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Computed tomography (CT) has made a profound impact on the diagnosis and treatment of neuroblastomas and ganglioneuromas. The size, location, calcification, composition, and contiguous spread of the tumors has been well demonstrated by CT. CT is essential for their staging, subsequent treatment, and follow-up. Seventy-seven children were reviewed, 67 with neuroblastoma and 10 with ganglioneuroma seen between 1976 and 1980. Fifty-eight had one or more body CT scans, 22 had metrizamide myelography and/or CT metrizamide myelography, and three patients had cranial CT. Intraspinal extension of tumor occurred in 11 instances, several requiring decompressive surgery. A workup plan for optimal use of CT and CT metrizamide myelography was developed from this experience.

Neuroblastoma and ganglioneuroma are among the most common neoplasms of infancy and early childhood, exceeded only in frequency by Wilms tumor of the kidney. Staging serves to identify tumor subgroups and clinical prognosis. Several factors indicate a favorable prognosis including: onset of the tumor before 1 year of age [1–7], tumors arising from the chest or posterior mediastinum [8–11], or a paravertebral location with extradural extension into the spinal canal [1–3, 12–15]. Ganglioneuroblastoma and benign ganglioneuroma have a more favorable prognosis. Spontaneous regression from the more malignant to the more benign forms may occur [7].

Our purpose was to develop an imaging protocol in which CT played a central role in determining the location and overall geography of the tumor. A retrospective study of the accuracy of CT in demonstrating the size, location, calcification, composition, and contiguous and metastatic spread of the tumor as well as intraspinal extension provides the basis for this report of its effectiveness.

Materials and Methods

From the medical records of the Hospital for Sick Children, Toronto, The Tumor Registry, and the computer retrieval system of the Division of Special Procedures, we found 77 patients with either neuroblastoma or ganglioneuroma between 1976 and 1980. All tumors were histologically verified in our Department of Pathology.

Body CT and metrizamide myelography were first used together at the Hospital for Sick Children in 1976. Initially, the Ohio Nuclear Delta-50, and later the General Electric 8800 CT-T scanners were used. One or more CT scans, including either the chest and abdomen or cranium, were obtained in 58 of the 77 patients and CT metrizamide myelograms in 18. Thirty-two were boys and 26 were girls. Seven patients had ganglioneuromas first presenting at a mean age of 7 years (range, 4–14.5 years). Fifty-one patients had neuroblastomas with a mean age of onset of 2.7 years (range, 1 day to 16 years). Of the 11 patients with intraspinal extension of the tumor, only six had neurologic symptoms suggesting involvement of the spinal cord or lumbar nerve roots. The clinical findings included pain, scoliosis, paraparesis, or paraplegia.

Plain radiography, excretory urography, conventional tomography, radionuclide imaging,

Fig. 1.—Three patients. **A**, Paravertebral mass with amorphous calcification displacing kidney. **B**, Primary thoracic neuroblastoma with discrete punctate calcifications. Displacement of thoracic dural sac (*arrow*) indicates intraspinal tumor extension. **C**, Rim calcification. Thoracic neuroblastoma.
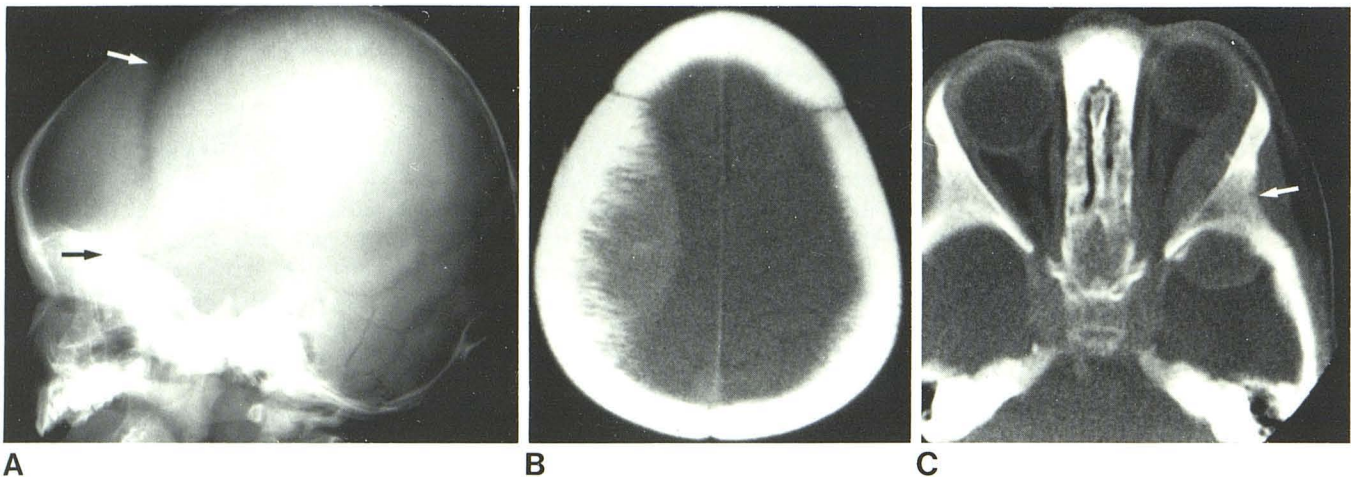
Fig. 2.—**A**, Typical plain radiographic findings of metastatic neuroblastoma to skull. Striated new bone formation, sutural separation (*white arrow*), and sclerosis of sphenoid and orbital roof (*black arrow*). **B**, Hair-on-end appearance of inner table in response to dural metastasis well shown by CT. **C**, Enhancing extradural mass in left middle cranial fossa and intraorbital mass with resultant proptosis of left eye. Metastatic invasion of sphenoid bone (*arrow*). **D**, Low-density round metastatic deposits in liver.

Fig. 3.—**A**, Ganglioneuroma erodes transverse process (*white arrow*) and widens intervertebral foramina. Extension of primary chest ganglioneuroma into neck. Slight but definite indentation on left side of cervical dural sac (*black arrow*) indicates also intraspinal extension. **B**, Ganglioneuroma (*arrow*) extended higher into soft tissues of neck than was clinically suspected.

A   B
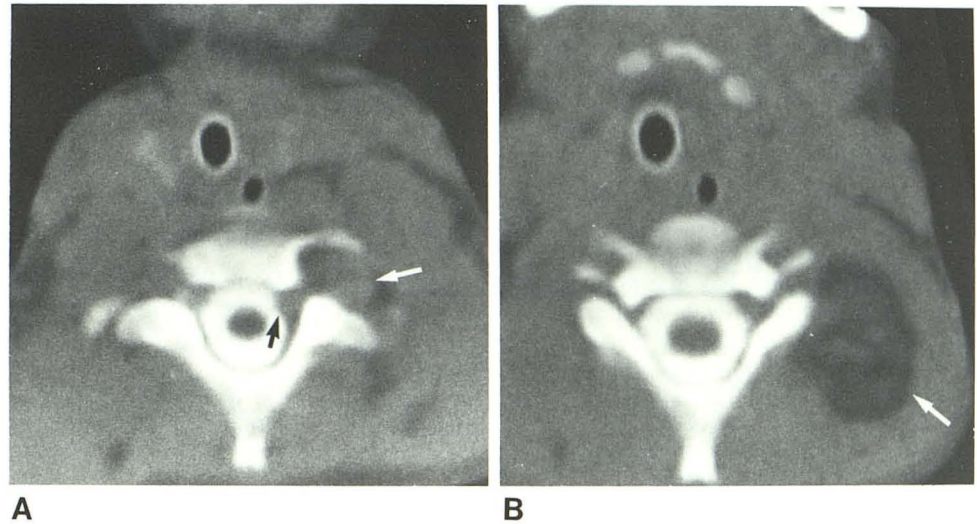
sonography, and angiography were the other methods used in localization. Radionuclide bone scintigraphy helped localize bone metastases.

All radiographic and scintigraphic films obtained were restudied by at least two radiologists. In the few instances where the original film reports differed from surgical or pathologic reports, new interpretation of the studies by an unbiased observer was made.

Results

Computed Tomography

Calcification. Standard radiography demonstrated calcification in 10% of chest lesions and 25% of abdominal lesions. Incidences of less than 5% of chest lesions and about 25% of abdominal lesions were previously reported [2, 6, 9, 10, 15–16]. CT demonstrated calcification in 25% of the 18 chest lesions and 43% of the 39 abdominal lesions in our patients; calcification was seen by CT in 40% of the neuroblastomas and 20% of the ganglioneuromas. Calcification of the intraspinal component of neuroblastoma was seen in only one case.

The CT pattern of calcification more often appeared as amorphous (cloudlike) calcification (fig. 1A) and less commonly, discrete punctate calcifications (fig. 1B) or rim calcifications (fig. 1C).

Skull and Orbits. Recent reports [17–22], show the usefulness of cranial computed tomography in the evaluation of metastatic neuroblastoma to the skull and orbits. Three of our patients had cranial CT because of proptosis, orbital swelling, ecchymosis, and/or a soft-tissue mass over the cranium. CT showed extradural involvement and the intraorbital mass of the metastatic neuroblastoma (figs. 2A and 2B). Special CT reconstruction for bone (General Electric Review Program) enhanced the display of bone metastases (fig. 2C).

Neck. Neuroblastoma or ganglioneuroma uncommonly presents as a mass in the neck. In two patients, a chest radiograph revealed a larger posterior mediastinal mass with
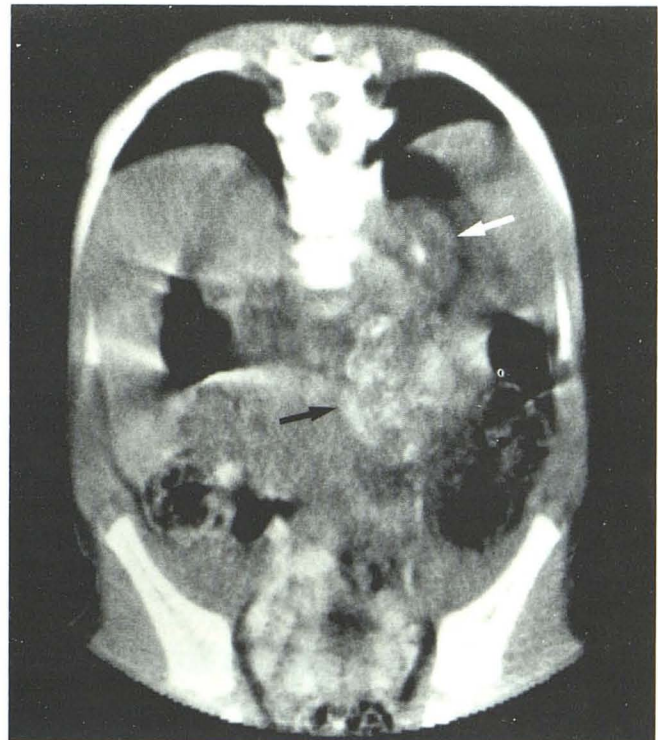
Fig. 4.—True coronal CT scan. Left paravertebral calcified mass (*white arrow*) just below diaphragm was primary abdominal neuroblastoma. Inferior to this is contrast-filled small bowel and there is also contrast-filled small bowel (*black arrow*) in pelvis. This projection makes determination of radiation port possible.

extension into the neck. CT demonstrated displacement of the carotid artery in one case and extension into the extradural space through the neural foramen in a second case (fig. 3).

Chest. Tumor involved the chest in 18 patients scanned with CT. Primary tumor, contiguous spread from an abdominal primary, and, in the case of the neuroblastoma, metas-

tases along the paravertebral sympathetic chain can all occur in the chest. Rarely, parenchymal and subpleural nodules or pericardial metastases have occurred.

Abdomen. Thirty-three neuroblastomas and six ganglioneuromas were abdominal. Twenty-nine of these were paravertebral and 10 were adrenal. Sagittal and coronal

reconstruction or direct coronal CT imaging [23] (fig. 4) were used in treatment planning and determining radiation portals. Abdominal CT also documented the presence of liver metastases (fig. 2D).

Metrizamide Myelography, Intraspinal Tumor Extension, and CT Metrizamide Myelography

With the availability of metrizamide, the advent of body computed tomography, and computer software capable of increasing bone resolution, CT metrizamide myelography has become exceptionally useful in evaluating intraspinal and paraspinal neoplasms in infants and children [24]. Early in the experience with metrizamide, both conventional myelography using water-soluble contrast material and CT scanning after the conventional examination were performed. This has been referred to as secondary or postmyelogram CT metrizamide myelography. In cases with specific clinical indications, a primary CT metrizamide myelography procedure for evaluating the presence of intraspinal extension of the tumor has been developed. A smaller volume and more dilute concentration (170 mg/dl metrizamide) has been used and better definition of the subarachnoid space, cord, cauda equina, and nerve roots has been obtained with fewer side-effects.

The use of metrizamide myelography and CT metrizamide myelography is summarized in table 1. Intraspinal extension of the tumor was found in 11 of the 77 patients. Two of the 10 ganglioneuromas and nine of the 67 neuroblastomas showed intraspinal involvement. In patients having CT scans, 11 of the 58 had intraspinal tumor extension. Four of 18 chest tumors and seven of 39 abdominal tumors had intraspinal extension. Abdominal tumors localized to the adrenal had no intraspinal extension.

Nine neuroblastoma patients with intraspinal tumor extension presented at a mean age of 19 months. Five of the nine had neurologic symptoms suggesting cord involvement at the time of initial diagnosis. An 8-year-old died of widespread metastatic disease including metastases to the spinal canal. The surviving younger patients (mean, 9 months;

TABLE 1: **Spinal Canal Studies**

	Tumor Type		Total
	Neuroblastoma	Ganglioneuroma	
No. patients	67	10	77
CT	50	8	58
CT metrizamide myelography only ..	6	3	9
Metrizamide myelography only	5	3	8
Metrizamide myelography and CT			
metrizamide myelography	7	2	9
Total metrizamide studies	18	8	26

Fig. 5.—Conventional metrizamide myelogram. Complete extradural block at T12–L1 (*large arrow*). Soft-tissue paraspinal mass (*small arrow*). At surgery, neuroblastoma encircled dural sac.

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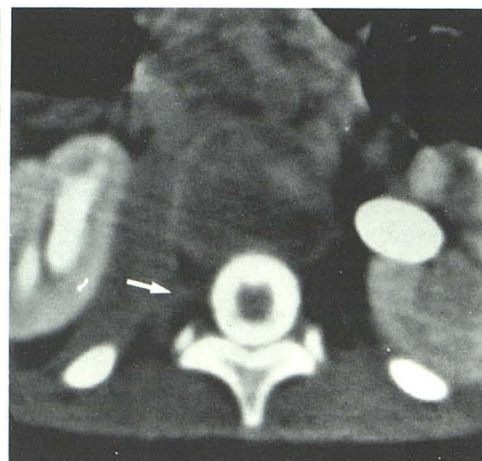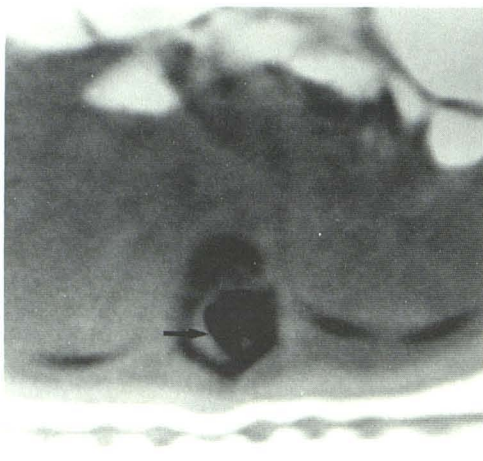Fig. 6.—Thoracoabdominal neuroblastoma. Conus markedly displaced to left (*arrow*) indicating intraspinal tumor extension.

Fig. 7.—Abdominal ganglioneuroblastoma. At level of intervertebral disk on this scan, there is evidence of paravertebral mass with extension of tumor into extradural space (*arrow*) without any displacement of metrizamide-filled lumbar subarachnoid space. Slight lateral displacement of right kidney.

range, 1–24 months) had direct spread of the primary tumor. Follow-up of 1.5–3.0 years (mean, 2.5 years) had indicated that only two have mild residual neurologic deficits. Previous reports [1–3, 13–15] indicate that this presentation of the disease is associated with a relatively favorable prognosis. Most patients with intraspinal extension of neuroblastoma were younger than 1 year, and it is known that the prognosis of neuroblastoma occurring in infancy is better than in later childhood.

In the two intraspinal ganglioneuromas, the mean age at the time of diagnosis was 6.75 years. One patient with an intraspinal ganglioneuroma had later morbidity associated with a severe scoliosis.

Intraspinal extension was demonstrated as a complete block by conventional myelography (fig. 5) in three patients or, on CT, as gross displacement of the cord, surrounded by metrizamide in the subarachnoid space (fig. 6), flattening of one side of the dural sac (fig. 3A), paravertebral tumor extending extradurally and displacing the cord (fig. 7), and widening of an intravertebral foramen (fig. 3A).

Discussion

CT imaging can define the location, extension, calcification, and composition of the tumors. After evaluating the various imaging methods, we have concluded that it is important to select those methods that yield the maximum information to answer the clinical problem presented. CT, sonography, plain radiography, radionuclide scintigraphy, and angiography are all of value in tumor localization. CT, however, provides better spatial representation of the pathologic process.

Myelography and CT metrizamide myelography are the only methods available to determine intraspinal tumor extension. Distant metastases to bone, brain, lungs, or abdominal viscera are evaluated best with CT, plain radiography, and radionuclide scintigraphy. Careful examination of the vertebral bodies, foramina, and pedicles at the time of CT body scanning can show tumor involvement of the spine (fig. 7). The cystic, necrotic or avascular, or hypervascular characteristics of the tumor are best imaged with CT with vascular enhancement, sonography, or angiography. CT is the most sensitive method of detecting tumor calcification but cannot predict benignity. Sonographic acoustic shadowing or high-level echoes may occur when tumor calcification is present, but sonography is less sensitive than CT for calcification.

With modern CT scanners, a scout view or digital radiograph can be obtained after intravenous enhancement and can show opacification of the kidneys, ureters, and bladder, eliminating the need for a conventional excretory urogram.

Sagittal and coronal reconstruction or direct coronal CT [23] can be used to determine radiation therapy portals, and CT can also be used to follow the effect of treatment on the mass. However, sonography may be all that is necessary in routine cases.

We suggest an imaging protocol, a combination of CT and CT metrizamide myelography, after the tumor is first identified by plain radiography or sonography. If the tumor is paraspinal, CT metrizamide myelography should be the next step. A lumbar puncture is performed, a small amount (2–5 ml) of low concentration (170 mg/dl) metrizamide is injected into the lumbar subarachnoid space, and the patient is taken immediately to the CT scanner. Masses that are primarily adrenal, or are located far anteriorly, are unlikely to have intraspinal extension. After localization by sonography, patients with these should initially have only a CT body scan before and after administration of contrast material.

CT examination after intrathecal and intravenous enhancement used as a primary diagnostic tool can demonstrate contiguous spread, displacement of visceral organs and genitourinary tract, and evidence of intraspinal tumor extension extremely accurately. The tumor can be staged, and if radiation therapy is planned, the radiation portal can be determined from the axial scan, coronal reconstruction, or direct coronal CT scan. A sonogram, if not previously used in the investigation, should then be obtained as a baseline for follow-up of response of the tumor to therapy.

REFERENCES

1. Traggis DG, Filler RM, Druckman H, Jaffe E, Cassady JR. Prognosis for children with neuroblastoma presenting with paralysis. J Pediatr Surg 1977;12:419–425
2. King D, Goodman J, Hawk T, Boles ET, Sayers MP. Dumbbell neuroblastomas in children. Arch Surg 1975;110:888–891
3. Punt J, Pritchard J, Pincott JR, Till K. Neuroblastoma: a review of 21 cases presenting with spinal cord compression. Cancer 1980;45:3095–3101
4. Wilson LMK, Draper GJ. Neuroblastoma, its natural history and prognosis: a study of 487 cases. Br Med J 1974;3:301–307
5. Evans AE, Albo V, D'Angio GJ, et al. Factors influencing survival of children with non-metastastic neuroblastoma. Cancer 1976;38:661–666
6. deLorimier AA, Bragg KU, Linden G. Neuroblastoma in childhood. Am J Dis Child 1969;118:441–450
7. Bolande RP. Benignity of neonatal tumours and the concept of cancer regression in early life. Am J Dis Child 1971;122:12–14
8. Gale AW, Jelihovsky T, Grant AF, Leckie BD, Nicks R. Neurogenic tumors of the mediastinum. Ann Thorac Surg 1974;17:434–443
9. Filler RM, Traggis DG, Jaffe N, Vawter GF. Favorable outlook for children with mediastinal neuroblastoma. J Pediatr Surg 1972;7:136–143
10. Eklöf O, Gooding CA. Intrathoracic neuroblastoma. AJR 1967;100:202–207
11. Bar-Ziv J, Nogrady MB. Mediastinal neuroblastoma and ganglioneuroma: the differentiation between primary and secondary involvement on the chest roentgenogram. AJR 1975;125:380–390
12. Hamilton PK. Neuroblastoma of the spinal cord. Am J Clin Pathol 1951;21:846–851
13. Balakrishnan V, Rice MS, Simpson DA. Spinal neuroblastomas: diagnosis, treatment and prognosis. J Neurosurg 1974;40:631–638
14. Rothner AD. Congenital "dumbbell" neuroblastoma with paraplegia. Clin Pediatr 1971;10:235–236
15. Fagan CJ, Swischuk LE. Dumbbell neuroblastoma or ganglioneuroma of the spinal canal. AJR 1974;120:453–460
16. Perez CA, Vietti T, Ackerman LV, et al. Tumors of the sympa-

thetic nervous system in children: an appraisal of treatment and results. *Radiology* **1967**;88:750–760

17. Keating JW, Cromwell LD. Remote effects of neuroblastoma. *AJR* **1978**;131:299–303
18. Curless RG. Cranial computerized tomography in childhood neuroblastoma. *Arch Neurol* **1980**;37:326–327
19. Zimmerman RA, Bilaniuk LT. CT of primary and secondary craniocerebral neuroblastoma. *AJNR* **1980**;1:431–434
20. Damgaard-Pedersen K. Neuroblastoma follow-up by computed tomography. *J Comput Assist Tomogr* **1979**;3:274–275
21. Naheedy MH, Kido DK, O'Reilly GV. Computed tomographic evaluation of subdural and epidural metastases. *J Comput Assist Tomogr* **1980**;4:311–315
22. Chirathivat S, Donovan Post MJ. CT demonstration of dural metastases in neuroblastoma. *J Comput Assist Tomogr* **1980**;4:316–319
23. Kaiser MC, Pettersson H, Harwood-Nash DCF, Fitz CR, Chuang S, Armstrong EA. Direct coronal CT of the spine in infants and children. *AJNR* **1981**;2:465–466
24. Resjo IM, Harwood-Nash DCF, Fitz CR, Chuang SH. CT metrizamide myelography for intraspinal and paraspinal neoplasms in infants and children. *AJR* **1979**;132:367–372