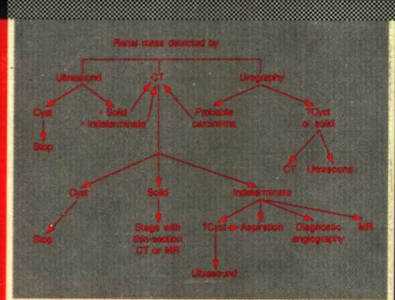
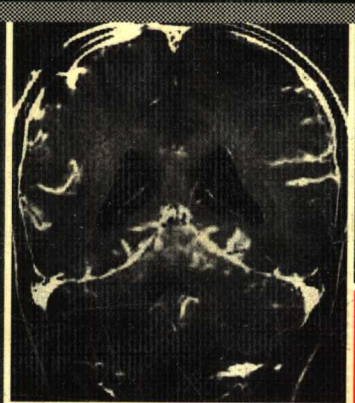
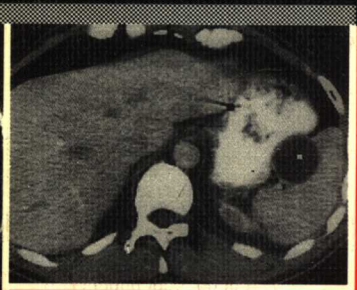
Daniel Vanel
David Stark

Imaging Strategies in Oncology







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Imaging Strategies in Oncology

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Wiley-Liss

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First published in the United States of America
in 1993 by John Wiley & Sons Inc., Wiley-Liss
Division, 605 3rd Avenue, New York, NY 10158-
0012

First published in the United Kingdom in 1993
by Martin Dunitz Ltd, The Livery House, 7–9
Pratt Street, London NW1 0AE

Library of Congress Cataloging-in-Publication Data

Imaging strategies in oncology/edited by Daniel Vanel, David Stark:
editorial board, Scott Atlas . . . [et al].
p. cm.
Includes bibliographical references and index.
ISBN 0-471-59069-X
1. Cancer--Imaging. I. Vanel, Daniel. II. Stark, David D.
III. Atlas, Scott W., 1955–
[DNLM: 1. Diagnostic Imaging--methods. 2. Neoplasms--diagnosis.
3. Neoplasms--radiography. QZ 241 I306]
RC270.3.D5314 1993
616.99'40754--dc20
DNLM/DLC
for Library of Congress 92-48264
CIP

Composition by Scribe Design,
Gillingham, Kent, United Kingdom
Origination by Imago Publishing Ltd
Manufactured by Imago Publishing Ltd
Printed and bound in Singapore

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Foreword

The imaging needs of the patient with cancer are complex challenges and the physician's response must be based upon an understanding of the specific neoplasm, its biological characteristics and its response to treatment.

This text, organized by major anatomic sites, is a practical working guide to the application of radiology to oncologic patients. Decision trees and illustrations will serve as procedural guidelines to assist the reader in understanding the proper applications and limitations of our technology. Although the text is addressed primarily to a radiologic audience, it will also serve to guide the oncologic clinician responsible for patient management.

The authors have been selected from Europe and the United States to balance the oncologic experience presented. Some variation may exist in the various protocols used to treat cancer among the authors' institutions and countries, but the editors have ensured a cohesive presentation. The TNM staging language is now virtually uniform worldwide. Some tumor sites do not, admittedly, lend themselves to the TNM classification system for cancer staging (for example, gynecologic, prostatic and urologic neoplasms and the lymphomas). Nevertheless, tremendous strides have been made in the recent past in unifying the staging language and systems of the American Joint Committee with those of the Union Internationale Contre le Cancer; the resulting TNM system should be used whenever possible in our reports.

I am pleased to have been a participant in this text and look forward to its integration in our daily oncologic practice.

David G. Bragg

Preface

This book attempts to provide a cohesive approach toward oncologic imaging. A group of distinguished authors from the United States and Europe discusses the appropriate timing and sequence of imaging studies in oncologic diagnosis. Extensive illustration and decision trees guide the practical application of these recommendations.

In these days of cost-containment, efficient diagnostic algorithms must be defined and adopted as the standard of care. Understanding the specific value of each imaging modality can conserve resources, save time, and help radiologists and clinicians interact to provide optimal care.

We would like to thank the associate editors and our distinguished contributors for their helpful advice and expertise in describing the diagnostic approach to various oncologic conditions.

We hope that our readers will enjoy and learn as much from this book as we did in editing it.

In dedicating this book to our patients and colleagues, we acknowledge the support of our familes: Christine, David, Stephane, Lila, Maïa and Zoë; and Susan and Elizabeth.

Daniel Vanel
David Stark

Contents

1

The brain

Danielle Balériaux, William O. Bank and Celso Matos

Introduction

In this chapter we discuss an imaging strategy that can be used whenever a cerebral neoplasm is suspected. Since most extra-axial intracranial tumors are benign (meningioma, schwannoma, etc.), they will not be considered here, although malignant tumors can exist in this location. The 20% of all childhood cancers that involve the brain are also excluded here; they are discussed separately in Chapter 3.

Intracerebral tumors are rare in adults. They are slightly more frequent in men than in women. The global incidence reported in the literature varies from 4.5 to 15.0 per 100 000. The variations are a function of the methodology used by the investigators and variations in their patient populations.[1-3]

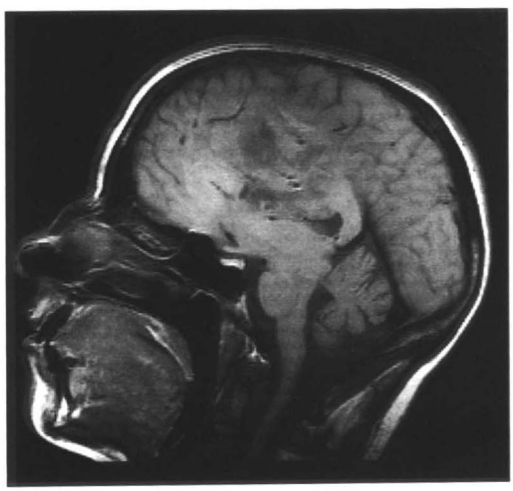
Sixty per cent of brain tumors in adults are hemispheric lesions. Histologic differences will be addressed later, but it is important to note here that the type of neoplasm encountered most frequently in a given population varies with the age of that population. In like manner, the frequency and malignancy of the tumors encountered both increase with the age of the population studied, up to an age of 62 years, at which point both decrease abruptly.

A list of brain neoplasms is given in Table 1.1.

Although it is clear that the prognosis in brain tumors is poor, it is closely related to the histologic type of the tumor and the treatment chosen. While age plays a role, that role is variable. Supratentorial low-grade astrocytomas exhibit a potentially long period of latency during which time the patient remains asymptomatic or has minimal symptoms that can be controlled medically. The median survival is 7 years, with malignant transformation occurring in half of the patients during the first 6 years. In oligodendrogliomas, median survival falls to 5 years.[4]

Anaplastic astrocytomas (Figure 1.1) fall into a category on which age, surgical debulking and irradiation have a definite effect on longevity.[5,6] In patients under the age of 50, the 2-year survival is about 50%, with median survival of 100 weeks. In patients over the age of 50, the median survival falls to 48 weeks, with 2-year survival of only 10%, almost identical to that of the glioblastomas. While gross total resection is associated with longer and better-quality survival in glioblastomas,[5,7] 1-year survival falls to 15%, with patients less than 50 years old having a 1-month longer median survival. Nevertheless, if reoperation with extensive tumor resection is feasible, the patient may enjoy a good-quality prolongation of life of 10 weeks with a glioblastoma and 83 weeks with an anaplastic astrocytoma.[6,8]

The supratentorial low-grade astrocytomas (Figure 1.2) are the tumors in which imaging makes the biggest impact. Newer non-invasive techniques are providing conclusive diagnosis of these lesions at an earlier time in their development. The median interval until malignant transformation is now 56 months from radiologic diagnosis.[9] This apparent lengthening of the quiescent period before transformation may be related to earlier diagnosis, implying that the low-grade gliomas in previous studies may already have been in or close to malignant transformation at the time of diagnosis. It has been shown recently that biopsy and treatment regimens during the quiescent period make no difference in the eventual outcome, and their use in this period is thus controversial.[9] Imaging follow up remains



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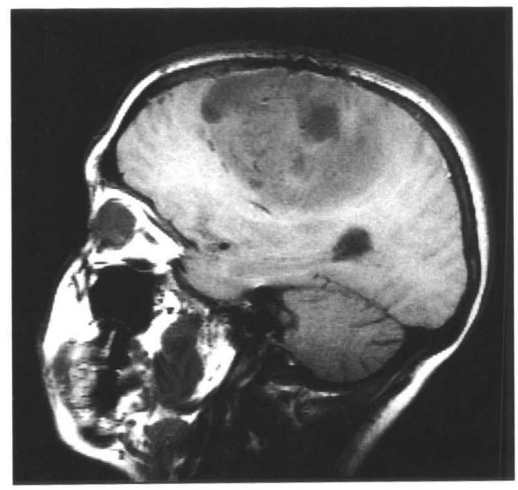

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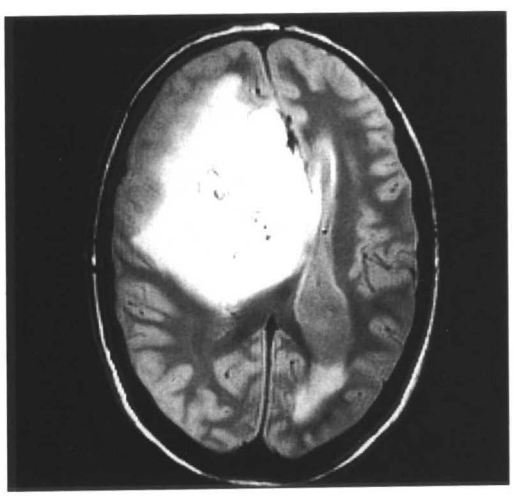

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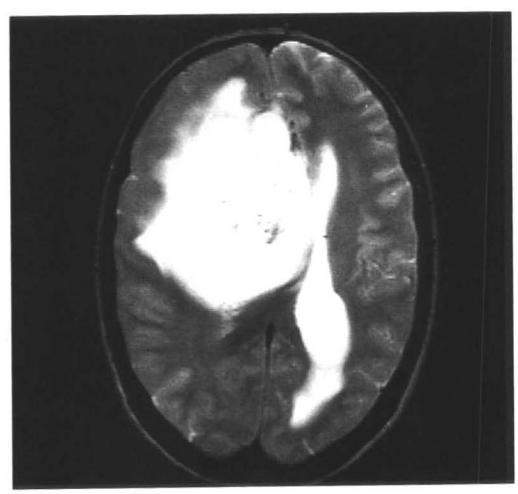

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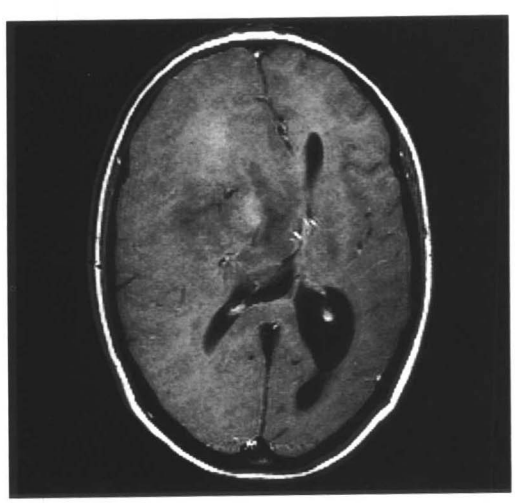

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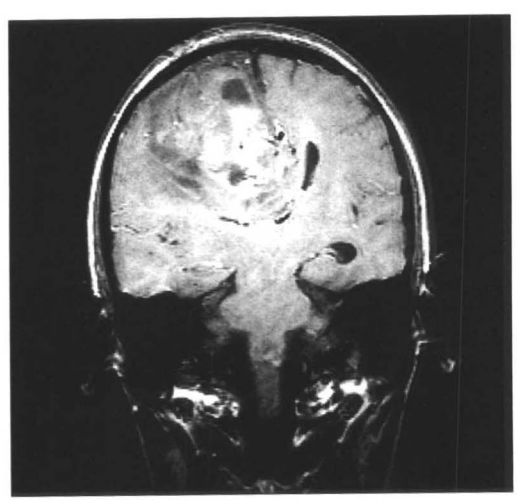

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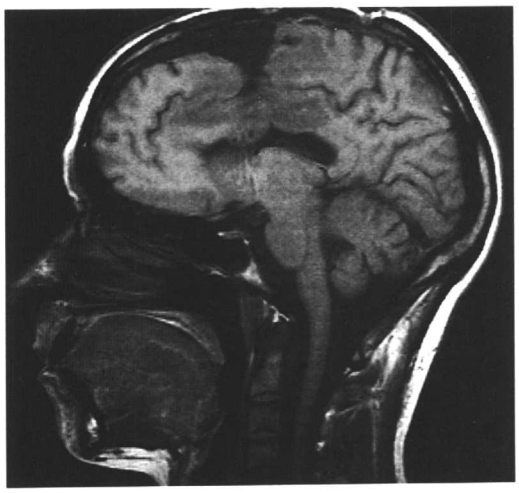

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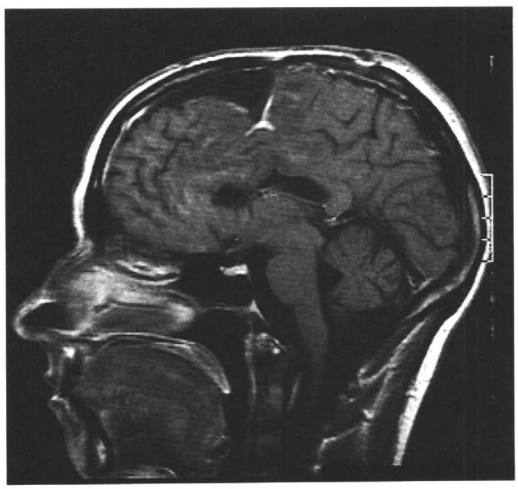

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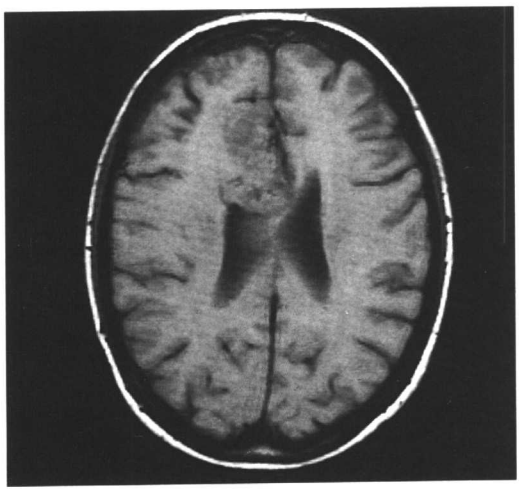

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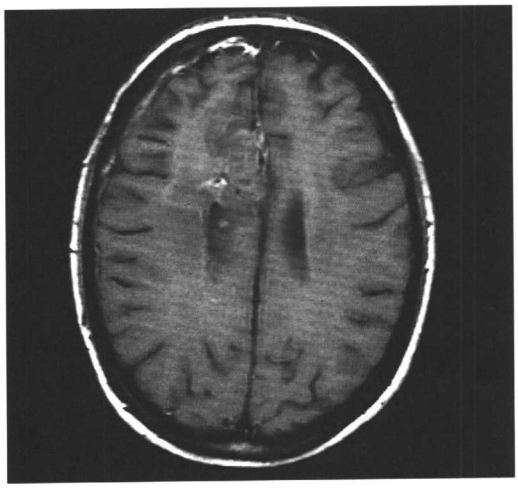

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Figure 1.1

Frontal anaplastic astrocytoma with involvement of the corpus callosum pre and post partial resection. The images demonstrate the large amount of tumor that can be resected and the appearance of meningeal and intracerebral contrast enhancement following surgery.

A and **B** Sagittal T1-weighted images from the initial MR evaluation.

C and **D** Axial proton density (**C**) and T2-weighted (**D**) images.

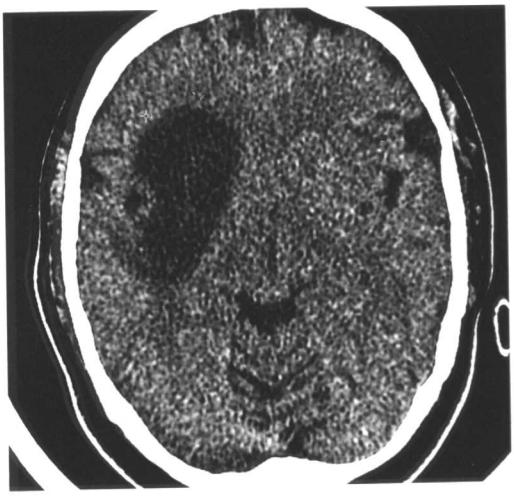
E and **F** Axial **E** and coronal (**F**) T1-weighted images after gadolinium injection.

Although one might be tempted to call this tumor inoperable, armed with the multiplanar depiction of the large frontal tumor, the neurosurgeon can make preoperative preparations for an extensive debulking of clinically silent areas while preserving adjacent eloquent areas. In this case the sagittal images suggest that the rolandic sulcus is displaced posteriorly, allowing a more complete resection than might be attempted otherwise. Rapidity of regrowth is a function of the amount of tumor 'left behind'.

G and **H** Sagittal T1-weighted images before (**G**) and after (**H**) gadolinium injection obtained 5 months after extensive partial resection.

I and **J** Axial T1-weighted images before (**I**) and after (**J**) gadolinium injection.

5-month follow-up MR demonstrates the striking amount of tumor that could be removed without producing significant neurologic deficit. Note the enhancement at the margins of tumor resection. Only by repetitive follow-up examinations will we be able to identify the tumor progression.



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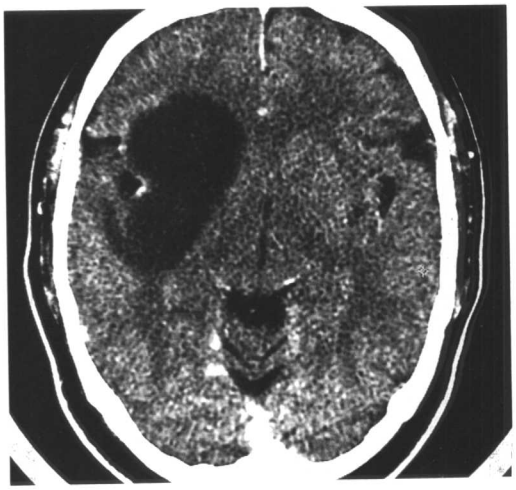

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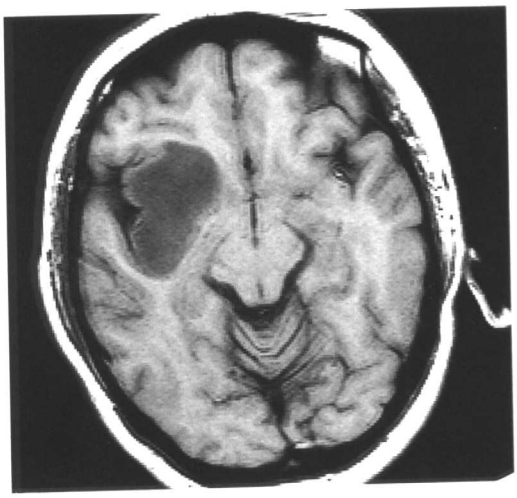

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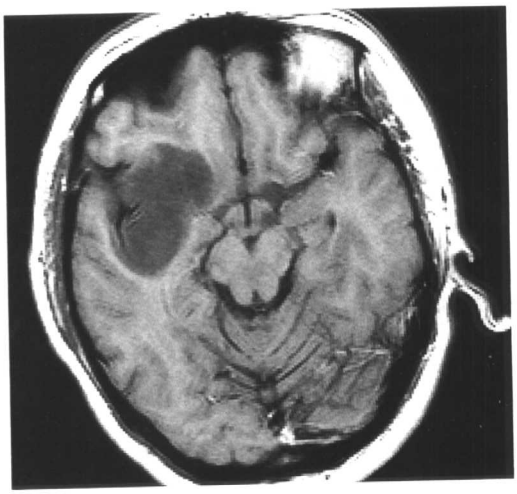

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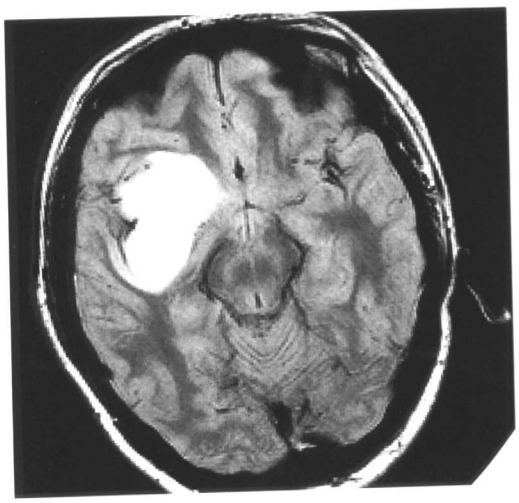

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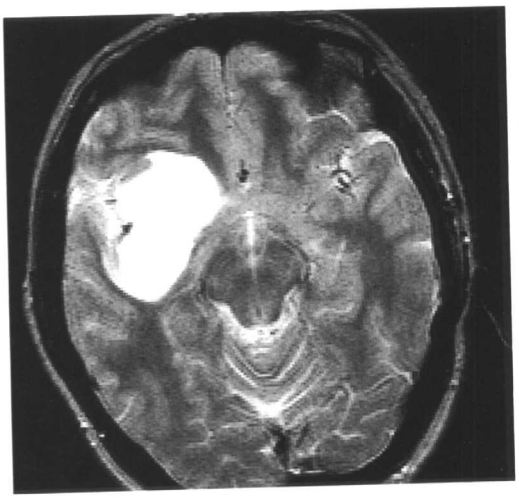

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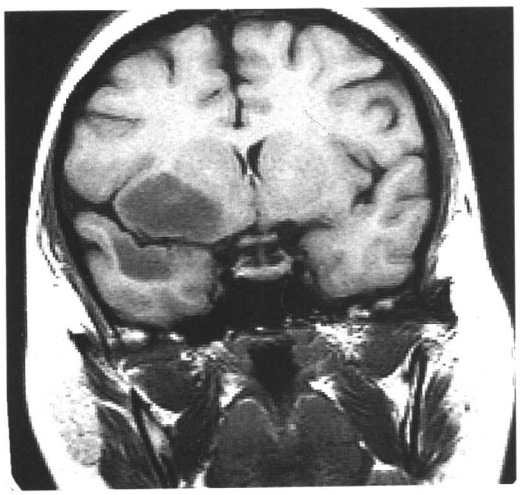

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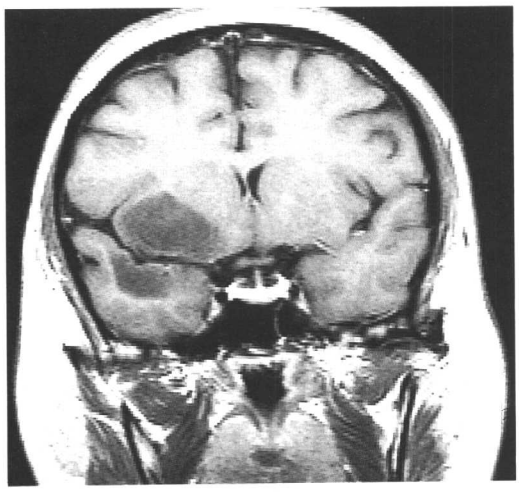

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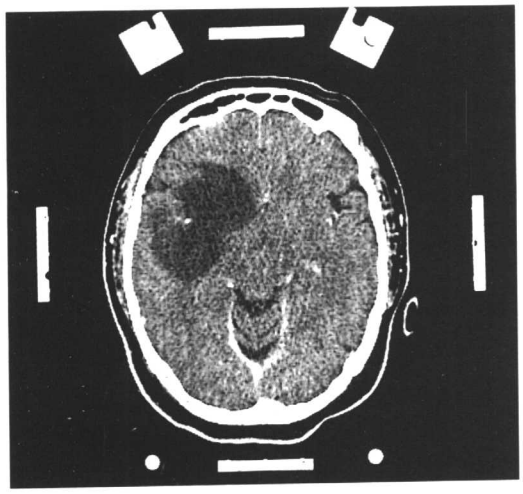

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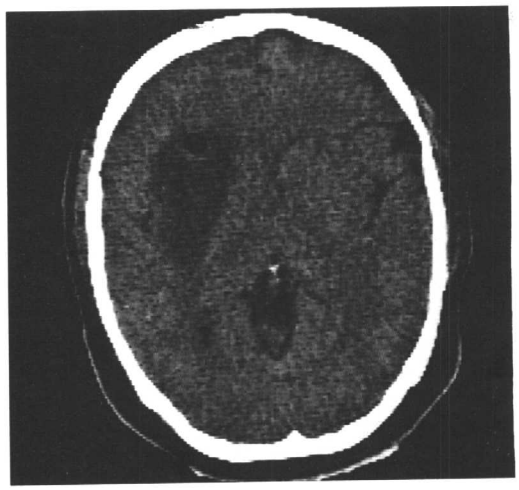

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Figure 1.2

Low-grade frontotemporal astrocytoma. The images demonstrate the typical presentation of low-grade gliomas.

A and **B** CT scan before (**A**) and after (**B**), contrast administration obtained as part of an evaluation for a clinically suspected pituitary adenoma, reveals a vast well-defined low-density lesion with minimal mass effect that exhibits no contrast enhancement.

C and **D** Axial T1-weighted images before (**C**) and after (**D**) gadolinium injection demonstrate a homogeneous, hypointense, well-delimited mass with no contrast enhancement.

E and **F** Axial proton density (**E**) and T2-weighted (**F**) images show hyperintensity (T2 prolongation) in the region of the tumor without surrounding edema.

G and **H** Coronal T1-weighted images before (**G**) and after (**H**) gadolinium injection show the extension of the tumor into the frontal and temporal opercula.

The tumor remained static for three years before onset of symptoms necessitated biopsy.

I and **J** Enhanced CT performed in the stereotactic frame (**I**) immediately prior to biopsy and 24 hours post biopsy (**J**) shows no hemorrhagic complications, but the presence of an intentionally injected small bubble of air confirms the site of the tumor biopsy.

The localization of this tumor in the frontotemporal region, its incidental discovery in a young asymptomatic patient, and its slow evolution are fairly typical of low-grade gliomas.

Table 1.1 Histologic classification of neuroepithelial cerebral neoplasms.

ASTROCYTIC TUMORS
Astrocytoma
  Fibrillary
  Protoplasmic
  Gemistiocytotic
Pilocytic astrocytoma
Subependymal giant-cell astrocytoma (the ventricular tumor of tuberous sclerosis)
Astroblastoma
Anaplastic

OLIGODENDROGLIAL TUMORS
Oligodendroglioma
Mixed oligoastrocytoma
Anaplastic oligodendroglioma

EPENDYMAL AND CHOROID PLEXUS TUMORS
Ependymoma
  Myxopapillary ependymoma
  Papillary ependymoma
  Subependymoma
Anaplastic ependymoma
Choroid plexus papilloma
Anaplastic choroid plexus papilloma

PINEAL GLAND TUMORS
Pineocytoma
Pineoblastoma
Pineal germinoma
Embryonal carcinoma

NEURONAL TUMORS
Gangliocytoma
Ganglioglioma
Ganglioneuroblastoma
Gangliocytoma and anaplastic ganglioglioma
Neuroblastoma
Primitive neuroectodermal tumors

POORLY DIFFERENTIATED AND EMBRYONAL TUMORS
Glioblastoma
  Sarcomatous glioblastoma
  Giant-cell glioblastoma
Medulloblastoma
  Desmoplastic medulloblastoma
  Medullomyoblastoma
Medulloepithelioma
Primitive polar spongioblastoma
Cerebral gliomatosis

important for early identification of the onset of malignant transformation.

In view of the relative rarity of primary brain neoplasms, routine screening of the general population for these lesions has not been performed or even advocated to our knowledge. However, as soon as a patient falls into a category at high risk of having an intracranial tumor, sensitive screening methods must be employed. For example, screening techniques become appropriate in a patient with a primary neoplasm that has a known potential to metastasize to the brain, or in a patient with a rare condition associated with intracranial tumors, such as phacomatomatoses. The strategies for screening in these cases is discussed later.

Clinical presentation of cerebral neoplasm

The symptoms and signs caused by brain tumors can be classified as follows.

- *Direct focal effects* related to focal tumor invasion and destruction of cerebral parenchyma.
- *Indirect focal effects* due to displacement and/or compression of normal brain by the tumor itself, and displacement and/or compression of normal brain by surrounding edema.
- *Remote or generalized effects* due to:

(1) Impairment of the vascular supply or drainage of otherwise normal brain by direct tumor invasion or compression of the feeding arteries or draining veins of the involved vascular territory.
(2) Secondary hydrocephalus caused by cerebrospinal fluid (CSF) overproduction, obstruction of CSF pathways by the tumor itself, or obstruction caused by tumor compression or displacement of these same pathways.
(3) Increased intracranial pressure caused by the volume of the mass itself and/or any of its secondary effects.

Although it appears at the end of the list, this etiological category is in fact the most frequently encountered.

The rate of tumor growth is an important factor in determining the clinical manifestations observed in brain tumors. Slowly growing tumors become symptomatic at larger volumes, while rapidly growing tumors do not allow the brain time to compensate for their presence and become symptomatic sooner. On the average, malignant tumors become symptomatic when they attain a volume of approximately 100 ml. In certain critical locations such as the brainstem, however, much smaller tumors can produce neurologic deficits. Hemorrhage into a pre-existent but previously asymptomatic tumor, or obstruction of the CSF pathways with sudden onset of obstructive hydrocephalus, may produce an abrupt onset of neurologic symptoms. Since the cranial vault cannot expand in adults, intracranial hypertension develops when anything within the confines of the calvarium expands too much or too rapidly.

Headache is the most common symptom in patients with brain tumors. It was found to be the initial manifestation of supratentorial malignant gliomas in over 50% of the patients included in the EORTC (European Organization for Research and Treatment of Cancer) brain tumor group studies. Typically these headaches are generalized but often predominate at the site of the tumor. They are aggravated by coughing and Valsalva maneuvers.

Bilateral papilledema is a common fundoscopic sign in older children and adults with intracranial hypertension. Arterial hypertension, bradycardia and depressed respiratory rate tend to be found during advanced stages of cerebral neoplastic diseases, but seldom at the time of diagnosis. Another clinical feature seen in late stages is tentorial herniation which initially produces ipsilateral mydriasis due to the compression of the 3rd cranial nerve, followed by a typical sequence of events leading to coma and death.[10]

The effects of intracranial hypertension and remote mass largely account for the rather poor correlation of clinical presentation and tumor location in comparison with cerebral infarcts. One of the best examples of a misleading focal sign is paralysis of the 6th cranial nerve; this sign has no localizing value whatsoever.

In most cases, the neurologic deficit caused by tumors is slowly progressive. An abrupt, stroke-like onset is not uncommon, however, in malignant gliomas and metastatic tumors. Intratumoral hemorrhage and acute peritumoral edema best explain such rapid clinical course (Figure 1.3). Intermittent symptoms may be caused by a pedunculated intraventricular tumor that intermittently produces an acute obstructive hydrocephalus. Seizures may occur either as an early or late manifestation in about a third of patients with brain tumors.[11,12] These seizures are usually focal, although they may generalize rapidly. A careful history may allow localization of the tumor, especially when seizures are an early manifestation of the neoplastic process.

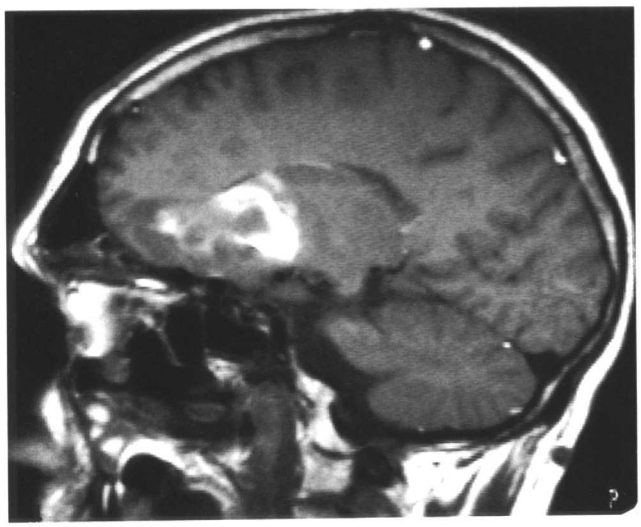
Behavioral changes and cognitive disorders, such as aphasia, apraxia and memory deficits, are common in various types of brain tumors. Slowly growing tumors, especially in the frontal region, may lead to dementia.

In search of an imaging strategy

Whenever a brain neoplasm is clinically suspected, the neuroradiologist is expected to answer fundamental questions. These questions guide the subsequent strategic decisions and fall into five categories as follows.

- *Sensitivity*: Are the patient's clinical signs and symptoms caused by an intracranial expansile lesion?
- *Specificity*: With what kind of lesion are we dealing? Is it a neoplasm? Is it benign or is it malignant? Can we suggest a histopathologic diagnosis?
- *Location*: If a tumor is found, where is it located exactly, is it solitary or multiple, and what are its precise limits?
- *Treatment*: What kind of useful information may be provided in order to give appropriate treatment? Is this tumor resectable? What approach should the surgeon use? Where are the ideal locations from which to take an open or a stereotactic biopsy? What are the limits of the area to be irradiated?
- *Monitoring*: How can the neuroradiologist monitor and evaluate the efficacy of the treatment?

Answering these questions will lead us to the establishment of the most effective strategic approach to these diagnostic problems. Different neuroradiologic imaging modalities are presently available and are discussed here; they include primarily CT and/or MR, as well as cerebral angiography.



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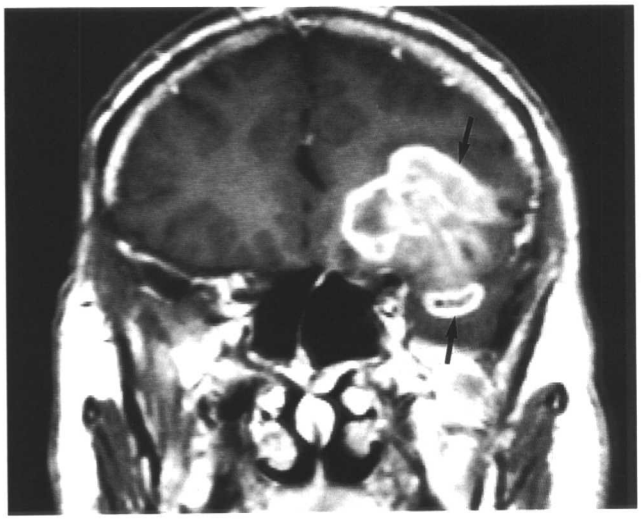

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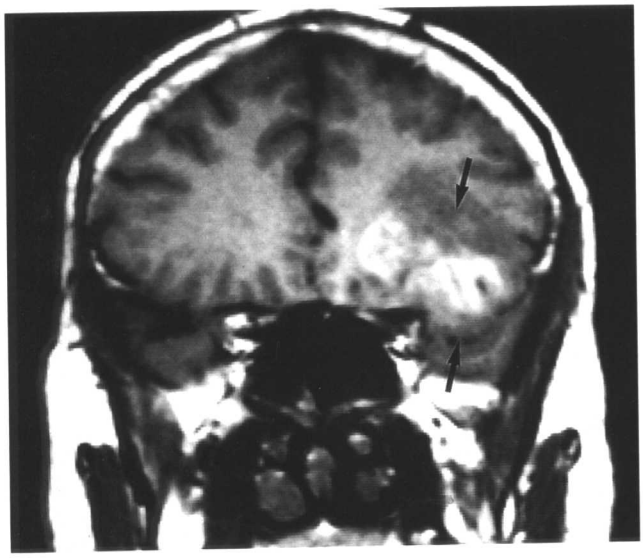

B

Figure 1.3

Hemorrhagic frontal glioblastoma. The images demonstrate a frontal hemorrhage with underlying neoplasm.

A Sagittal unenhanced MR.

B and **C** Coronal MR before (**B**) and after (**C**) gadolinium injection.

The location of the hemorrhage in this part of the frontal pole and the nodular non-homogeneity strongly suggest the presence of an underlying tumor. Enhancement of the large hypointense areas above and below the zones of hemorrhage (arrows, **B** and **C**) confirm this suspicion.

Standard radiography and tomography

Standard radiographs and standard tomographic images of the skull are known to be of little value in the detection of intracranial tumors and cannot be considered as a screening procedure. Brain neoplasms almost never invade the bony elements of the skull. Erosion of the clinoids or displacement of a calcified pineal gland, while classical indirect radiologic signs of intracranial expansive lesions, are not early signs of tumor and they are only occasionally recognized nowadays. Tumor calcifications may be seen on plain tomographs mainly in slow growing tumors such as oligodendrogliomas, subependymal giant-cell astrocytomas or choroid plexus papillomas (Figure 1.4), but are usually seen long after the tumor is clinically apparent and readily evident on CT and MR.