Intracranial Neuroblastoma and Abnormal Catecholamine Excretion in a 42-Year-Old Woman*

Case Report

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It is difficult to estimate the frequency of neuroblastomas of the central nervous system because of inconsistency in classification of brain tumors composed of neuroblasts, ganglion cells, and glial elements. Nevertheless, such tumors are rare in adults.1-8 This report describes the clinical and diagnostic findings in a patient who had an intracranial neuroblastoma associated with markedly elevated urinary catecholamine excretion.

Case Report

Three months preceding hospitalization this 42-year-old woman developed intermittent severe headaches which started in the occipital area and spread to involve the entire head. Three days before admission she experienced an episode of headache, nausea, vomiting, and stiff neck followed by urinary incontinence, loss of consciousness, and repeated bouts of hot and cold sweats. Upon arrival at her local hospital the patient was comatose and unresponsive. A spinal tap showed blood-stained spinal fluid, and she was transferred to State University Hospital in Syracuse for neurosurgical evaluation.

Examination. On admission the patient's blood pressure was 140/80 mm Hg, and her pulse rate 96 per minute. No thyroid, breast, or abdominal masses were palpable. There was no adenopathy. She was deeply comatose and unresponsive to painful stimulation, her right pupil was larger than the left, and both were nonreactive to light. The corneal reflexes were markedly decreased or absent. Ophthalmoscopic examination showed marked bilateral papilledema and small hemorrhages, especially on the left. There was decerebrate posturing in all extremities and Babinski responses were present bilaterally. The admitting diagnosis was an intracranial space-occupying lesion on the right side.

A lumbar puncture was done, and the opening pressure was 600 ml H2O. The spinal fluid contained 5500 red blood cells and 1 monocyte/mm³, 84 mg% protein, and 74 mg% glucose. Blood glucose was 135 mg%. The hematocrit was 31 vol%, and white blood count was 12,600 cells/mm³ with 91% neutrophiles, 8% lymphocytes, and 1% monocytes. No malignant cells were found on subsequent analysis of sternal bone marrow aspirate. Routine urinalysis, blood urea nitrogen, and serum sodium, potassium, chloride, and CO₂ content were normal. The skull x-ray films showed dilated occipital emissory veins and demineralization of the intrasellar aspect of the dorsum sellae. The pineal gland was calcified and shifted from right to left approximately 5 mm. Chest x-ray was normal. Right carotid arteriography showed a marked shift of the anterior cerebral artery from right to left. There was posterior displacement of the first opercular branch of the middle cerebral artery and posterior displacement of the supraclinoid portion of the internal carotid artery. The anterior portion of the internal cerebral vein was displaced posteriorly and to the left. A large meningeal artery extended anteriorly along the greater wing of the sphenoid to supply an extracerebral lesion in the frontal region. The radiological diagnosis was meningioma in the right frontal region.

Operation. A right frontotemporal craniotomy was performed (E.S.W.) Subarachnoid hemorrhage was found as well as massive tumor arising from bone immediately above the right orbital roof and extending...
Intradurally, and intracerebrally, at the frontotemporal tip of the right frontal lobe. The major portion of the tumor was excised and a right frontal lobectomy was performed to secure decompression. The involved bone in the frontal region was removed down to the supra-orbital ridge.

Pathological Examination. Grossly, the tumor was soft and hemorrhagic. It contained much necrotic material, and there were spotty areas of calcification. Histological examination revealed a highly malignant small cell tumor with pseudo-rosettes and fibrillary cytoplasm resembling a neuroblastoma (Fig. 1).

Postoperative Course. Urine collected postoperatively over a 24-hour period contained markedly elevated quantities of dopamine, norepinephrine, and 3-methoxy-4-hydroxymandelic acid (VMA). No epinephrine was found (Table 1). The patient never regained consciousness. Routine clinical efforts to detect a primary tumor after craniotomy were unsuccessful. She died 3½ months later at the referring hospital; unfortunately no postmortem examination was done.

Discussion
Neuroblastoma is one of the most common solid tumors of infancy and early childhood. The peak incidence occurs before 3 years, and few cases are found after 7 to 8 years of life. The tumor usually arises from adrenal sympathetic tissue or from sympathetic ganglia in the posterior mediastinum or retroperitoneal area. Cerebral metastases often occur as retro-orbital masses which cause unilateral proptosis and erosion of bone. The disease generally is fatal within a few months when bony metastases are present. In rare instances, neuroblastosomas mature into ganglioneuroblastomas and ganglioneuromas in older children and young adults.

Table 1
Postoperative urinary catecholamine excretion

<table>
<thead>
<tr>
<th>Adult Patient</th>
<th>Dopamine</th>
<th>Norepinephrine</th>
<th>VMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Our Patient</td>
<td>31,900</td>
<td>3817.5</td>
<td>61,125</td>
</tr>
<tr>
<td>Adult Mean</td>
<td>249.1 ± 74.9</td>
<td>50.7 ± 15.7</td>
<td>3192 ± 699</td>
</tr>
</tbody>
</table>

![Fig. 1. Histologic section of the neuroblastoma demonstrating a typical nest of undifferentiated neuroblasts. Some cells are arranged in pseudo-rosette formation. H. & E., x280.](image)

Neuroblastomas and ganglioneuroblastomas are capable of synthesizing norepinephrine, its precursors, and metabolites; abnormally high urinary levels of these compounds are found in most patients with these tumors. Such studies are helpful in diagnosis and in following response to treatment. Despite increased pressor amine production, hypertension and paroxysmal episodes of headache, sweating, tachycardia, etc., are seldom found in children with neuroblastoma possibly due to defective storage of catecholamines within the neoplasm. The presence of a highly anaplastic neuro-
blastoma in the frontal lobe of a person in the fourth decade of life was an unexpected finding. The age of the patient and the location of the tumor suggested a diagnosis of meningioma, and, indeed, this was thought to be correct until microscopic sections of tumor slices were viewed. Since a tumor of neuroectodermal origin was not suspected, tissue was not saved at operation for electronmicroscopy and biochemical analysis.

It is possible that the tumor of this patient was a metastatic neuroblastoma deposit since it was extracerebral, although heterotopic neural tissue in the subarachnoid space can give rise to neuroblastoma. Unfortunately, necropsy was not performed so the presence of a primary neoplasm within the chest or abdomen was not excluded. The absence of hypertension, despite markedly elevated pressor amine excretion, is not surprising in view of general experience in children with neuroblastoma. In view of the late onset of the paroxysmal episodes of headache, vomiting, and unconsciousness, these symptoms probably were secondary to increased intracranial pressure rather than to any secretory function of the tumor.

To our knowledge this case represents the first instance wherein abnormally high urinary catecholamine excretion has been reported in an adult with an intracranial neuroblastoma. Previous studies in this laboratory (M.L.V.) have failed to demonstrate significantly elevated urinary dopamine, noradrenaline, and VMA output from patients with astrocytomas and medulloblastomas. It seems unlikely that meningiomas can secrete catecholamines because they are mesodermal in origin and do not contain neurosecretory cells. Measurement of urinary catecholamine excretion may be helpful in verifying the diagnosis of intracranial neuroblastoma particularly when accurate histological interpretation of the cell type is difficult. Clearly, when this tumor is found in the central nervous system, routine systematic search should be made for a primary lesion arising from sympathetic nervous tissue elsewhere in the body.

Summary

A 42-year-old comatose woman whose preoperative clinical and diagnostic findings suggested a meningioma in the right frontal region was found to have an extracerebral neuroblastoma and markedly elevated urinary catecholamine secretion.

Acknowledgment

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References