in three cases; character change, convulsions, pubertas praecox, and diabetes insipidus were found in two cases (Table 3). These signs and symptoms are explained by unilateral involvement of the thalamus, hypothalamus, limbic system, and visual pathway. One of the cases with pubertas praecox (Case 2) showed a high serum level of LH and low FSH at the time of admission. The LH level had decreased to 220 mIU/ml after removal of the tumor and became undetectable after the irradiation. It was concluded that the precocious puberty was due to hypersecretion of HCG by the tumor.

The diagnosis of germinoma in the thalamus and basal ganglia is difficult at an early stage because of its rarity and nonspecific findings. Electroencephalography and cerebral angiography were not diagnostic at that stage. However, these cases showed nonspecific changes compatible with unilateral thalamus and basal ganglia tumor at a later stage of this condition. Pneumoencephalography and pneumoventriculography were found to be more valuable diagnostic aids: asymmetry of the lateral ventricle, elevation of the floor of the lateral ventricle of the involved side, and/or a shift of the third ventricle toward the contralateral side were found in all cases so tested. Dilatation of the lateral ventricle on the involved side was found in three cases, and ipsilateral cortical atrophy in two. Radioisotope scans using radioactive iodinated serum albumin (RISA) or 99mTc showed a higher uptake of the isotope corresponding to the lesion in two cases. In one case (Case 2), the area of greatest uptake disappeared after partial removal of the tumor and radiation therapy. Recent progress of CT has enabled more specific and accurate diagnosis of intracranial germinomas to be made. Plain CT showed a circumscribed, homogeneous high-density area in one patient (Case 3), and a large, irregular, mixed high- and low-density area in another (Case 1). Both of the lesions were highly enhanced on contrast media administration. Of special interest in the diagnosis of intracranial germinomas was the comparison of CT scans taken before and after irradiation. Intracranial germinomas are highly radiosensitive, and a rapid response to initial doses of radiation was confirmed in both cases. Cytology testing of the CSF in four cases showed increased cell count in all cases, but the tumor cells were identified only in one (Case 1). The
reliability of CSF findings in diagnosing intracranial germinoma remains to be studied. At present, a definitive diagnosis is still only obtained on biopsy. In this series, pathological diagnosis was made in five cases and all were two-cell types of pinealoma. The diagnosis of germinoma was suspected in one case (Case 3) from the clinical signs, CSF findings, and the responsiveness to irradiation.

Glioblastoma of basal ganglia and thalamus can be differentiated from germinoma by age distribution, the rapid clinical course, and the characteristic neuroradiological findings. Glioblastomas do not usually respond to irradiation. Malignant lymphoma of the basal ganglia may show CT findings and radiosensitivity similar to germinoma; however, its multiple distribution and fulminating course help in the differential diagnosis.

Treatment and Prognosis

We performed a partial removal of the tumor in three cases, and biopsy in two, followed by irradiation to the whole brain. One case (Case 3) was treated by radiation therapy only. The efficacy of the treatment was confirmed by improvement of clinical signs in all cases, by repeated CT scans in two cases, and by radioisotope scans in one. Five patients survived for more than a year without signs of recurrence. The longest survival periods have been 20 years 7 months and 18 years 6 months. The outcome is considered “excellent” and “good” in two (Cases 2 and 3) and “fair” in three (Cases 1, 5, and 6). Only one patient (Case 4) died 6 months after the treatment. Kwak, et al., reported six cases of germinoma in the thalamus (three were their own), and stated that five of them died. Three of their cases had been irradiated with or without removal of the tumor, and two had received no treatment. Only one patient had survived 10 years 10 months after subtotal removal of the tumor and radiation therapy.

The prognosis without proper treatment is poor. From our experience, germinoma in the thalamus and basal ganglia responds to radiation therapy, as do other intracranial germinomas. Major surgery to the tumor should be avoided because of serious damage to the region, with undesirable neurological deficits. Moreover, the danger of seeding tumor cells during operation is always present. It will be necessary to determine the critical dose of radiation and also the indication for spinal irradiation and chemotherapy in cases with recurrence or seeding into the CSF space.

References


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