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CT of Primary and Secondary Craniocerebral Neuroblastoma

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Eleven children with craniocerebral neuroblastoma (three primary and eight metastatic) were examined by computed tomography (CT). The findings in both primary and secondary neuroblastoma correlate well with the known neuropathologic findings. Primary cerebral neuroblastoma originates in the brain parenchyma of the supratentorial space, and may extend into the cerebrospinal fluid pathways. Secondary neuroblastoma is confined to the osseous structures of the calvarium and orbit, and adjacent subperiosteal spaces (epidural and epicranial). In both forms of neuroblastoma, intratumoral hemorrhage is frequent. Separation of the cranial sutures often relates to epidural deposits of tumor extending to the sutural margins. In this form of sutural diastasis, intracranial pressure is not elevated. When elevated intracranial pressure accompanies sutural diastatis, CT findings reveal epidural deposits compressing the major dural venous sinuses in the region of their confluence.

Neuroblastoma may arise as a primary intracerebral neoplasm [1] or may metastasize to the skull, epidural space, and orbit. There is a difference between the primary and secondary craniocerebral forms in their clinical presentation and in their computed tomographic (CT) appearance. Computed tomography is superior to other radiologic studies in the diagnosis of both the primary and secondary forms of craniocerebral neuroblastoma because it demonstrates with a very low morbidity the full tumor extent and specific characteristics of the tumor. A relatively frequent finding is intratumoral hemorrhage.

Subjects and Methods

During a 5 year period (1974–1979), 11 patients with craniocerebral neuroblastoma have been examined by CT at the Hospital of the University of Pennsylvania. Three patients, all male, had no evidence of extracerebral neuroblastoma either at autopsy (one case), or during the course of followup (two cases, 3–5 years after CT diagnosis), and are therefore thought to have primary intracerebral neuroblastoma. Eight patients (three male and five female) had secondary craniocerebral neuroblastoma.

Computed tomographic scans were done on either an EMI, Mark One head scanner (160 × 160 matrix), an EMI 1005 head scanner (160 × 160 matrix), or an EMI 5005 body scanner (160 × 160 or 320 × 320 matrix). Slice thickness was 13, 8, or 6 mm. Coronal scans were performed on the body scanner. Iodinated radiographic contrast medium (Conray 60) was administered as an intravenous bolus in a dose of 1 ml/lb up to a maximum of 100 cc.

Observations

The three patients with primary intracerebral neuroblastoma were 2,4, and 8 years old at the time of diagnosis. Two of the three primary tumors presented as

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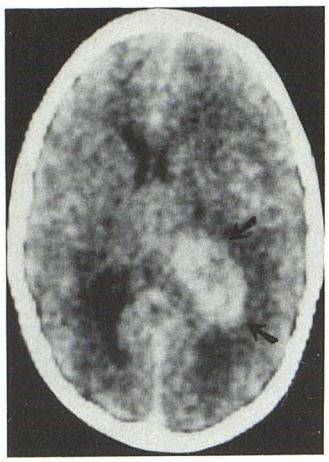
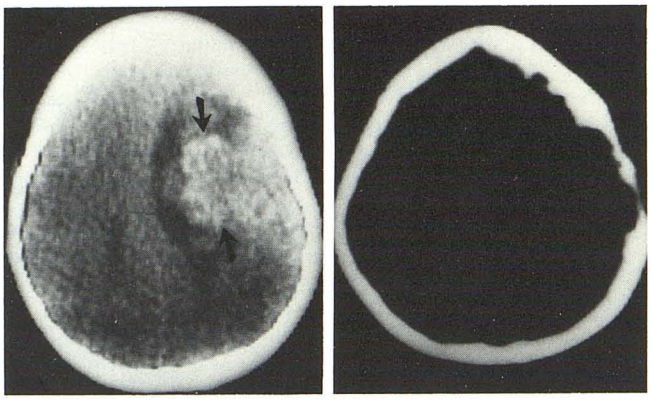


Fig. 1.—Primary craniocerebral neuroblastoma with intratumoral hemorrhage. Postcontrast scan. Dense left periatrial mass (*arrows*). Mass unchanged in density from preinjection study (not shown) and measures in range of clotted blood.



A B

Fig. 2.—Secondary craniocerebral neuroblastoma; intratumoral hemorrhage into calvarial metastasis with intracerebral extension of hemorrhage. **A**, CT scan without contrast agent injection. Irregular hemorrhagic mass (*arrows*) surrounded by edematous zone. **B**, Higher section, at bone density setting. Several lytic lesions erode both tables of skull. Area is contiguous with site of hemorrhage in **A**.

acute intratumoral hemorrhages (fig. 1); the other was an intraventricular mass associated with hydrocephalus.

In the eight patients with metastatic craniocerebral neuroblastoma, the primary tumor had been diagnosed at ages ranging from 3 months to 12 years. In four of the patients, the initial medical evaluation was brought on by orbital manifestations of metastatic neuroblastoma. The other four patients presented with constipation, diarrhea, enlarged neck nodes, and pneumonia, respectively.

With the secondary craniocerebral neuroblastomas, there was evidence of bone, dural, brain, or skin involvement (figs. 2–4). Four patients developed evidence of craniocerebral metastases between 6 months to 5 years after the diagnosis of the extracranial primary.

The CT appearances varied, and abnormalities were seen in seven of the eight patients. In one patient, an extensive osseous metastasis hemorrhaged and ruptured into the cerebral parenchyma (fig. 2). In two patients the metastatic neuroblastoma involved the epidural space and compressed the confluence of the transverse and straight sinuses and/or superior sagittal sinus producing clinical evidence of intracranial hypertension (fig. 4). Compression of the sinus confluence in one of these patients led to the development of a thrombus within the straight sinus (fig. 4D). In three patients with metastatic neuroblastoma, the osseous walls of the orbit were involved (fig. 3). In one patient, who also had orbital involvement, neuroblastoma involved the region of the cranial sutures as epidural deposits (fig. 3C) and the skull radiographs showed splitting of the sutures. In one patient CT demonstrated a tumor of the eyelid, and in one patient with a facial soft-tissue mass, the CT was normal.

Discussion

Primary cerebral neuroblastoma arises anywhere within the cerebral hemispheres [1], while secondary craniocerebral neuroblastoma is manifested most often as osseous metastases involving the calvarium, orbit, or skull base [2]. Metastatic calvarial lesions may extend to produce epidural deposits, occasionally subdural, but only rarely produce subarachnoid spread [3]. In contradistinction, primary central nervous system neuroblastoma arises intraparenchymally and frequently invades leptomeninges and seeds the subarachnoid space [5]. Cerebral parenchymal metastases are extremely rare, but can occur by retrograde seeding of the cerebrospinal fluid pathways. When this occurs, it usually follows intraspinal extension of a retroperitoneal primary tumor [4].

Histologically, both primary and secondary forms of cerebral neuroblastoma are similar [5]. They are highly cellular tumors with numerous mitotic figures, scant cytoplasm, and poor differentiation [3]. Grossly, they appear lobulated and well defined, but show frequent cystic degeneration, blood staining of cysts, and occasionally extensive hemorrhages [3]. In this series, two of the three patients with primary cerebral neuroblastoma had catastrophic symptoms due to a hemispheric mass. Computed tomography showed massive intratumoral hemorrhage (fig. 1) in one patient, and in the other both hemorrhage and nonhemorrhagic tumor (fig. 5). One of the patients with known secondary craniocerebral neuroblastoma had similar symptoms, and on CT examination was found to have a large hemorrhagic tumor mass that extended from the calvarium through the dura into the cerebral parenchyma (fig. 2).

Metastatic involvement of the bony orbit and skull has been found in up to 25% of cases [6], and is one of the most frequent clinical forms, a presentation that often precedes direct evidence of the primary tumor. In three patients of this series, periorbital soft-tissue hematomas (black eyes) were the initial manifestation of the secondary craniocerebral neuroblastoma. These hematomas arise from hemorrhage into osseous or soft-tissue metastases in the orbital region. In two of these patients CT demonstrated metastatic involvement of the sphenoid bone (fig. 3A) with contiguous subperiosteal intra- and extraorbital tumor masses (figs. 3A and 3B).

Metastatic involvement of the skull and orbit produces

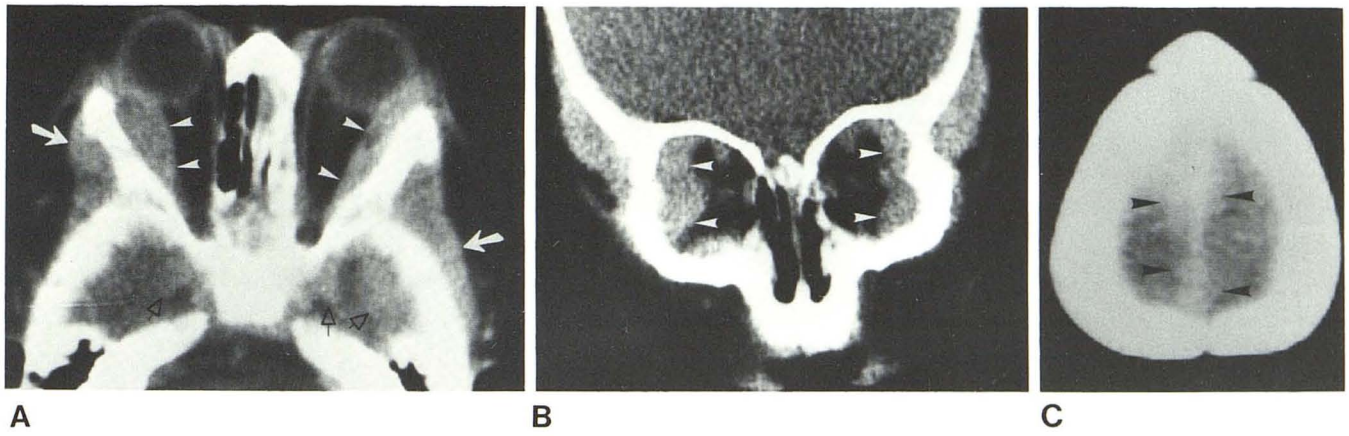


Fig. 3.—Secondary craniocerebral neuroblastoma. **A**, Postcontrast. Bilateral subperiosteal masses intraorbitally (*arrowheads*) arise from metastasis in the sphenoidal walls of the orbit. Tumor also extends subperiosteally into both temporal fossae (*arrows*) and both middle cranial fossae (*open arrows*). Marked bilateral proptosis. **B**, Coronal section through orbit. Inferosuperior extent of lateral subperiosteal tumor masses (*arrowheads*). **C**, Epidural tumor deposits outline margins of sagittal suture (*arrowheads*).

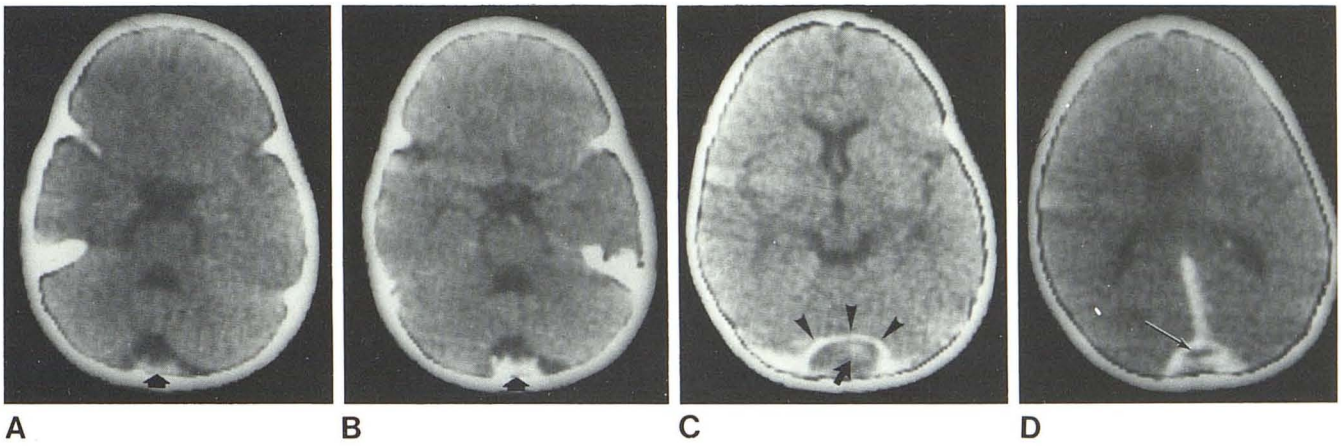


Fig. 4.—Secondary craniocerebral neuroblastoma with dural metastasis and venous thrombosis. **A**, CT scan without contrast material injection. Calcified mass (*arrow*) projects into cisterna magna from dura of calvarium. This represents the spiculated hair-on-end hyperostosis that can be seen on skull radiographs. **B**, Postcontrast at same level as **A**. Enhancement of tissue containing calcification (*arrow*). **C**, Postcontrast at level above **A** and **B**. Confluence of lateral sinuses is displaced forward (*arrowheads*) by partially enhancing tumor mass (*arrow*). **D**, Next level higher. Lucent filling defect (*arrow*) at juncture of straight and lateral sinuses. At autopsy, this was thrombus within sinus confluence.

several possible radiographic findings; thickened bone, the so-called "hair-on-end" periosteal reaction (spiculated bone), lytic defects, and separation of the sutures. Skull radiographs were normal in all three cases of primary cerebral neuroblastoma. In the eight cases of secondary craniocerebral neuroblastoma, the skull radiographs demonstrated hyperostosis of the sphenoid bone due to tumor in two cases, splitting of the cranial sutures in four cases, and destructive calvarial lesions in one case.

Computed tomographic findings reflect the known pathologic processes involved in neuroblastoma metastases to the skull and orbit. The "hair-on-end" appearance is a periosteal response to tumor cells extending from the calvarial metastasis (figs. 4A and 4B). The inner aspect of the periosteum is particularly resistant to penetration by tumor cells so that the tumor, as it breaks out of the bone, lifts the periosteum producing plaque-like epidural deposits of tumor (figs. 3C, 4C, and 4D). Secure anchoring of the dura at the suture margins limits the tumor to the adjacent sutural edges. Resulting pressure from tumor deposits adjacent to the sutures results in sutural diastasis. Intracranial hypertension is not usually associated with this form of sutural separation [7,8]. The computed tomographic counterpart of this form of sutural diastasis is an extensive epidural deposit of tumor on either side of the sutural margins (fig. 3C).

In the presence of clinically evident intracranial hypertension, one should look for venous sinus compression or occlusion by epidural tumor deposits. Carter et al. [2] stated that this finding is rare. However, two of the eight patients with secondary craniocerebral neuroblastoma in this series

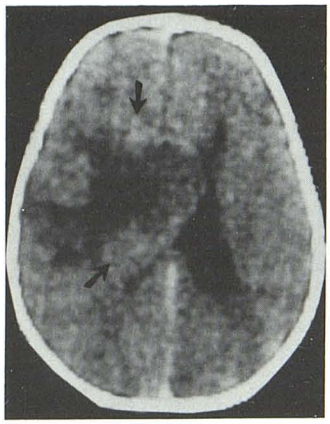


Fig. 5.—Primary central neuroblastoma. Postcontrast. Large right frontoparietal mass of decreased density with minimal peripheral enhancement (*arrows*). Marked compression and contralateral shift of right lateral ventricle. Intratumoral hemorrhage demonstrated on higher cuts (not shown).

had clinically evident increased intracranial pressure, and both showed displacement of the sinus confluence and adjacent dural venous sinuses by epidural tumor deposits (fig. 4C). A venous thrombus contributed to the increased intracranial pressure in one patient (fig. 4D).

Early involvement of the skull may not produce obvious radiographic changes, but may be detected by radionuclide bone scanning [8]. The radionuclide bone scan was positive for cranial tumor in six of the eight patients with secondary craniocerebral neuroblastoma. Computed tomography, skull radiography, and radionuclide bone scans were negative in one patient whose only finding was a soft-tissue metastasis adjacent to the bridge of the nose.

It should be noted that in four of the eight patients with secondary craniocerebral neuroblastoma, the initial presentation of the neuroblastoma was due to the craniocerebral involvement. All patients with secondary craniocerebral neuroblastoma had an advanced clinical stage of the disease at the time of the computed tomographic examination. The other sites of metastatic involvement in these patients were the skeletal system in six, the bone marrow in four, liver in one, and the cervical lymph nodes in one. In the patients with primary craniocerebral neuroblastoma there has been no evidence of extracerebral disease (autospy, one; clinical follow-up, two).

As reported in the literature [5], and as was true in this series, 50% or more of the patients with the primary cerebral form and more than 70% of those with the primary extracerebral form of neuroblastoma were 5 years old or younger. A gender predilection has not been reported in either the cerebral or extracerebral form of neuroblastoma [3], but in this series, all three cases of primary cerebral neuroblastoma occurred in boys.

Computed tomography is the most useful single diagnostic method to demonstrate the pathophysiologic consequences of secondary craniocerebral neuroblastoma. Hyperostotic sphenoidal metastases, orbital and intracranial subperiosteal epidural tumor deposits, and tumor deposits displacing and compressing adjacent venous sinuses are all well shown on computed tomographic studies. CT also demonstrates the presence of intratumoral hemorrhage in both the primary and secondary forms of craniocerebral neuroblastoma.

By using the computed tomographic information, the primary and secondary forms of craniocerebral neuroblastoma can be differentiated. The primary form is limited to the brain parenchyma and subarachnoid space, and is often hemorrhagic. The secondary form is associated with osseous and epidural tumor deposits and shows a predilection for certain sites that is almost pathognomonic. Primary cerebral neuroblastoma presenting without hemorrhage may resemble other malignant hemispheric tumors in the young child.

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