Extrapyramidal disorder with pineal germinoma

Case report

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Space-occupying lesions of the basal ganglia are a rare cause of extrapyramidal dysfunction in children. Metastatic pineal germinoma in both basal ganglia produced dystonia in a 12-year-old boy. The literature is reviewed. Extrapyramidal manifestations in this child are compared with previously reported cases of basal ganglia neoplasms.

Key Words • involuntary movements • basal ganglia neoplasms • pineal germinoma • dystonia

Extrapyramidal dysfunction due to neoplasms involving the basal ganglia and thalamic nuclei is rare in children; only 24 cases have been reported previously. In most of these cases, the neoplasms were of glial origin and either infiltrated the basal ganglia or affected their function secondarily by compression or by interruption of neural pathways between the basal ganglia and thalamus. In the following case, a child with pineal germinoma metastatic to both basal ganglia presented with progressive dystonia, a heretofore unreported manifestation of this neoplasm. This patient's history is described in detail because of the unusual clinical course.

Case Report

This 12-year-old, right-handed, Caucasian boy of non-Jewish descent was admitted to University Hospitals on October 8, 1973, with a 1-year history of progressive movement disorder. There was no family history of progressive psychological or neurological disease. In September, 1972, he had developed difficulty with concentration and penmanship, and his teacher reported that he had a poor attention span. He progressively lost fine motor skills in the right arm and developed clumsiness of the right leg. By December, 1972, his right foot was maintained in an equinovarus position, and his gait was awkward. He was quiet and socially withdrawn.

When evaluated at another hospital in January, 1973, the boy was reluctant to speak, but articulation was clear. He was voluntarily mute because tongue movements precipitated painful dystonic contortion of both axial and limb musculature. Facial ex-
pression was decreased on the right side. There were gross fibrillations of the tongue and occasional involuntary tongue protrusion and movement of the right side of the upper lip. The right upper limb was maintained in extension at the elbow and fingers, and exhibited intermittent dystonic movement. Muscle strength was normal. Deep tendon reflexes were diffusely hyperactive and right plantar response was extensor. Gait was lurching with a tendency to maintain the right lower limb in an extensor posture. The following diagnostic studies were within normal limits: skull x-ray films, brain scan, electroencephalogram (EEG), hemogram, urinalysis, serum ceruloplasmin, serum electrolytes, fasting blood sugar, urea nitrogen, serum calcium, triiodothyronine (T3), thyroxine (T4), creatine phosphokinase (CPK), glutamic oxaloacetic transaminase (GOT), lactic dehydrogenase (LDH), urinalysis for metachromatic substances, and cerebrospinal fluid (CSF) examination. A pneumoencephalogram revealed only minimal dilatation of the left temporal horn. Treatment with diazepam was of minimal benefit in controlling dystonia, and the patient was referred to University Hospitals on October 8, 1973.

**First Admission.** Examination revealed an alert, cooperative youth who would not talk but who understood and followed commands readily. He was thin and somewhat small for his age. Facies were flat. He had frequent dystonic movements of the limbs (Fig. 1), in the right extremities more than the left, and the dystonia was enhanced by tactile stimulation.

Eye movements and fundi were normal; Kayser-Fleischer rings were absent. Visual fields were normal on confrontation. The right corner of the mouth was drawn slightly upward, the uvula deviated to the right, and the gag reflex was slightly diminished on the right. Tongue protrusion was clearly unpleasant to the patient and precipitated painful dystonic movements of the right arm and leg. Undulating movements were noted in the protruded tongue. All limbs were hyperreflexic and mildly hypertonic. Plantar responses were extensor bilaterally. The Hoffman reflex was absent and abdominal and cremasteric reflexes were normal. Tactile stimulation produced increased dystonic posturing in the right lower limb. His gait was unsteady, with the right arm adducted at the side or behind the trunk and the right leg extended at the ankle with the foot inverted. Alternate motion rate was markedly diminished on the right side but fairly good on the left. Finger-to-nose test was done well on the left but he refused to perform it on the right.

Significant intellectual deterioration had been documented over a 4-year period. In October, 1969, he had attained an I.Q. score of 101 on the Otis Intelligence Test. In December, 1972, he obtained a Verbal Scale I.Q. of 83, Performance Scale I.Q. of 70, and Full Scale I.Q. of 76 on the Wechsler Intelligence Scale for Children. In October, 1973, repeat Wechsler testing yielded a Full Scale I.Q. of 64.

An EEG on October 9, 1973, was normal except for abundant movement artifact. Laboratory test results were normal including hemogram, urinalysis, electrolytes, calcium, urea nitrogen, fasting blood sugar, serum cortisol levels, serum ceruloplasmin, and serum and urinary copper levels. The clinical impression was one of rapidly progressive degenerative basal ganglia disorder. He was discharged on a therapeutic trial of Haldol (haloperidol). This medication...
was soon discontinued because it seemed to aggravate his dystonia.

Second Admission. He was readmitted on December 13, 1973, because of dysphagia and marked progression of dystonia. He was unable to feed himself or walk; he had become emaciated and was confined to a wheel chair. The severe dystonic movements (Fig. 2) consisted of slow extension of the right arm followed by adduction of the arm behind his back with forearm hyperpronation and wrist flexion. Simultaneously, the right leg was adducted and flexed. Similar, but less severe movements were present on the left. There was frequent arching of the back and torsion of the trunk to the left side. Dystonic movements were often accompanied by a high-pitched cry. He was able to grip voluntarily with the left hand and release with a sudden jerk; grip was much weaker on the right. The tongue was tightly retracted and attempts to protrude it precipitated painful dystonia. All laboratory tests were again normal.

An EEG on December 12, 1973, revealed delta waves at 1 to 3/sec over the right posterior temporoparietal region with loss of fast 15 to 20/sec beta activity over the right posterior hemisphere. The posterior alpha frequency was decreased to 8/sec. Pneumoencephalography demonstrated lateral ventricular dilatation and slightly increased cortical sulcal air (Fig. 3). The third ventricle, aqueduct, and fourth ventricle were normal with no evidence of obstruction or mass lesion. Cerebrospinal fluid protein, sugar, and cell count were normal; spinal fluid was not submitted for cytological examination.

Operation. On January 31, 1974, he underwent stereotaxic thalamotomy with placement of lesions in the left nucleus ventralis oralis anterior, nucleus ventralis oralis posterior, and zona incerta. Biopsy was not performed. This operative procedure did not change his dystonia. He continued to deteriorate, and died at another hospital on May 4, 1974.

Postmortem Examination. Postmortem examination was limited to the brain. The...
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ganglia revealed an infiltrating neoplasm composed of nests and sheets of cells with large vesicular nuclei and abundant pale-staining cytoplasm admixed with lymphocytes (Fig. 6). Similar neoplasm was seen in tissue adjacent to the stereotaxic lesion and in the pineal gland, although the pineal gland was of normal size. The cytological morphology of the neoplasm was that of pineal germinoma (dysgerminoma).

Discussion

Extrapyramidal syndromes are a nonspecific manifestation of basal ganglia involvement by a myriad of disease processes: congenital, degenerative, inflammatory, toxic, metabolic, vascular, traumatic, and neoplastic. In addition, extrapyramidal signs may accompany functional or hysterical disorders. Neoplasia is probably the least frequent cause.

Table 1 summarizes the 24 previously reported cases of extrapyramidal syndrome caused by space-occupying lesions in children. Among this group, extrapyramidal manifestations consisted of chorea, athetosis, rigidity, parkinsonian and atypical tremor, dystonia, and unclassified involuntary movements. In most cases, there was a combination of extrapyramidal signs; when a single sign was present, tremor was the most common. Dystonia was infrequent and usually occurred in combination with other extrapyramidal signs, such as tremor, or pyramidal signs, such as spasticity and paresis. Both extrapyramidal and pyramidal signs occurred in 18 of the 25 cases (72%). Intracranial pressure...
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<tr>
<th>Authors, Year</th>
<th>Age (yrs), Sex</th>
<th>Initial Symptoms</th>
<th>Clinical Manifestations</th>
<th>Tumor Location</th>
<th>Tumor Histology</th>
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<tbody>
<tr>
<td>Parker, 1923</td>
<td>12, M</td>
<td>disturbance of gait</td>
<td>parkinsonian syndrome; choreoathetosis</td>
<td>thalami</td>
<td>glioma</td>
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<td>Brzezicki, 1929</td>
<td>12, M</td>
<td>headache, vomiting</td>
<td>parkinsonian tremor; rigidity, Lt side</td>
<td>rt cerebral hemisphere</td>
<td>cyst</td>
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<td>Ody, 1932</td>
<td>3, F</td>
<td>hypokinesia, rigidity</td>
<td>behavior disorder; anorexia</td>
<td>basal ganglia</td>
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<td>Masten, 1938</td>
<td>12, F</td>
<td>gait disturbance</td>
<td>tortion spasms</td>
<td>thalami, ventricular nucleus, hypothalamus</td>
<td>spongioblastoma</td>
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<td>Bailey, et al., 1939</td>
<td>6, F</td>
<td>headache</td>
<td>constant tremor, upper &amp; lower limbs</td>
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<td>Globus &amp; Kuhlenbeck, 1942</td>
<td>15, F</td>
<td>headache, vomiting</td>
<td></td>
<td>thalami</td>
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<td>Urechia, et al., 1943</td>
<td>14, M</td>
<td>spasm, rt hand</td>
<td>painful extension, lt leg</td>
<td>lt hemisphere, basal ganglia</td>
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<td>Mettler, et al., 1947</td>
<td>6, F</td>
<td>intention tremor, lt arm</td>
<td></td>
<td>lt thalamus, midbrain</td>
<td>spongioblastoma</td>
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<td>Scott, 1947</td>
<td>4, F</td>
<td>headache, vomiting</td>
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<td></td>
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<td>Sciarr &amp; Sprofkin, 1953</td>
<td>15, F</td>
<td>spasm, lt hand</td>
<td>involuntary movements, lt great toe; athetosis</td>
<td>lt frontal lobe, lt caudate, rt basal ganglia</td>
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<td>Millichap, et al., 1962</td>
<td>6, M</td>
<td>chorea, lt arm</td>
<td>bilat choreo-athetosis &amp; dystonia, lt &gt; rt</td>
<td>rt thalamus</td>
<td>astrocytoma</td>
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<td>Chorobski, 1962</td>
<td>12, F</td>
<td>limp, lt leg</td>
<td>vertical nystagmus; lt Babinski response</td>
<td>upper brain stem</td>
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<td>6, M</td>
<td>tremor, rt extremities</td>
<td>—</td>
<td>lt hemisphere</td>
<td>sarcoma</td>
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<td>Arseni, et al., 1972</td>
<td>5, M</td>
<td>tremor, rt extremities</td>
<td>increased ICP; mental disturbance; rt hemiparesis</td>
<td>lt frontal-temporal lobes; lt basal ganglia</td>
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<td>Arseni, et al., 1972</td>
<td>5, F</td>
<td>headache; vomiting</td>
<td>choreoathetoid movements; hypertonia; cogwheel rigidity</td>
<td>lt basal ganglia</td>
<td>spongioblastoma, protoplastic astrocytoma</td>
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<td>Arseni, et al., 1972</td>
<td>14, M</td>
<td>headache; vomiting; tremor, rt arm</td>
<td>rt pyramidal syndrome; mental disturbances; increased ICP</td>
<td>lt caudate nucleus &amp; thalamus</td>
<td>astrocytoma</td>
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### TABLE 1 (Continued)

<table>
<thead>
<tr>
<th>Authors, Year</th>
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<th>Clinical Manifestations</th>
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<th>Tumor Histology</th>
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<tr>
<td>Lins, et al., 1978</td>
<td>12, M</td>
<td>poor coordination, rt arm extensor</td>
<td>bilat Babinski response; mutism; dementia</td>
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<td>bilat basal ganglia; pineal</td>
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<td>10, F</td>
<td>involuntary movements, rt arm</td>
<td>involuntary movements &amp; generalized dystonia precipitated by external stimulus</td>
<td>rt hemiparesis; rt focal seizures; somnolence, papilledema</td>
<td>lt basal ganglia</td>
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<td>tremor, lt arm; headache; vomiting</td>
<td>atypical tremor, lt arm; cogwheel phenomenon</td>
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<td>frontal horn, rt lateral ventricle</td>
<td>hydatid cyst</td>
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<td>11, M</td>
<td>headache; apathy</td>
<td>bilat Parkinson-like tremor, rt &gt; lt; cogwheel phenomenon</td>
<td>rt pyramidal syndrome; mental changes; increased ICP</td>
<td>lt thalamus</td>
<td>fibrous astrocytoma</td>
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<tr>
<td>11, F</td>
<td>tremor, lt arm; headache; vomiting</td>
<td>tremor &amp; choreoathetoid movements, lt extremities; cogwheel phenomenon</td>
<td>increased ICP; lt hemiparesis; Parinaud syndrome; rt hypacusis</td>
<td>brain stem &amp; rt basal ganglia</td>
<td>not verified</td>
</tr>
<tr>
<td>7, M</td>
<td>tremor, rt arm; headache; vomiting</td>
<td>bilat Parkinson-like tremor; cogwheel phenomenon; hypertonia; bilat choreoathetoid movements</td>
<td>quadripareisis; increased ICP; Parinaud syndrome</td>
<td>pineal</td>
<td>not verified</td>
</tr>
<tr>
<td>10, F</td>
<td>tremor, rt arm; headache</td>
<td>Parkinson-like tremor rt arm; rt hypertonia</td>
<td>rt hemiparesis; papilledema</td>
<td>lt parietal</td>
<td>hydatid cyst</td>
</tr>
<tr>
<td>10, M</td>
<td>tremor, all extremities</td>
<td>tremor, all extremities; hypertonia, generalized dystonia</td>
<td>lt peripheral facial palsy; papilledema; dementia</td>
<td>brain stem (superior)</td>
<td>glioma</td>
</tr>
</tbody>
</table>

was increased in 12 patients (48%), and correct diagnosis often was not established until such manifestations appeared. In some cases, diagnosis was delayed because of the slow clinical evolution. In many cases, the onset of extrapyramidal signs was preceded by a febrile illness, prompting diagnosis of post-infectious or postencephalitic extrapyramidal syndrome.¹,¹³,¹⁸ Neoplasm involved the basal ganglia in 12 cases (48%), the thalamus in eight cases (32%), the cerebral hemisphere in seven cases (26%), the brain stem in five cases (20%), and the pineal region in two cases (8%). In one case, an intraventricular cyst was present in the right frontal horn. In many cases, more than one anatomical structure was diffusely infiltrated by neoplasm. Tumors of neuroglial origin

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were the most common with 17 cases (68%) verified histologically. Two of the unverified brain-stem neoplasms were probably also of neuroglial origin. If the latter are included, the percentage of neuroglial tumors increases to 76%. Other verified space-occupying lesions included three cysts (12%), one sarcoma, and one pinealoma. The tumor in one case was also thought to be a pinealoma on the basis of neuroradiological studies, but it was not biopsied. Inclusion of this unconfirmed case would increase the percentage of pinealomas to 8%.

This patient is thought to be the first with histologically verified pineal germinoma to present primarily with progressive movement disorder. There was diffuse bilateral infiltration of the basal ganglia including the caudate nuclei and putamina, with cavitary destruction of the globi pallidi; the hypothalamus was also involved. There was no intraventricular extension.

Pineal neoplasms usually disseminate along the third ventricle and may secondarily invade the brain stem, hypothalamus, pituitary, and optic chiasm. Subependymal implants and seeding of the cerebrospinal fluid with subsequent implantation along the neuroaxis are common findings. White matter adjacent to the ventricular system may be invaded, but this is uncommon. Fowler, et al., reported one case of internal capsule involvement without infiltration of the basal ganglia. Suzuki and Iwabuchi reported a case of ectopic pinealoma infiltrating the left basal ganglia. Hemiplegia was present but there were no extrapyramidal signs. Arseni, et al., reported a case in which the patient presented with signs referable to the pineal region, basal ganglia, and brain stem. A diagnosis of pinealoma was based on characteristic ventriculographic changes, and the patient's response to irradiation therapy lent support to that diagnosis.

In reviewing the literature, we were unable to find other cases of pineal germinoma infiltrating the basal ganglia. In our patient the pineal germinoma behaved like a glioma, producing diffuse bilateral parenchymal infiltration without distortion of the ventricular system. Had neoplasm been suspected at the time of the patient's stereoeencephalotomy, the diagnosis of germinoma might have been made by stereotaxic biopsy as the lesion was made within an area that was involved by neoplasm at autopsy. His clinical course might then have been altered in view of the known sensitivity of pineal germinoma to radiation therapy.

The mechanism of dystonia is an interesting point for speculation in this patient. The massive infiltration and destructive change in the caudate nuclei and putamina is comparable to destruction seen with Huntington's chorea, but this patient had no chorea. The degree of destructive change in the lentricular nuclei was comparable to that seen in Wilson's disease, but there was no tremor. An unmodified thalamic influence on cortical neurons is an unlikely mechanism because both the thalamus and internal capsule were equally involved. Cerebellofugal fibers to the thalamus, of course, were also involved, adding to the complexity of functional interpretation. Cooper's concept is that dystonia is a manifestation of impairment of the efferent system rather than the afferent system. It would seem that dystonia in this patient was a manifestation of widespread diffuse basal ganglia impairment with lost inhibition of normal afferent influences on the final motor pathways.

The curious feature of tongue movements precipitating severe, sustained, painful dystonic movements indicates diffuse loss of reflex motor inhibition. It is analogous to a strychnine-like suspension of inhibition where light stimulation or movement precipitates cataclysmic movements referable to both bulbar and spinal segments. This action dystonia, combined with other positive criteria such as dystonia hyperkinesia, passive dystonia, dystonic postural disturbances, and restricted sustained muscle spasm seemed to support a diagnosis of dystonia musculorum deformans (DMD). Zeman and Dyken's negative criteria of rigidity and spasticity, indicating internal capsule involvement, mitigated against the diagnosis of DMD, as did the patient's progressive dementia.

Primary brain neoplasms commonly involve the basal ganglia by infiltration or direct compression, but rarely produce involuntary movements. When such manifestations do occur, they are difficult to analyze in functional terms. Although neuronal destruction undoubtedly occurs secondary to neoplastic compression, more than a mechanical mechanism must be involved since mass lesions of the thalamus and basal
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ganglia usually do not present with abnormal movements. Chorobski favors a functional mechanism for movement disorders associated with neoplasms, based on the observation that extrapyramidal signs often disappear following removal of the tumor and that neoplasm may infiltrate the basal ganglia without producing abnormal movements. The mechanism of dystonia is likely a combination of anatomic and physiological dysfunction. The clinical presentation and pathological anatomy in this patient would seem to support the supposition that widespread impairment of basal ganglia function must exist in order to produce a dystonic movement disorder.

Summary

Extrapyramidal syndromes in children caused by neoplasms or other space-occupying lesions in the basal ganglia are rare. The majority of such neoplasms are of neuroglial origin. Tremor and choreoathetoid movements are the most common presenting symptoms. This patient presented with extrapyramidal movement disorder attributed after autopsy to pineal germinoma metastatic to both basal ganglia. The clinical course was consistent with a progressive degenerative disease of the basal ganglia, and pneumoencephalography was consistent with diffuse cerebral atrophy. This is but one example of diagnostic problems that may arise when movement disorders result from neoplastic infiltration of the basal ganglia. Diagnosis may be increasingly difficult if an infectious process preceded the onset of abnormal movements. Basal ganglia neoplasms are a small but important group to consider in the differential diagnosis of movement disorders in children. Stereotaxic biopsy may establish an antemortem diagnosis so that appropriate therapy may be instituted.

Acknowledgment

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