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Cranial Computed Tomography of Malignant Melanoma

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Two hundred seventy-five cranial computed tomography (CT) scans performed on 179 patients with malignant melanoma were reviewed. Of the 101 patients with confirmed cerebral metastases, CT demonstrated lesions in 93. In 72% of these, areas of increased attenuation were present in the precontrast scan. These lesions also enhanced after contrast infusion. There was a direct correlation between the extent of bleeding in the neoplasm and the density of the metastasis, at least 20% red blood cells per high power field were consistently present within lesions of increased attenuation. Cerebral metastases were occasionally associated with subdural or intracranial hemorrhage. Meningeal melanomatosis was recognized by CT only when associated with adjacent parenchymal metastases. In nine (11%) of 74 patients without clinical evidence of brain involvement, CT revealed cerebral metastases; this suggests that a staging CT scan might be useful on patients with diffuse or advanced local extracranial disease prior to definitive therapy.

The cranial computed tomographic (CT) features of malignant melanoma usually consist of single or multiple nodules of increased attenuation that enhance after the infusion of contrast material [1-3]. These metastases are often located in the gray matter or at the subcortical gray-white matter junction surrounded by varying amounts of edema and frequently associated with hemorrhage. At times, the CT manifestation is that of intracerebral, subarachnoid, or subdural hemorrhage alone [4, 5]. Meningeal melanomatosis has been detected by CT in combination with parenchymal disease or, on occasion, as an isolated finding [2]. In this report, we detail these features and their relative incidence in 101 patients with established cerebral involvement by malignant melanoma. The value of CT as a staging procedure in 74 other patients with melanoma but with no obvious neurologic signs and symptoms is also discussed.

Materials and Methods

We analyzed retrospectively 275 CT examinations in 179 patients with proven malignant melanoma. The 107 males and 72 females were 9-81 years old. The interval between diagnosis of the primary melanoma and CT demonstration of cerebral metastases in the 101 patients with cerebral disease was 6 months to 22 years.

The examinations were performed on an EMI 1010S head scanner. Most patients (80%) were examined before and after infusion of 42.3 g of iodine in 300 ml of 30% meglumine diatrizoate. More recently, the CT studies were done after rapid infusion (in about 10 min) of 84.6 g of iodine in 600 ml of 30% meglumine diatrizoate. In selected cases (nine patients) repeat images were obtained 1 hour after rapid high-dose infusion. As many as eight studies were done in some patients during the course of their disease to monitor the effects of treatment.

The primary tumors were located in the head and neck in 36 patients, in the upper extremities in 34, in the lower extremities in 28, on the chest wall in 21, on the back in 32, and on the abdominal wall in seven. Unusual sites of primary tumor localization were in the vulva in two patients and one each in the vagina, gallbladder, scrotum, stomach, thoracic

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TABLE 1: Distribution of Metastases with Cerebral Melanoma

Site of Metastases	No. Metastases/No. Patients (%)		
	Single	Multiple	Total
Cerebral alone	14 (15.0)	9 (9.7)	23 (24.7)
Cerebral and extracranial	22 (23.7)	48 (51.6)	70 (75.3)
Total	36 (38.7)	57 (61.3)	93 (100.0)

extradural space, and cerebral leptomeninges. In 13 cases, the site of the primary neoplasm was unknown.

In 74 patients with no neurologic findings, CT was performed to stage the disease. In the other 105 patients, the examination was done at the onset of neurologic symptoms or during the course of the cerebral disease.

Results

Overview

Of the 179 patients examined by CT, clinical evidence of intracranial involvement was found in 101. Of these 101 patients, 75 were studied before and after intravenous injection of contrast material; in 22 patients CT was performed only after contrast material; in the other four patients no contrast material was used because of a known history of sensitivity. CT findings were positive in 93 patients, while in eight with clinical evidence of intracranial disease established by cerebrospinal fluid cytology, CT examinations were interpreted as negative.

In 92 of the 93 patients with abnormal features, foci of metastatic melanoma were identified in the pre- and/or postcontrast studies. In one case, characterized by an inhomogeneous area of low density, we were unable to differentiate between postsurgical changes and recurrent tumor. Surgery performed because of progressive neurologic findings confirmed the presence of melanoma.

The distribution of the metastases demonstrated in 93 patients was as follows: in 50 (53%), the lesions were in one hemisphere, while in 43 (47%) they were diffuse. A single metastasis was seen in 36 (38%) and multiple lesions in 57 (62%).

In 23 (24.7%) of the 93 patients, central nervous system involvement was clinically suspected and confirmed by CT as the only site of metastatic melanoma. Of this group of 23, a single metastasis was found in 14 (15%) of 93 patients, while in nine (9.7%) multiple cerebral lesions were seen. The other 70 of the 93 patients had cerebral plus extracranial involvement. Of these, 22 (23.7%) of the 93 patients had a single cerebral metastasis while 48 (51.6%) had multiple brain lesions (table 1).

The frontal lobe was the most common site followed by the temporoparietal region. In seven cases, metastatic nodules were periventricular in location and in one case, a single lesion was identified arising from the lateral ventricle (fig. 1). Posterior fossa metastases were found in 21 patients, more commonly with diffuse cerebral disease, while the posterior fossa was the only site of involvement in six. Hydrocephalus was associated with posterior fossa metastases in seven patients.

Ventricular distortion or shift by mass effect was noted in

52 (56%) of the 93 cases and varied from minimal flattening of the ventricles to marked obliteration and herniation (fig. 2). In two cases, metastases were in the orbits (fig. 3). Osteolytic metastases of the skull were identified in five patients, four of whom also had contiguous parenchymal extension (fig. 4). One patient had scalp metastases (fig. 5).

Specific CT Features

Of the 93 patients with positive CT, 80 had precontrast studies. In 57 (71%) of these, the metastases were visualized as circumscribed masses of increased attenuation as compared with normal brain (fig. 6) (table 2).

In two patients, an intracerebral hematoma was diagnosed because of a fluid level identified within the area of increased density. Three other patients developed intracerebral hemorrhages as defined by attenuation coefficients greater than 30 EMI units. Two of these three patients were subjected to craniotomy, which confirmed the presence of tumor cells mixed with blood (fig. 2). An isolated subdural hematoma was discovered by CT in still another patient and proved by surgery to contain tumor cells in the blood.

In all 75 patients studied before and after infusion of contrast material, there was enhancement of cerebral lesions. In three of these, additional lesions were demonstrated after contrast material; and in four, lesions were seen only after contrast infusion. A "ring" lesion was seen in 14 (15%) of the 88 patients with positive CT who received contrast material (fig. 7). This pattern was present only after irradiation in four of these 14. Areas of decreased attenuation (presumably edema) surrounding the enhanced lesions were demonstrated in 78 of 93 (84%) positive cases and varied from a few millimeters to occupying most of the hemisphere.

In nine patients delayed images were obtained 1–1½ hr after administration of contrast material, in addition to immediate postinjection scans. This did not modify the characteristics of the metastatic disease in one patient but did enhance the lesions in two others without altering the number of metastases detected. The density of the lesions was less obvious, that is, more isodense with the brain in one patient, while in another the ring lesions filled in completely. In three other patients, the delayed study confirmed the absence of disease.

Of the 93 patients with positive CT, meningeal melanoma was found in six cases in conjunction with parenchymal metastases. In the other eight patients with clinical evidence of intracranial disease and positive cerebral spinal fluid cytology there were no CT manifestations of meningeal neoplasm. This included one patient with a hairy nevus syndrome and primary leptomeningeal melanoma.

In nine (11%) of 74 patients without clinical evidence of brain involvement, CT revealed cerebral metastases. Two of these patients had single metastases in the liver and lung. Two other patients with recurrent local disease in the skin of the back were found to have cerebral metastases. In the other five patients with several systemic metastases and no neurologic findings, CT performed for staging revealed cerebral lesions.

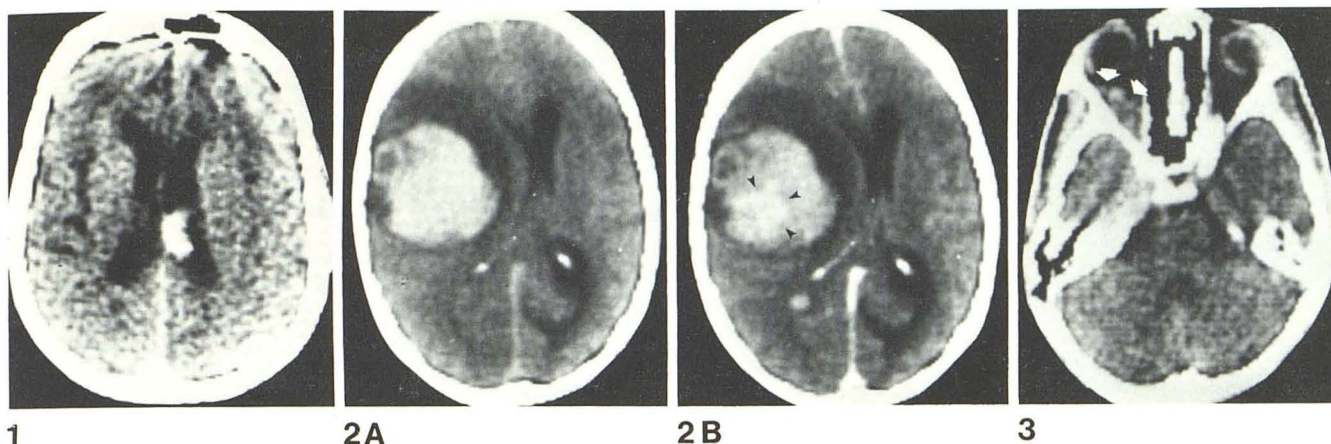


Fig. 1.—Enhanced image. Intraventricular melanoma metastasis.
Fig. 2.—A, Unenhanced image. Major mass effect secondary to acute hemorrhage into melanoma metastasis. B, Enhanced image. Eccentric contrast enhancement (*arrowheads*).

Additional enhancing lesions, left occipital. Nonenhancing right occipital lesion.

Fig. 3.—Unenhanced image. Metastatic melanoma to posterior left orbit. (*arrows*).

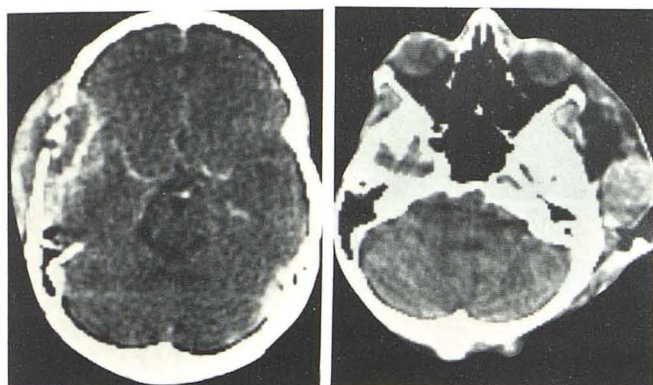


Fig. 4.—Enhanced image. Melanoma metastasis to bony calvarium. Intra- and extracranial extension.

Fig. 5.—Unenhanced image. Right temporal, extracranial melanoma metastasis.

Intracranial involvement by metastatic melanoma was established in 76 of the 101 patients by surgery, cytologic examination of the cerebrospinal fluid, or by autopsy within 3 months after CT. In 25 patients, the clinical course of the disease, primarily diffuse metastases, appeared to confirm the CT findings.

The nature of the metastatic foci was best defined from the histologic examination of the surgical and autopsy specimens in 25 patients. The metastases were evaluated as to the presence and proportion of hemorrhage, hemosiderin, and neoplasm. All nodules, whether they exhibited increased attenuation before contrast infusion or not, contained some evidence of hemorrhage. There was a direct relation between the size of the neoplasm and the extent of hemorrhage. The larger the lesion, the more extensive was the hemorrhagic component. Metastases with a minimum of 20% red blood cells per high power field exhibited increased attenuation before contrast infusion. Four patients with

amelanotic melanoma had increased attenuation on the precontrast study. Consequently, the increased attenuation may be related to the percent of hemorrhage and/or hemosiderin in the tumor and not to the presence of melanin.

Discussion

Malignant melanoma occurs in 1.8 persons per 100,000 annually [6]. Eighteen percent of cerebral neoplasms are metastases and of these 5%–10% are from melanoma [7, 8]. At M. D. Anderson Hospital, over 50% of patients dying of malignant melanoma have cerebral metastases [9]; the average survival time from the beginning of neurologic symptoms is 65 days [10, 11]. Even with chemotherapy and radiotherapy, this is extended to only 4 months with a maximum of 2 years and 2 months [9].

Metastatic brain tumors may be associated with subdural, subarachnoid, intracerebral, and intraventricular hemorrhage or a combination of these [4, 5, 12–14]. Massive hemorrhage is a complication of metastases in 14% of patients compared with 0.8% of those with glioma [13]. With multiple metastases, hemorrhage occurred with large as well as small lesions and was at times the first manifestation of cerebral disease. In order of frequency, the tumors most prone to develop such hemorrhage were metastatic choriocarcinoma, melanoma, bronchogenic carcinoma, and hypernephroma. Madonick and Savitsky [15] reviewed the subject of subarachnoid hemorrhage in cerebral melanoma and found 26 cases of bloody or xanthochromic spinal fluid in 56 cases of metastatic melanoma in contrast to two of 56 with metastases from other primary sites.

Increased attenuation of metastases on the precontrast scans was almost invariably associated with some degree of recent hemorrhage within the tumor. Histologic evidence of hemorrhage was also found in those lesions showing decreased attenuation on unenhanced scans. A finding of 20% or more red blood cells per high power field was associated with increased attenuation. Why this increased

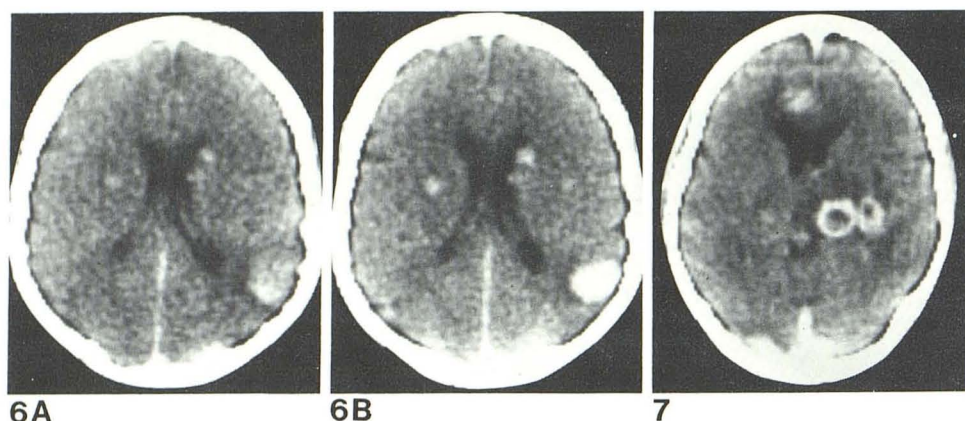


Fig. 6.—A, Unenhanced image. Several hyperdense nodules. Minimal peritumoral edema. No mass effect. B, Enhanced image. Several enhancing lesions.

Fig. 7.—Enhanced image. Ring-enhancing melanoma metastases right thalamic and deep temporal lobe. Other enhanced lesions on left.

TABLE 2: CT Features of Cerebral Metastatic Melanoma

Feature	No. (%)	(n = 93)*
Edema	78 (84)	
Increased attenuation (postcontrast)	57 (71)	
Mass effect	52 (56)	
Intra- or periventricular	8 (9)	
Obstructive hydrocephalus	7 (8)	

* For increased attenuation (precontrast), n = 80.

attenuation persists on follow-up examinations performed at intervals of 1–3 months remains unclear but may be related to recurrent hemorrhages or the accumulation of hemosiderin. The presence of melanin was not responsible for the increased density. Four patients with amelanotic melanoma had hyperdense lesions.

Computed tomographic findings of multiple (62%), bilateral (53%) nodules of increased attenuation (72%) were the most common features in our series of 101 patients with malignant melanoma involving the brain (fig. 6). Occasionally, secondary foci of melanoma may be without edema or mass effect (16% and 44%, respectively). Solitary hyperdense dural-based lesions that enhanced dramatically after infusion of contrast material were impossible to differentiate from meningioma (fig. 8). However, if the patient has known metastases the diagnosis of meningioma is less likely; if there are no known metastases, melanoma should be included in the differential diagnosis of a lesion that looks like a meningioma.

Cerebral involvement has been reported as the first focus of metastasis in 7%–22% of patients with malignant melanoma [16] and was seen in 24% of our patients. For the most part, intracranial metastases occurred in association with more widespread disease [76%].

Eleven percent of cerebral metastases were discovered during the staging procedure of melanoma patients without neurologic findings. These patients had several foci of disease and were evaluated before more aggressive local therapy was instituted. In view of the high incidence of cerebral metastases in neurologically intact patients, CT should be performed for staging in patients with advanced

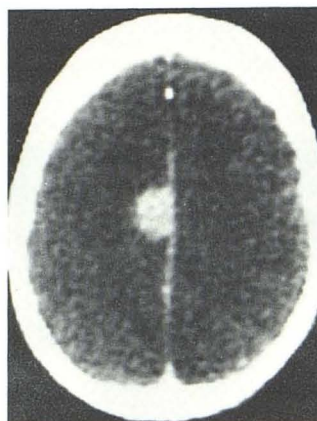


Fig. 8.—Enhanced image. Enhancing, dural-based melanoma metastasis indistinguishable from parafalcine meningioma.

local disease or with extracranial metastases. The discovery of additional cerebral metastatic foci will help avoid unnecessary treatment.

Computed tomography was most disappointing in the detection of meningeal involvement with melanoma unless associated with parenchymal metastases. However, this diagnosis may even be difficult at autopsy, that is, microscopic changes may be minimal when infiltration is confined to the leptomeninges [17]. In none of the eight patients with positive cerebrospinal fluid cytology was there diffuse contrast enhancement of the subarachnoid space as reported by Enzmann et al. [2]. In our one case of primary leptomeningeal melanoma, CT was normal in the face of positive cytology [18].

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