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Melanotic Neuroectodermal Tumor of Infancy: Clinical, Radiologic, and Pathologic Findings in Five Cases

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Five pathologically proved melanotic neuroectodermal tumors of infancy are reported. These rare neoplasms of infancy exhibit a distinct predilection for the maxillary bone. Three tumors originated in the maxilla, one in the calvaria, and one in the cerebellar vermis. Those occurring in bone did not metastasize but were locally invasive, as reflected in their radiologic appearance. Bone erosion, expansion, hyperostosis, and osteogenesis can occur in the same neoplasm and were appreciated best on CT. MR imaging showed the soft-tissue component and extent of the neoplasm better than CT did. The pathologic findings from all five cases (and one possibly related melanotic tumor of the face) revealed abundant melanin. MR imaging of two melanotic tumors showed isointense T1-weighted and slightly hyperintense T2-weighted signals. This appearance is contrary to that of most melanin-containing tumors, which exhibit enhanced T1 and T2 relaxation, and indicates that variables other than the absolute amount of melanin may determine the MR signal. Clinically, rapid neoplastic growth and excessive melanin production by the tumor cells caused facial disfigurement and visible blue black discoloration. All five melanotic neuroectodermal tumors were resected and the vermian tumor was also irradiated. Four of five children were well and free from disease 1 month to 7 years after resection. The calvarial tumor was incompletely resected and involved the underlying brain, eventually causing death. The clinical, radiologic, and pathologic features of melanotic neuroectodermal tumors of infancy are reviewed.

Melanotic neuroectodermal tumors of infancy that involve bone can be diagnosed from the clinical and radiologic findings. Prompt diagnosis and surgical resection are essential for cure.

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Melanotic neuroectodermal tumor (MNT) of infancy is a rare and unusual neoplasm. Characteristically, an infant has a firm tumor mass near the midline that is adherent to bone in the maxilla, mandible, or calvaria [1-5]. The neoplasm is locally aggressive, and rapid enlargement causes visible facial disfigurement. Blue black discoloration due to melanin pigment in the neoplasm may be seen through the skin. Five MNTs of infancy and one similar melanotic neoplasm of the face have been treated at our institution. Five of six infants had the clinical signs and symptoms described above. The other infant had ataxia, and an MNT was discovered in the cerebellar vermis [6].

Materials and Methods

A retrospective review of six infantile melanotic neoplasms was undertaken to correlate their clinical, radiologic, and pathologic features. The six patients, four boys and two girls, were 1-21 months old at the time of imaging. Five infants were examined to evaluate a rapidly growing facial or calvarial mass; the other was examined because of worsening ataxia. CT scans were obtained before and after contrast administration in five patients. Axial and coronal images were obtained with a slice thickness of 5 mm. Two patients were studied

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with MR at 1.5 T. Imaging parameters included a 256 × 256 matrix, 20-cm field of view, and 5-mm section thickness (interslice gap, 2.5 mm). Sagittal spin-echo (SE) 500/20/1 (TR/TE/excitations) images, coronal SE 700/20/2 and SE 2800/30,70 images, and axial SE 700/20/2 and SE 2800/30,70 images were obtained. Angiograms were obtained in three patients with standard pediatric techniques.

The images were assessed for tumor extent, soft-tissue invasion, and bone involvement. The CT, MR, and angiographic appearances were compared and correlated with pathologic findings. All six tumors

were resected, and pathologic examination was performed on representative fixed-tissue samples embedded in paraffin and stained with H and E. In five cases, immunocytochemistry was performed with antisera and tumor cells were examined with electron microscopy.

Results

The results of the clinical, laboratory, and radiologic studies are given in Table 1, along with the surgical findings and

TABLE 1: Summary of Patients With Melanotic Tumors

Case No.	Age (months)	Sex	Location	Radiologic Features	Treatment	Pathology	Outcome
1	4	M	R premaxilla and oral cavity	Unenhanced CT showed an expansile, lytic tumor enclosing a tooth with focal extension through posterior cortex; moderate homogeneous enhancement was seen on enhanced CT	Total resection	MNT	No recurrence; alive at 2 years
2	6	M	L premaxilla and oral cavity	CT appearance similar to that in case 1; tumor was isointense on T1-weighted and slightly hyperintense on T2-weighted MR sequences when compared with muscle	Total resection	MNT	No recurrence; alive at 1 month
3	2	F	L maxilla, infratemporal fossa, L orbit	Locally invasive tumor causing marked hyperostosis; soft-tissue component contained punctate calcification and showed homogeneous enhancement on CT	Total resection	MNT	No recurrence; alive at 3 years
4	1	F	L maxilla, infratemporal/temporal/pterygopalatine fossae; L globe	Lytic and expansile bone changes indicating a locally aggressive tumor; large lobular, otherwise homogeneous soft-tissue component on CT and MR; deep invasion could not be excluded on CT; tumor margins and extent clearly seen on MR; signal characteristics similar to those in case 2; vascular tumor on contrast-enhanced CT and angiography; blood supply mostly from external carotid artery	Total resection ^a	Congenital melanoma (possible MNT variant)	No recurrence; alive at 5 months
5	12	M	L occipital calvaria with intracranial extension	Radiographs showed a large, dense, and aggressive neoplasm; calvarial hyperostosis and bony spicules in tumor caused increased density; angiography revealed a vascular tumor supplied mostly by external carotid artery	Incomplete resection	MNT	Died 8 months postoperatively from extensive brain invasion
6	21	M	Cerebellar vermis	Homogeneous increased attenuation compared with brain on unenhanced CT; marked vascularity on enhanced CT and angiography; blood supply from superior cerebellar and vermian arterial branches	Total resection; craniospinal irradiation	MNT (atypical medulloblastoma indistinguishable from other MNTs of infancy)	No recurrence; alive at 7 years

Note.—R = right; L = left; MNT = melanotic neuroectodermal tumor.

^a This infant received one course of chemotherapy (vincristine, adriamycin, cyclophosphamide) and radiation treatment prior to surgery.

postoperative courses. The clinical histories in five of six patients were similar and consisted of a rapidly enlarging maxillary or calvarial mass, most occurring in the first 6 months of life and discovered by the parents. One child (case 6) had ataxia. Vanillylmandelic acid (VMA) levels measured in three patients were normal.

Unenhanced and enhanced CT, performed in five of six patients, identified four homogeneous enhancing maxillary neoplasms (cases 1–4) and one cerebellar vermian neoplasm (case 6). In two patients (cases 1 and 2), the neoplasm expanded the premaxilla, eroded the anterior margin of the hard palate, and protruded into the oral cavity (Figs. 1 and 2). Both tumors contained a tooth, and the initial interpretation was dentigerous cyst or dermoid.

One maxillary tumor (case 3) showed marked hyperostosis involving the ipsilateral orbit and ethmoid sinus (Fig. 3A). The soft-tissue component, located in the infratemporal fossa, could not be separated from the muscles of mastication and contained new bone formation (Fig. 3B). The radiologic appearance suggested osteosarcoma, neuroblastoma, or Ewing sarcoma.

One maxillary neoplasm (case 4) was a large, lobular, disfiguring, soft-tissue mass that eroded and expanded the left maxilla and orbit. The neoplasm was present at birth and rapidly enlarged during the first few weeks of life despite one course of chemotherapy and radiation treatment (Fig. 4A). The diagnosis at admission to our institution was schwannoma. Enhanced CT showed tumor filling the infratemporal fossa, bulging medially into the pharynx, laterally into the temporal fossa, and superiorly into the orbit and globe (Figs. 4B and 4C). Invasion of the ipsilateral tongue and muscles of deglutition could not be excluded.

Two infants (cases 2 and 4) were examined with MR. In both cases the neoplasm appeared homogeneous, demonstrating isointense T1-weighted (Figs. 2D and 4D) and slightly hyperintense T2-weighted (Figs. 2E and 4E) signal compared with that of muscle. The margins of the large neoplasm (case 4) were clearly seen on the T1-weighted images (Fig. 4D), and there was no evidence of deep muscle invasion or intracranial extension on the T2-weighted images (Fig. 4E).

Three patients (cases 4–6) underwent angiography prior to

surgery; a vascular tumor stain persisting into the venous phase was demonstrated in each case. The maxillary neoplasm (case 4) was supplied predominantly by the left external carotid artery (Fig. 4F), with some contribution from the ophthalmic artery (Fig. 4G). The calvarial neoplasm (case 5) was supplied by the external carotid artery, and the intracranial component parasitized middle and posterior cerebral artery branches. The cerebellar vermian neoplasm received blood supply from superior cerebellar and vermian arterial branches.

Skull radiographs of the large calvarial neoplasm (case 5) showed a large, dense, spiculated lesion involving most of the left parietooccipital bone, initially believed to represent a sarcoma (Fig. 5A).

The posterior fossa neoplasm (case 6) was located in the midline and had well-defined margins, slightly increased attenuation compared with surrounding brain on unenhanced CT (Fig. 6A), and marked homogeneous enhancement after IV contrast administration (Fig. 6B). The CT features were believed to represent a medulloblastoma. A choroid plexus papilloma was also considered.

All six neoplasms were completely resected, except the calvarial tumor (case 5), which recurred and invaded the brain (Fig. 5B). Grossly, the maxillary and calvarial neoplasms appeared blue black because of abundant melanin. Four neoplasms (cases 1–3 and 5) showed the typical microscopic pathology of MNT, including clusters of small round cells and large epithelioid cells, both cell types containing melanin and derived from the neural crest (Fig. 7). Occasional primitive glandlike structures were identified.

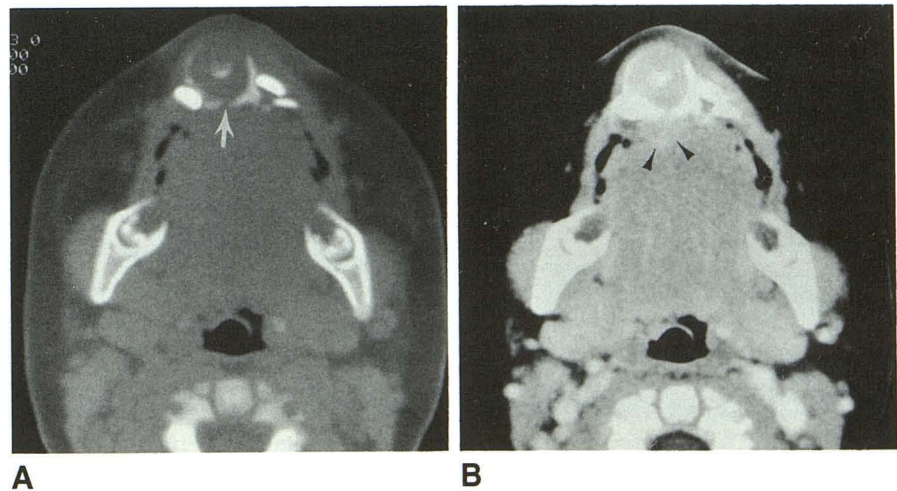
On gross examination, the cerebellar tumor (case 6) showed foci of brownish discoloration. The tumor was composed of many small round cells with hyperchromatic nuclei. Astrocytic and neuronlike cells were also present. Many cells contained melanin and were arranged in tubular configurations suggesting primitive glands. The pathologic diagnosis was atypical melanotic medulloblastoma; however, the melanotic component was indistinguishable from MNT of infancy located elsewhere.

The large maxillary melanotic neoplasm (case 4), initially thought to be a schwannoma, was pathologically diagnosed

Fig. 1.—Case 1: 4-month-old boy with a melanotic neuroectodermal tumor (MNT) in right premaxilla.

A, Axial bone-algorithm CT scan shows a 2-cm lytic expansile lesion in right premaxilla that contains a tooth. Initially this appearance suggested a dentigerous cyst. However, inferior margins are irregular and cortex has been eroded (arrow), indicating locally invasive nature of MNT of infancy.

B, Axial enhanced CT scan shows homogeneous, enhancing solid tumor in right premaxilla protruding into oropharynx (arrowheads).



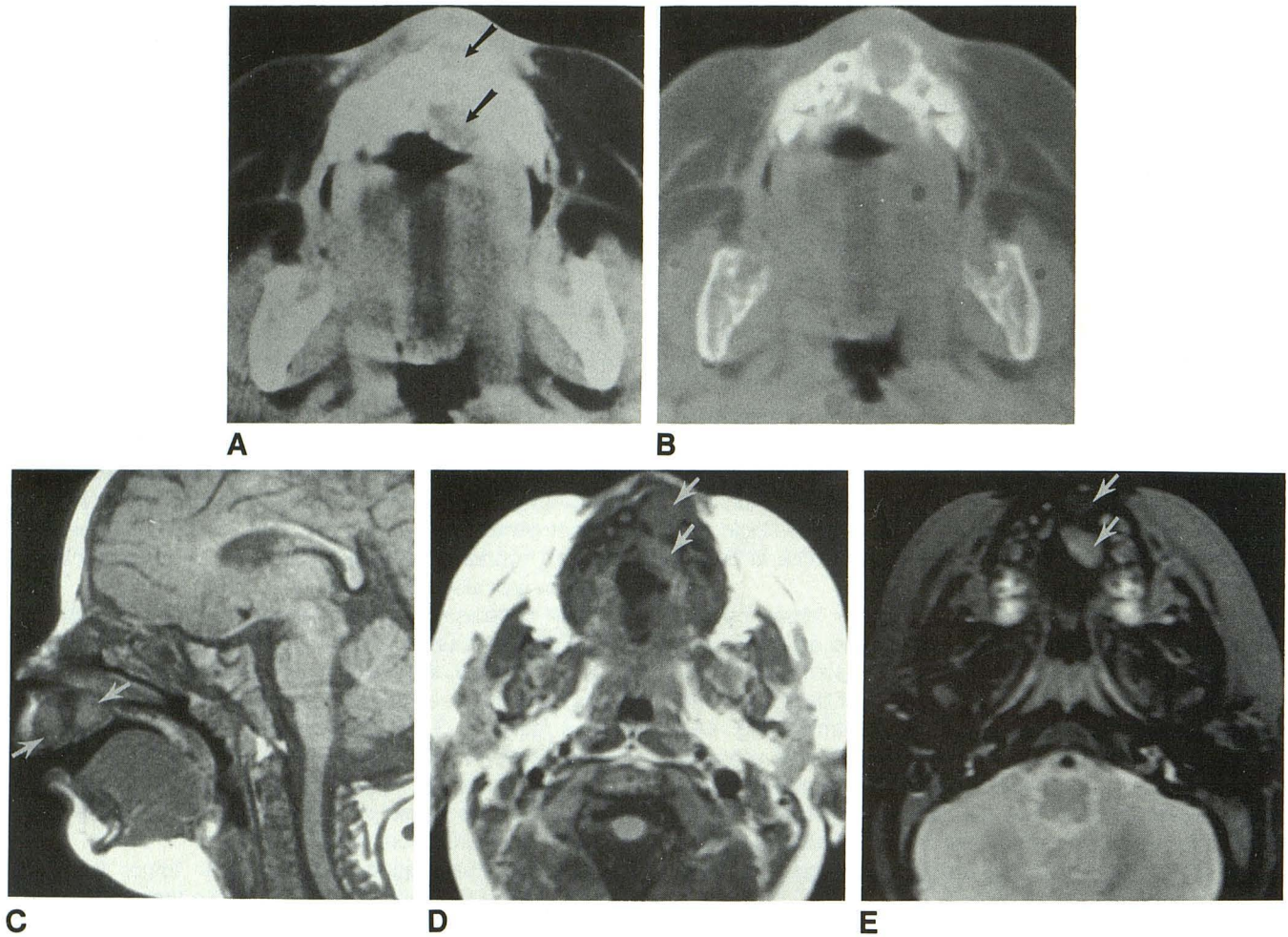


Fig. 2.—Case 2: 6-month-old boy with a melanotic neuroectodermal tumor in left premaxilla.

A and B, Axial enhanced soft-tissue (A) and bone-algorithm (B) CT scans show a solid enhancing lesion (arrows) expanding left premaxilla and protruding into oropharynx through a focal area of cortical destruction. As in case 1, neoplasm encloses a tooth. Bone changes, best appreciated on CT, again reflect locally aggressive nature of this tumor.

C–E, Sagittal T1-weighted SE 500/20/1 (C), axial T1-weighted SE 700/20/2 (D), and axial T2-weighted SE 2800/70 (E) MR images also show a homogeneous neoplasm (arrows) expanding premaxilla. Tumor signal is similar to that of muscle on T1-weighted images and slightly hyperintense on T2-weighted image. Tumor margins are better defined on MR, when compared with CT, owing to superior soft-tissue contrast resolution, and MR correctly predicted extent of tumor as confirmed at surgery.

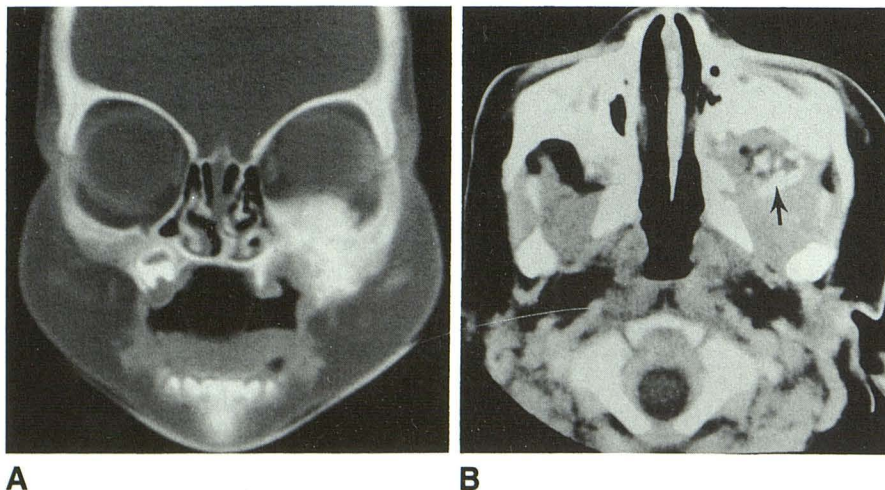


Fig. 3.—Case 3: 2-month-old girl with a melanotic neuroectodermal tumor originating in left maxilla, extending into floor of orbit.

A, Coronal bone-algorithm CT scan reveals marked hyperostosis involving left maxilla and floor of orbit. Hyperostosis is reactive and may be exuberant.

B, Axial enhanced CT scan shows an enhancing soft-tissue mass containing foci of calcification (arrow), representing ossification in tumor. Neoplasm has enlarged left infratemporal fossa.

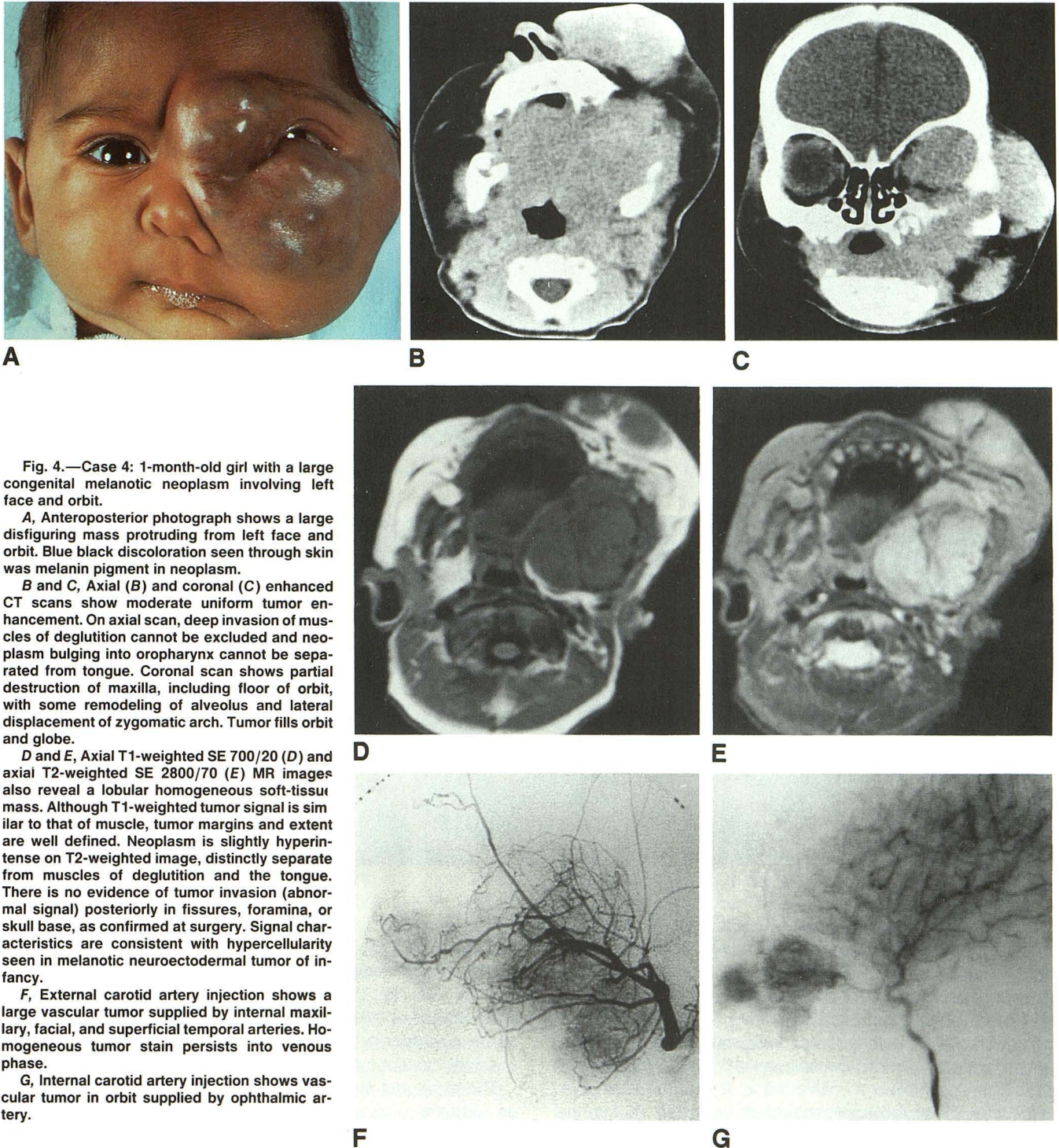


Fig. 4.—Case 4: 1-month-old girl with a large congenital melanotic neoplasm involving left face and orbit.

A, Anteroposterior photograph shows a large disfiguring mass protruding from left face and orbit. Blue black discoloration seen through skin was melanin pigment in neoplasm.

B and C, Axial (B) and coronal (C) enhanced CT scans show moderate uniform tumor enhancement. On axial scan, deep invasion of muscles of deglutition cannot be excluded and neoplasm bulging into oropharynx cannot be separated from tongue. Coronal scan shows partial destruction of maxilla, including floor of orbit, with some remodeling of alveolus and lateral displacement of zygomatic arch. Tumor fills orbit and globe.

D and E, Axial T1-weighted SE 700/20 (D) and axial T2-weighted SE 2800/70 (E) MR images also reveal a lobular homogeneous soft-tissue mass. Although T1-weighted tumor signal is similar to that of muscle, tumor margins and extent are well defined. Neoplasm is slightly hyperintense on T2-weighted image, distinctly separate from muscles of deglutition and the tongue. There is no evidence of tumor invasion (abnormal signal) posteriorly in fissures, foramina, or skull base, as confirmed at surgery. Signal characteristics are consistent with hypercellularity seen in melanotic neuroectodermal tumor of infancy.

F, External carotid artery injection shows a large vascular tumor supplied by internal maxillary, facial, and superficial temporal arteries. Homogeneous tumor stain persists into venous phase.

G, Internal carotid artery injection shows vascular tumor in orbit supplied by ophthalmic artery.

as a congenital melanoma. Specifically, electron microscopy showed abundant premelanosomes and melanosomes, but neurofilaments characteristic of MNT of infancy were absent. All the patients were treated with surgical resection, and the child with the cerebellar neoplasm (case 6) also received irradiation therapy (5000 cGy cranial and 2500 cGy spinal). Five of six children were well and free from disease 1 month to 7 years after resection. As mentioned, the calvarial MNT recurred, causing the infant's death 8 months after surgery.

Discussion

MNT of infancy is a controversial, rare neoplasm. It occurs most often in the maxilla, followed by the calvaria and mandible [1, 5, 6, 8–10]. Unusual locations include the shoulder, mediastinum, epididymis, and uterus. Since the original description by Krompecher [11] in 1918, between 150 and 200 cases have been reported [6, 12]. Krompecher believed the tumor was a congenital melanocarcinoma. Other names for

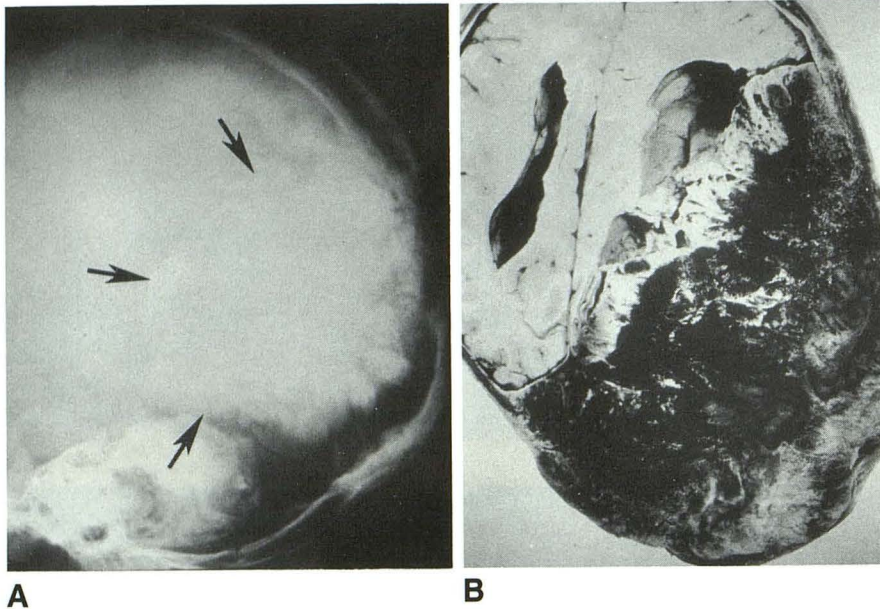


Fig. 5.—Case 5: 12-month-old boy with a left occipital melanotic neuroectodermal tumor that invaded brain and caused child's death.

A, Lateral skull radiograph shows increased bone density (*arrows*) in occipitoparietal region secondary to spiculated calcifications in tumor and marked reactive hyperostosis in adjacent calvaria.

B, Postmortem axial-cut brain shows a large tumor that has destroyed and protrudes through left occipitoparietal calvaria. There is extensive invasion of underlying brain parenchyma. Solid black appearance of tumor is from abundant melanin pigmentation.

(Reprinted with permission from Harwood-Nash and Fitz [7].)

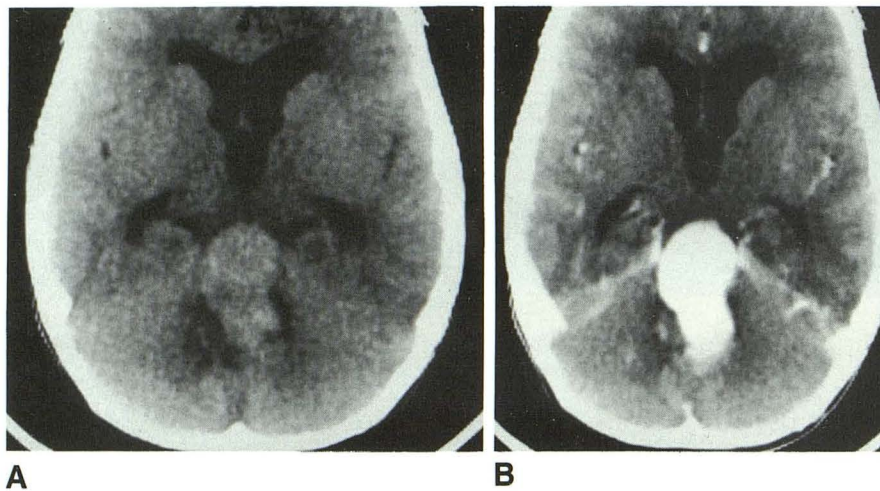


Fig. 6.—Case 6: 21-month-old boy with a melanotic neuroectodermal tumor in the vermis.

A, Unenhanced axial CT scan shows a well-defined, midline, posterior fossa, homogeneous tumor that is slightly denser than adjacent brain. There is hydrocephalus associated with compression on fourth ventricle.

B, Enhanced axial CT scan. Tumor demonstrates marked homogeneous enhancement.

the same entity, which were based on theories of tumor cell origin, have included pigmented ameloblastoma, melanoameloblastoma, pigmented epulis, retinal anlage tumor, and melanotic progonoma [2, 4, 5].

The term *retinal anlage tumor* frequently appears in older reports because the microscopic cellular structures seen in MNTs may resemble a primitive retina. It was theorized that a pinching off of the neuroepithelium occurred during the formation of the embryonic eye [4, 5, 10]. The embryologic development of the eye, however, is complete when the maxilla forms.

The most widely accepted theory of origin is that this tumor derives from the neuroectoderm [1, 2, 4, 6, 10, 12–17]. The term *melanotic progonoma* implies derivation or ancestry from precursors of the sensory (neural crest) neuroectoderm, specifically the vomeronasal organ of Jacobson [4, 6, 10]. This structure is seen in lower vertebrates, and chick embryo neural crest cells labeled with tritiated thymidine have been shown to migrate to the upper face [16]. This is the theory of

atavism. However, in the early human embryo, the vomeronasal organ is present for a transient period only and is absent in later fetal life and infancy when MNTs occur. It is not currently known how neural crest cells, which arise from cords of neuroectoderm, become trapped or diverted and end up in aberrant locations such as the maxilla.

The strongest support for neural crest cell origin is based on electron microscopic ultrastructure and biochemical evidence. Specifically, on electron microscopy, neuritelike processes, neurofilaments, and neurosecretory granules have been identified by several investigators [1, 4, 6, 12–17]. The neurofilaments or microtubules, approximately 10 nm in diameter, are located in the cytoplasm of small neural type cells and are believed to represent a transportation mechanism for neurosecretory substances. These features are morphologically compatible with a neuroblast or immature melanocyte of neural crest origin. Melanin-containing cells typically occur in the sympathetic ganglia and adrenal medulla, further supporting neural crest origin.

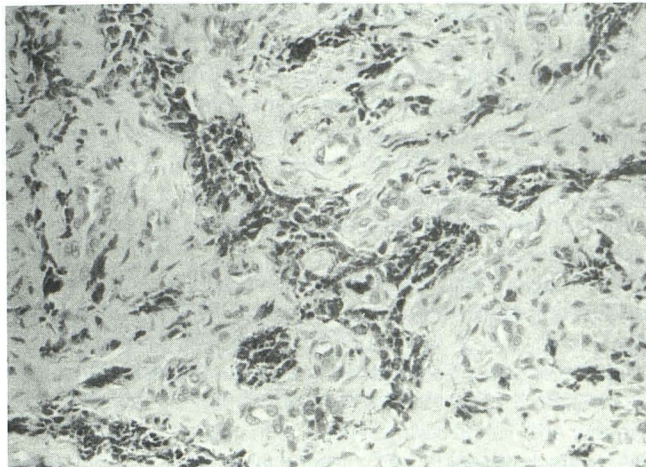


Fig. 7.—Melanotic neuroectodermal tumor of infancy, representative histologic section. Numerous clusters of small round cells and polygonal epithelioid cells are seen in vascular fibrous connective tissue stroma. Both cell types are derived from neuroectoderm. Some cells are so densely pigmented with melanin that cellular structures are obscured. (H and E, original magnification $\times 200$)

Borello and Gorlin [15] described a group of patients with elevated urine levels of VMA that returned to normal after the MNTs were resected. VMA is the major urine breakdown product of the catecholamines produced by amine precursor uptake and decarboxylation cells, derivatives of the neural crest. Therefore, tumors of the neural crest may have elevated levels of VMA. Bolande (cited in [16]) first recognized this relationship and proposed the concept of neurocristopathy to explain the origin of several neoplasms with elevated VMA levels, including pheochromocytoma, ganglioneuroblastoma, neuroblastoma, ganglioneuroma, and retinoblastoma.

Most infants with MNTs are less than 6 months of age and have a solid, sessile facial mass located in the maxillary bone. Occasionally the neoplasm is visible at birth, but most often it is discovered by the parents during the first few months of life [1]. Rapid tumor enlargement typically occurs over a few weeks and produces facial disfigurement. Blue black discoloration seen through the skin indicates melanin pigmentation in the neoplasm.

Maxillary, mandibular, and calvarial MNTs are locally aggressive. Cure is usually accomplished by complete excision alone [1, 2, 4–6, 9, 12]. There are case reports of recurrent or multicentric MNTs that also were treated with local resection and sporadic reports of adjuvant chemotherapy used in conjunction with surgery. Once considered universally benign, it is now known that definite malignant potential exists—reported to be 1.9–3.2% [6, 12].

More than two thirds of reported cases of MNT involve the maxilla. Of the cases reported here, three originated in the maxilla and were treated with surgical excision only. At the time of this report, all three patients were well and free of disease 1 month to 3 years after resection. An additional maxillary melanotic neoplasm was included that occurred in an infant with the clinical and radiologic features of an MNT of infancy. Pathologic evaluation, however, revealed a con-

genital melanoma (i.e., large epithelial cells only, containing melanosomes of varying maturation), which is exceedingly rare. Congenital melanoma may represent a variant or part of a spectrum of infantile melanotic neoplasms that includes MNT of infancy. As discussed, melanin-producing epithelial-like cells and neuroblasts are both known to originate from the neural crest. Absence or a decreased number of neuroblasts could explain the pathologic appearance in this case.

One MNT occurred in the left occipital calvaria near the posterior fontanelle. Unfortunately, the neoplasm invaded the underlying brain and caused the death of the 12-month-old boy. In 1982, Walsh and Strand [10] reviewed the literature and compiled 10 cases involving the calvaria. They found that calvarial MNTs occurred in or near the fontanelles, less frequently in the sutures, and appeared to arise from the pericranium. All the patients in their series were less than 1 year old and were cured with surgical resection. Sakamoto et al. [18] reported their 15-year experience with childhood brain tumors, which included a single calvarial MNT of infancy cured with surgery only.

This report also includes an atypical medulloblastoma of the cerebellar vermis. A large component of the neoplasm was melanotic and histologically similar to MNT of the maxilla. Intracranial MNTs contain abundant melanin pigment, but unlike those occurring in bone the intracranial neoplasms may spread by CSF seeding. Nearby vital structures may preclude total resection [7, 8]. Leptomeningeal disease is present in 50% of patients at the time of first diagnosis. The case reported here occurred in a 21-month-old boy with a vermian MNT but no leptomeningeal disease. The neoplasm was resected and the child was treated with craniospinal irradiation. Seven years after resection, he was still well and free of disease.

Hahn et al. [17] reported an intracranial MNT and reviewed the literature. Five of the 10 patients they discussed were alive (at an average of 22 months from diagnosis) at the time of their report. Among the survivors, two had undergone surgical resections, three had received radiation treatment, and one child had had both surgical excision and radiation treatment. Those who died were considered to have unresectable tumors, and evidence of widespread leptomeningeal disease caused by CSF seeding was seen in some. A propensity for leptomeningeal spread, similar to that seen in medulloblastoma, suggests that gadopentetate dimeglumine-enhanced MR of the craniospinal axis will be essential for assessing the extent of disease and follow-up after therapy [19–22].

There is little in the literature on imaging of MNTs of infancy or infantile melanotic maxillary neoplasms [1, 3, 23]. The radiologic appearance depends in part on the location of the MNT. In our series, CT showed predominantly lytic and expansile bone changes caused by the rapidly growing soft-tissue component in three of four maxillary neoplasms (Table 2). Two MNTs (cases 1 and 2) were located in the premaxilla, and each enclosed a tooth, adding dentigerous cyst and dermoid to the differential diagnosis (Table 3). The infantile melanoma (case 4) was a large soft-tissue neoplasm that destroyed the body of the maxilla, filled the orbit, and displaced the zygomatic arch and mandible laterally. Three-

TABLE 2: Radiologic Features of Maxillary Melanotic Neuroectodermal Tumors of Infancy

Lytic expansile tumor in maxilla, locally invasive with variable reactive hyperostosis/osteogenesis; may be exuberant. Bone changes best seen on CT. Homogeneous soft-tissue mass on CT that demonstrates uniform vascular enhancement with IV administration of contrast material. Angiography shows a vascular tumor stain supplied by the external carotid circulation (invasive tumors may parasitize the internal carotid circulation). MR imaging is better than CT for evaluating tumor extent and tissue invasion. The tumor exhibits homogeneous isointense T1-weighted and slightly hyperintense T2-weighted signal compared with that of muscle.

TABLE 3: Radiologic Differential Diagnosis of Maxillary Melanotic Neuroectodermal Tumors of Infancy

Diagnosis
Benign lesions
Dentigerous cyst
Dermoid
Eosinophilic granuloma
Giant cell tumor
Reparative granuloma
Malignant lesions
Neuroblastoma
Osteosarcoma
Ewing sarcoma
Rhabdomyosarcoma
Ameloblastoma

dimensional CT scans were useful during surgical planning and reconstruction. Less frequently, extensive hyperostosis and soft-tissue osteogenesis may occur, obliterating the normal bone architecture of the maxilla and causing increased density on radiographs and CT, as seen in case 3 [3, 24]. In this case, the differential diagnosis included osteosarcoma, neuroblastoma, and Ewing sarcoma.

The occipital MNT (case 5) probably originated in or near the posterior fontanelle and eroded both tables of the calvaria. Radiographs showed reactive hyperostosis at the bony margins and spicules of new bone within the neoplasm, similar to findings in previous reports [7, 10, 24]. Solitary destructive neoplasms of the infant calvaria are distinctly uncommon. Bony spicules perpendicular to the vault may be seen in hemangiomas, neuroblastomas, or Ewing sarcomas. A large soft-tissue mass with marked hyperostosis suggests a more malignant neoplasm such as sarcoma, usually of dural origin.

On unenhanced CT scans, the maxillary neoplasms were similar in density to the surrounding muscles, while the vermian lesion demonstrated slightly increased attenuation compared with the adjacent brain. In each case, the soft-tissue component was homogeneous, except for case 3, which showed some tumor osteogenesis. Following IV contrast administration, the maxillary and vermian MNTs showed uniform moderate and marked enhancement.

One expansile, lytic, premaxillary MNT of infancy (case 2) was evaluated with MR. The neoplasm exhibited homogeneous isointense T1-weighted signal and slightly hyperintense T2-weighted signal compared with that of muscle. Tumor destroying the posterior margin of the maxilla and protruding into the oral cavity was seen better on MR than on CT.

The large maxillary congenital melanoma (case 4) was also studied with MR. Both CT and MR showed a large soft-tissue mass that partially destroyed the left maxilla and extended into the ipsilateral infratemporal and temporal fossae, pterygopalatine fossa, and orbit. On CT it was difficult to separate the neoplasm from adjacent deep musculature before and after IV contrast administration. This was in part due to the relative absence of fat separating tissue planes in infants and young children.

MR imaging was very sensitive to subtle differences in tissue composition and water content. The extent and regional anatomy of the neoplasm were well shown on T1-weighted images. T2-weighted images distinguished the neoplasm from the normal tissues better than CT did owing to superior soft-tissue contrast resolution and correctly excluded deep muscle invasion and intracranial extension. As in case 2, the neoplasm exhibited homogeneous isointense T1-weighted and slightly hyperintense T2-weighted signal when compared with muscle, an appearance previously described in association with marked cellularity and consistent with the pathologic findings [25]. Contrary to a recent case report of MNT of infancy and despite abundant pathologically proved melanin, neither tumor exhibited T1 and T2 shortening (enhanced T1 and T2 relaxation), which typically occurs in melanin-containing tumors and appears as increased signal on T1-weighted images [23]. We have no explanation for this phenomenon, but factors other than the paramagnetic properties and the absolute amount of melanin may be involved [26]. IV gadopentetate dimeglumine was not administered in either infant; however, we predict moderate, uniform enhancement for MNTs of infancy based on the contrast-enhanced CT characteristics.

The blood supply to facial and neurocranial MNTs is from the external carotid circulation; this was seen in three patients (cases 4–6) who underwent angiography [10]. Each case showed vessel displacement caused by tumor mass and a vascular homogeneous tumor stain persisting into the venous phase. The cranial MNT, which invaded brain parenchyma, parasitized the ipsilateral posterior and middle cerebral arteries. The midline posterior fossa neoplasm displaced vermian branches anteriorly and superiorly, consistent with medulloblastoma originating near the roof of the fourth ventricle. The tumor stain, however, was more intense than usually seen in medulloblastoma.

All resected gross specimens exhibited blue black discoloration due to melanin pigment produced by the tumor. This pigmentation is often visible through the overlying skin and, in conjunction with the other clinical features, helps suggest the correct preoperative diagnosis. As mentioned, MNTs may be associated with elevated urine levels of VMA, reflecting increased catecholamine production. These levels return to normal after the tumor is resected. VMA levels, measured preoperatively in three cases, were all within the normal range.

Microscopically, MNTs of infancy consist of a nonencapsulated mass of tumor cells in a well-vascularized fibrous tissue stroma (Table 4), which explains the angiographic appearance [4–6, 8, 10, 17, 23]. Characteristically, there are clusters or islands of small cells with dark nuclei and minimal

TABLE 4: Pathologic Features of Melanotic Neuroectodermal Tumors of Infancy

Feature
Gross
Nonencapsulated, solid, homogeneous, cellular tumor adherent to contiguous structures; dark blue black discoloration caused by abundant melanin
Microscopic
Clusters of small, round cells with hyperchromatic nuclei and minimal cytoplasm and larger, polygonal epithelioid cells, both cell types originating from the neuroectoderm
Abundant melanin pigment that may occur in either cell type or the extracellular spaces
Other derivatives of the neuroectoderm may be present; for example, Schwann cells, astrocytes, and ganglia
Tendency to invade adjacent tissues; distant metastases reported in a few cases (intracranial variant may spread by leptomeningeal seeding)

cytoplasm. Larger epithelioid cells also are present and may form primitive glandlike structures resembling optic pits, which historically have led to the erroneous diagnosis of retinal anlage tumor [4]. Melanin granules may occur in either cell type, and frequently there are large extracellular deposits.

The large melanotic neoplasm involving the left face and orbit (case 4) was pathologically proved to be a congenital melanoma based on electron microscopic and immunohistochemical studies. Neuroectoderm morphologic features and immunohistochemical markers, pathologically characteristic of MNT of infancy, were absent. The melanoma was included in this report because the clinical and radiologic features were similar to other MNTs of infancy, suggesting that it may be a variant or part of a spectrum of melanotic neoplasms involving the maxilla in childhood.

Although MNT of infancy is a rare tumor, the correct diagnosis can be suggested from the clinical and radiologic findings described in this report. MR imaging and CT are complementary. Soft-tissue invasion and tumor margins are seen particularly well on MR, while CT is best for evaluating bone involvement. Except for two or three documented cases with metastases, MNTs of infancy occurring in bone are benign tumors. However, as observed in all our cases, rapid growth and local invasion are characteristic. The treatment is surgical excision, which, at the time of this writing, was curative in three of four cases (range, 1 month to 3 years after excision). The incompletely resected calvarial MNT (case 5) invaded the brain and caused the child's death 8 months later, emphasizing the importance of prompt diagnosis and complete resection.

The diagnosis, treatment, and outcome are less clear for the rarer intracranial MNT. Its similarity to medulloblastoma (regarding spread of leptomeningeal disease) suggests that contrast-enhanced MR will be essential for detecting and assessing the extent of disease. The infant with a cerebellar vermian MNT (case 6) was well and without recurrence 7 years after surgical excision and craniospinal irradiation.

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