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Cranial Computed Tomographic Abnormalities in Leptomeningeal Metastasis

Ya-Yen Lee, J. Peter Glass, Anne Geoffray and Sidney Wallace

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Ya-Yen Lee[1]
J. Peter Glass[2]
Anne Geoffray[1]
Sidney Wallace[1]

Sixty-four (57.6%) of 111 cancer patients with cerebrospinal fluid cytology positive for malignant cells had cranial computed tomographic (CT) scans within 2 weeks before or after a lumbar puncture. Twenty-two (34.3%) of the 64 had abnormal CT findings indicative of leptomeningeal metastasis: (1) sulcal-cisternal enhancement, (2) ependymal-subependymal enhancement, (3) widened irregular tentorial enhancement, or (4) communicating hydrocephalus. Thirteen (59.6%) of these 22 patients had associated parenchymal metastases. Recognition of leptomeningeal disease may alter the management of patients with parenchymal metastases. Communicating hydrocephalus in cancer patients should be considered to be related to leptomeningeal metastasis until proven otherwise.

Leptomeningeal metastasis is associated with a relatively poor prognosis. However, vigorous treatment with intrathecal chemotherapeutic agents and/or radiation therapy can improve symptoms and at times prolong survival [1]. The diagnosis of leptomeningeal metastasis by cranial computed tomography (CT) contributes to earlier treatment and sometimes alters the management of patients with parenchymal metastases. The findings and differential diagnosis of leptomeningeal metastasis are discussed from the evaluation of CT scans in 64 patients whose cerebrospinal fluid (CSF) cytologic examinations were positive for malignant cells.

Materials and Methods

During a 1 year period, 111 cancer patients at M. D. Anderson Hospital and Tumor Institute had a CSF cytology positive for malignant cells. The data were obtained from three major sources: cytopathology records; hematology records of CSF cell counts and differentials; and neurosurgical operative records of the placement of Ommaya reservoirs. The types of primary neoplasms are listed in table 1. Of the 111 patients, 44 (29.6%) had leukemia and 19 (16.2%) had lymphoma. The solid tumors included carcinoma of the breast in 21 (18.9%) patients and carcinoma of the lung in 11 (10%). Sixty-four (57.6%) of the 111 had CT scans within 2 weeks before or after a lumbar puncture.

CT studies were performed on GE CT/T 8800 or Siemens Somatom-2 or DR-3 scanners at 8 or 10 mm intervals using horizontal cuts from the base of the skull to the vertex. All examinations were done before and immediately after intravenous infusion of 300 ml of 30% meglumine diatrizoate (42.3 g iodine) over 10 min.

Results

Twenty-two (34.3%) of the 64 patients examined by CT had definite abnormalities that could be related to leptomeningeal metastasis, that is, sulcal-cisternal enhancement, ependymal-subependymal enhancement, widened irregular tentorial enhancement, or communicating hydrocephalus. All those studies with only suggestive or questionable findings were discarded.

Sixteen patients exhibited sulcal-cisternal enhancement that was localized in

TABLE 1: **Primary Neoplasms in Cancer Patients with CSF Cytology Positive for Malignant Cells**

Primary Neoplasm	No. of Patients with Positive CSF Cytology	No. of Cranial CT Studies	
		Total	Positive for Leptomeningeal Metastasis
Leukemia*	44	19	3
Lymphoma*	18	12	2
Breast	21	17	7
Lung	11	7	4
Multiple myeloma	4	2	2
Other tumors†	7	3	1
Pinealoblastoma	1	1	1
Medulloblastoma	3	2	1
Other brain tumors‡	2	1	1
Total	111	64	22

Note.—Cranial CT studies were performed within 2 weeks before or after the cerebrospinal fluid (CSF) examinations.
* Routine CSF cytology for all new patients staging and restaging.
† One retinoblastoma; one giant cell astrocytoma.
‡ One transitional cell carcinoma of the bladder; one neuroblastoma; one rhabdomyosarcoma; one undifferentiated carcinoma; two unknown primary; one Ewing sarcoma.

three and diffuse in 13 (fig. 1). There was ependymal-subependymal enhancement in three patients (fig. 2). Thickened irregular tentorial enhancement was seen in seven patients; it was localized in two and diffuse in five (fig. 3). Communicating hydrocephalus was noted in 13 patients (fig. 4).

Nine patients had one positive finding on CT: four with sulcal-cisternal enhancement, one with ependymal-subependymal enhancement, two with tentorial enhancement, and two with communicating hydrocephalus. Two or more CT findings related to leptomeningeal metastasis were seen in 13 patients, with sulcal-cisternal enhancement and communicating hydrocephalus in six as the most frequent combination (table 2).

Additional data collected revealed that 13 (59.6%) of the 22 patients with CT scans indicative of leptomeningeal metastasis also had parenchymal lesions; nine were metastatic and four were residual primary tumors.

Discussion

Leptomeningeal metastasis is defined as diffuse or widespread multifocal involvement of the subarachnoid space by metastatic tumor. The disease, also known as meningeal carcinomatosis or carcinomatous meningitis, has been discussed in the English-language literature since 1912 [2]. The incidence is variable, based largely on autopsy studies, and accounts for 8%–10% of all intracranial metastases [3]. There is presumptive evidence that this manifestation of cancer is increasing in frequency, particularly in lymphoma [4–6], breast carcinoma [7], and oat cell carcinoma of the lung [8]. This has occurred because of the availability of more effective systemic chemotherapeutic agents, which prolong survival, as well as the increased capacity of physicians to make the diagnosis of leptomeningeal involvement.

There are a number of proposed mechanisms for the spread of tumor to the leptomeninges [9]. A primary or metastatic parenchymal lesion is a frequently cited source of spread [10–
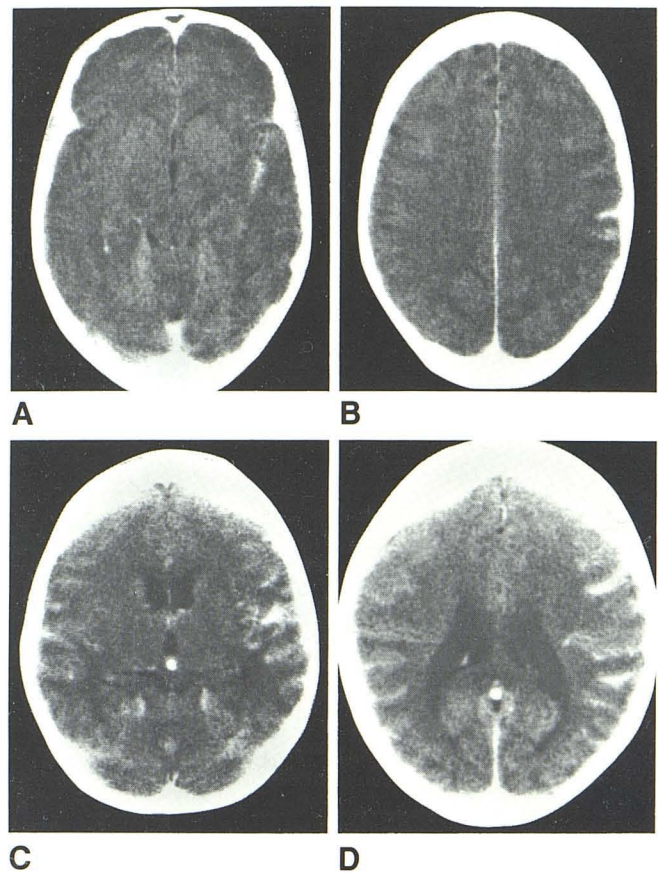

Fig. 1.—**A** and **B**, Localized abnormal leptomeningeal enhancement in left sylvian fissure and cortical sulci in adenocarcinoma of the lung with proven leptomeningeal metastasis. **C** and **D**, Diffuse sulcal enhancement with carcinoma of the breast. Obliteration of cortical sulci by leptomeningeal enhancement; associated communicating hydrocephalus.

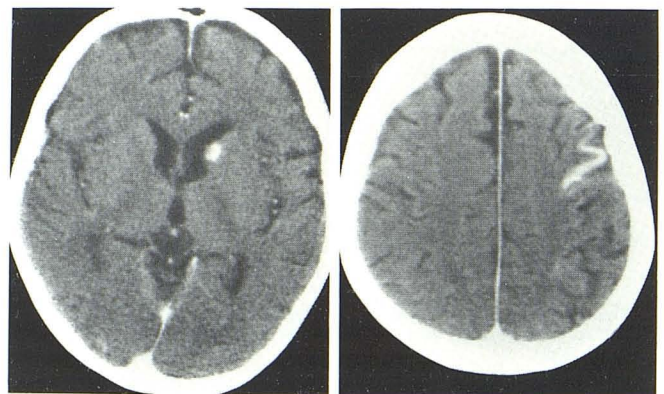Fig. 2.—Enhancing subependymal lesion in head of left caudate nucleus without surrounding edema in acute myelocytic leukemia with localized sulcal enhancement.

12]. However, the rupture of the pial surface by a parenchymal tumor is usually accompanied by a focal fibrous reaction that prevents the dissemination of exfoliated cells. Instead, rupture into the ventricular system is believed to be a more likely

Fig. 3.—**A**, Localized tentorial enhancement in malignant melanoma. **B** and **C**, Diffuse tentorial enhancement in carcinoma of the breast. Associated sulcal enhancement and ependymal-subependymal lesion in head of right caudate nucleus.

A   B   C
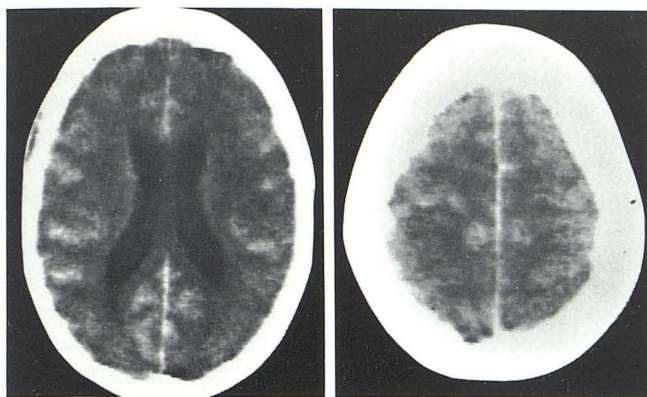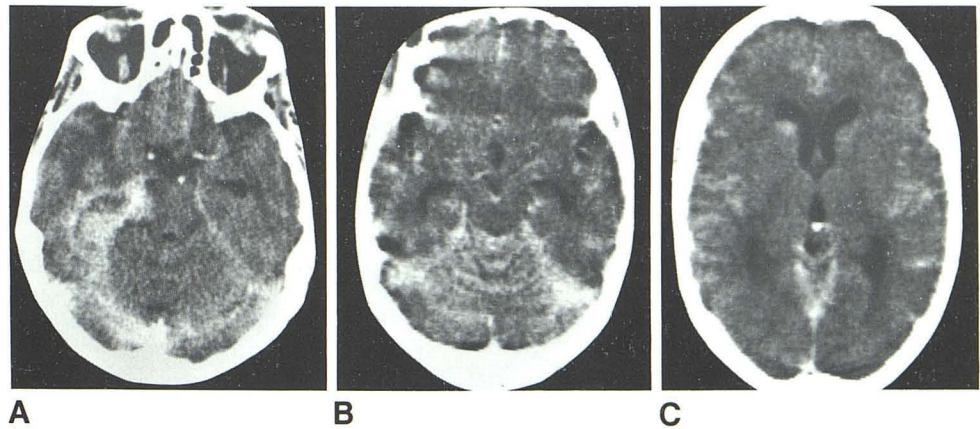

Fig. 4.—Symmetric ventricular dilatation of mild degree in 56-year-old patient with carcinoma of the breast. Obliteration of cortical sulci, consistent with communicating hydrocephalus, with diffuse leptomeningeal enhancement.

TABLE 2: **Cranial CT Abnormalities in Leptomeningeal Metastases**

Abnormalities	No. of Patients
Sulcal-cisternal enhancement	4
Ependymal-subependymal enhancement	1
Tentorial enhancement	2
Communicating hydrocephalus	2
Sulcal-cisternal and ependymal-subependymal enhancement	1
Sulcal-cisternal and tentorial enhancement	1
Sulcal-cisternal enhancement and communicating hydrocephalus	1
Tentorial enhancement and communicating hydrocephalus	3
Sulcal-cisternal and tentorial enhancement and communicating hydrocephalus	3
Sulcal-cisternal, tentorial, and ependymal-subependymal enhancement and communicating hydrocephalus	1
Total	22

route of dissemination because it is not associated with a surrounding tissue reaction [13]. The choroid plexus is considered by some to be the point of origin for leptomeningeal spread [14–17]. Others claim that choroid plexus involvement

is secondary to leptomeningeal metastasis elsewhere and does not represent the origin [18, 19]. Another plausible pathway is the perivascular space (Virchow-Robin) extending along the penetrating vessels [20, 21]. In addition, the subarachnoid space communicates with the perineural space of the nerve roots. These connections provide an accessible pathway through which tumor cells might reach the leptomeninges [22–25]. However, hematogenous spread through meningeal vessels is the most convincing theory for the dissemination of tumor into the subarachnoid space [26, 27].

In our institution, CSF cytology is a routine test for the initial staging and subsequent restaging of patients who have relapsed from leukemia and lymphoma. Once the diagnosis of leptomeningeal metastasis is established, the treatment is usually initiated immediately, without a CT scan. This group of patients is more apt to be detected and treated in the earlier stages of their leptomeningeal disease. Therefore, the percentages of positive CT scans in our patients with leukemia (15.8%) and lymphoma (16.9%) are significantly lower than in those with breast (41%) or lung (57%) carcinoma. In our series, the CSF was evaluated most often before a CT scan was obtained, and in general, the scan was requested for the detection of possible parenchymal lesions. On occasion the CSF cytologic examination was done because the CT findings were strongly suggestive of leptomeningeal metastasis.

Leptomeningeal metastasis is often associated with parenchymal neoplasms in the brain [28, 29]. The high incidence of parenchymal lesions on CT in association with findings indicative of leptomeningeal metastasis has not previously been emphasized in the literature [30]. Usually these lesions are irradiated or removed surgically, particularly if solitary and symptomatic. The CSF is rarely if ever looked at in metastatic parenchymal tumors. Given our data, CT evidence of parenchymal disease, without significant mass effect and with leptomeningeal disease, strongly indicates that a lumbar puncture be done. This may be extremely helpful in overall treatment.

The obliteration of the subarachnoid space, cisterns, and sulci can be appreciated on CT before infusion of contrast material. However, leptomeningeal metastasis is better dem-
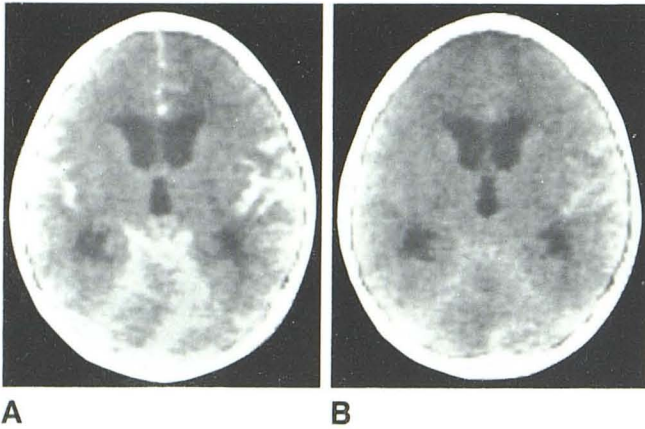
A   B

Fig. 5.—Postcontrast CT scans immediately (A) and 1 hr (B) after intrave-
nous injection. Leptomeningeal enhancement in sylvian fissures, quadrigeminal
cistern, and along tentorium has decreased markedly on delayed scan.
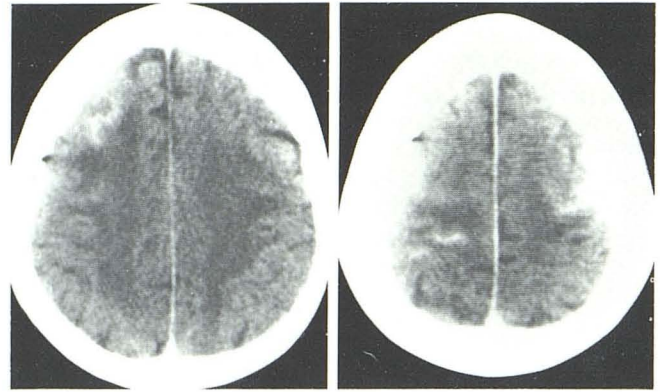

Fig. 6.—Postcontrast CT scans with oat cell carcinoma of the lung. Grand
mal seizures developed while receiving intravenous contrast material for spinal
CT study. An earlier cranial CT scan was normal, and CSF examination was
negative. Diffuse gyral enhancement in high convexity of both cerebral hemi-
spheres.

onstrated on the immediate postcontrast scans (fig. 5). The
most frequently observed abnormality is sulcal-cisternal en-
hancement. This finding may be diffuse or localized, and is
more often observed in the basal cisterns, sylvian fissures,
and the high-convexity cortical sulci. This may be because of
the vascularity of the tumor and/or the leptomeningeal reac-
tion to tumor infiltration. The latter may explain the persistence
of enhancement after the supposed disappearance of neo-
plastic cells, as reflected by repeated negative CSF cytologic
examinations after intrathecal chemotherapy.

Communicating hydrocephalus is the second most com-
mon abnormality from leptomeningeal metastasis. It is mani-
fested by symmetric dilatation of the ventricular system,
usually to a mild or moderate degree. It can occur early in the
disease before treatment and persist after the CSF is cleared
of tumor cells. Leptomeningeal metastasis impairs the ab-
sorption of CSF, which in turn leads to ventricular dilatation
and increased intracranial pressure. Brain irradiation and in-
trathecal chemotherapy have not been documented to be the
causes of communicating hydrocephalus. In the absence of
meningitis, subarachnoid hemorrhage, and previous treat-
ment by surgery, leptomeningeal metastasis is very likely the
cause of communicating hydrocephalus in the cancer patient.
Sometimes, repeated CSF examinations are required to con-
firm leptomeningeal spread.

Tentorial enhancement as a manifestation of leptomenin-
geal metastasis probably results from the same mechanisms
as those seen with sulcal-cisternal enhancement. Since ten-
torial enhancement normally occurs in the postcontrast scan,
it only becomes significant when the enhancement is over a
widened area representing a thickened tentorium, and is
irregular in configuration. This may be diffuse or localized. For
these reasons, tentorial enhancement is not as sensitive an
observation in the diagnosis of leptomeningeal metastasis.

Ependymal-subependymal enhancement in either a diffuse
or nodular pattern without surrounding edema frequently
results from the periventricular spread of leptomeningeal tu-
mor. It can be seen with metastases from extracranial neo-
plasms as well as with certain primary intracranial tumors

such as pinealoblastomas and medulloblastomas, which are
often associated with subarachnoid seeding. Ependymal-
subependymal enhancement usually disappears in response
to treatment. However, sulcal-cisternal and tentorial enhance-
ment may persist after negative cytologic examination.

Subarachnoid hemorrhage [31, 32] may be manifested by
increased attenuation in the cisterns and sulci on precontrast
studies. Arterial spasm related to subarachnoid hemorrhage
may be reflected in gyral enhancement mimicking sulcal en-
hancement on the postcontrast examination as a result of
gray-matter hypoxia. There may also be associated commu-
nicating hydrocephalus. Cerebral arteriography may be nec-
essary to establish the existence of arterial spasm. The clinical
features and evaluation of the CSF should confirm the diag-
nosis.

Similar CT observations occur in meningeal inflammation
from any etiology, particularly from granulomatous infection
such as tuberculosis [33]. The enhancement seen after infu-
sion of contrast material is on occasion virtually impossible to
differentiate from leptomeningeal metastasis. Sometimes
even the clinical presentation and CSF abnormalities such as
elevated protein and depressed glucose levels may be con-
fusing. CSF cytology and culture results frequently offer per-
tinent information in making the diagnosis.

Subacute infarction with gyral enhancement is another
consideration in the differential diagnosis [34]. The associated
edema with the resulting loss of cortical sulci and gyral
enhancement may mimic the sulcal enhancement seen in
leptomeningeal metastasis. However, the unilateral hemi-
spheric involvement in a vascular distribution in conjunction
with the clinical features should lead to a correct diagnosis.

On occasion, a CT scan obtained immediately after seizure
[35, 36], particularly if it is a grand mal seizure, may show
diffuse gyral enhancement (fig. 6).

In our experience, which agrees with previous reports [30,
37], the four major CT abnormalities seen in patients with
leptomeningeal metastasis are sulcal-cisternal enhancement,
ependymal-subependymal enhancement, widened irregular
tentorial enhancement, and communicating hydrocephalus.

Communicating hydrocephalus in cancer patients should be considered secondary to leptomeningeal spread of tumor until proven otherwise. In some cases, repeated CSF cytologic examinations may be necessary to make a definitive diagnosis. In addition, because of the relatively high incidence of leptomeningeal spread, patients with parenchymal lesions exhibiting symptoms, signs, and/or CT abnormalities suggestive of leptomeningeal metastasis should undergo a lumbar puncture unless contraindicated by mass effect.

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