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Educational Review

Management of Metastatic Brain Tumors

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Background: Brain metastases are the most common neurological complication of systemic cancer. They represent a serious cause of morbidity and mortality and a significant challenge for neurosurgeons. They outnumber all other intracranial tumors combined and, with advances in technology and treatment of systemic cancer, are on the increase as cancer patients live longer.

Methods: We have reviewed the major factors that influence the occurrences of metastases in the central nervous system: primary cancer, patient age and sex, clinical aspects of presentation, basic diagnostic modalities, diagnostic imaging (computed tomography and magnetic resonance imaging), and treatment considerations. In discussing these different aspects, we emphasize the efficacy of different treatment options, including recent information regarding multiple metastases that broadens the scope of surgical implications. The criteria we present are directed toward considerations made by general surgeons, as well as those made by neurosurgeons.

Conclusions: Although radiotherapy remains the main therapeutic modality, surgical excision has increasingly shown advantages in certain settings, as has stereotactic radiosurgery. Chemotherapy is less effective, but its advantages are reviewed, as are the implications of recurrent metastases.

Key Words: Brain metastasis—Brain neoplasms—Multiple brain metastases—Metastatic brain tumors.

The most common structural neurologic complication of systemic cancer is metastasis to the brain (1), an important cause of morbidity and mortality (2) that was first documented in 1898 by Bucholz (3). Since then, the central nervous system (CNS) has been recognized as a primary target site for metastases. Results of recent studies show that they outnumber all other intracranial tumors combined, occurring in 20–40% of the cancer patient population (1,4–6). That rate is reported rising as a result of more aggressive cancer therapy that has prolonged patient survival (2). Metastases usually reach the brain via arterial circulation (4); pulmonary cancer is a major source of brain metastasis, and any other primary tumor has likely metastasized to the lung before seeding the arterial circulation and reaching the brain (7). Metastases occur as "single," a term that refers to the presence of only one brain metastasis and implies nothing about the extent of cancer that may or may not be present elsewhere; "solitary," a term that signifies the presence of a single brain metastasis that is the only known cancer in the body (1); and "multiple," a term that refers to the presence of more than one brain metastasis and makes no distinction regarding the presence of systemic cancer.

Three major factors that influence brain metastases are primary cancer, age, and sex. Primary cancers of the lung, breast, melanoma, renal, and colon are the most common forms of metastasis, in

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contrast to sarcoma, ovarian, prostate, and bladder primary cancers, which are seldom the primary tumor in a brain metastasis (8). The primary cancer also influences the extent of metastasis: colon, pelvic, abdominal, and renal cancers are more often single, whereas melanoma and lung and breast cancer, as well as cancers of unknown origin, are more frequently multiple (5,9). Age has been shown to correlate with the incidence of certain cancers, and when it does, younger patients are more likely to develop brain metastases than are older patients. Gender has been implicated as well: men tend to have a higher incidence of metastases from lung cancer and to be more likely to develop brain metastasis from melanoma, whereas women have a higher incidence of breast primary cancer. However, rather than being due to a predilection, the male preponderance of metastases from melanoma may be a result of the greater propensity of men for melanoma arising on the head, neck, or trunk, locations with a greater tendency to spread to the brain (10). Quite frequently, symptomatic brain metastases occur in patients having no previously diagnosed systemic neoplasms, and inability to detect the primary cancer is not uncommon in these instances.

CLINICAL PRESENTATION

The clinical presentation is similar to that of other brain tumors (2). The most common presenting symptom is headache, but it occurs in only 50% of patients with a single brain metastasis. It may be mild, diffuse, or located bilaterally in the frontal or occipital regions, with little localizing value. When it does manifest, it often (40%) does so as an early morning headache, due possibly to increased intracranial pressure (ICP) (1). Patients with multiple metastases report a higher incidence of headache.

Most cerebral metastases (80%) are found within the cerebral hemispheres (followed by the cerebellum and brainstem) and show a predilection for the grey, rather than the white, matter. Because they produce symptoms consistent with their anatomic location, frontal metastatic lesions may cause mental changes and symptoms of increased ICP, frontoparietal lesions often cause motor weakness, occipital lesions often lead to visual field defects or cortical blindness, and cerebellar metastases usually cause ataxia or symptoms related to hydrocephalus (11). Metastases have a marked propensity to produce extensive edema in the surrounding brain, resulting in a frequent rapid pace of neurological deterioration, common symptoms of increased ICP, and neurological dysfunction (2). The most common neurological signs at diagnosis are focal weakness (usually mild or moderate) and mental or behavioral changes, the latter of which usually indicates multiple brain metastases or solitary lesions that increase ICP or cause hydrocephalus. Hemorrhage is common, particularly in cases of metastases from choriocarcinoma, gestational and testicular cancers, and malignant melanoma. On occasion, apoplectic symptoms and signs that are of unknown origin and that resolve completely, mimicking transient ischemic attacks, occur. Other symptoms may be confused state, gait unsteadiness, and unexplained vomiting, syncope, and seizures (the first sign in 10% of patients). Although scanning of asymptomatic patients who have been treated for systemic cancer is beyond the scope of routine examinations, any patient with known cancer who presents with any of these symptoms should be tested for a brain metastasis.

DIAGNOSIS

Diagnostic procedures begin with chest radiographs and imaging studies (computed tomography [CT] or, preferably, magnetic resonance imaging [MRI]) to verify suspected metastases. Surgical candidates require more rigorous radiological and laboratory tests to evaluate the status of the systemic cancer. The best diagnostic tools, other than biopsy, are CT and MRI. On CT scans, brain metastases usually appear as circumscribed parenchymal lesions. With contrast infusion, they have heterogeneous enhancement, with mild to severe surrounding edema and mass effect on adjacent structures and on the ventricular system (5). They generally can be differentiated from other types of brain lesions (on CT scans primary malignant tumors tend to be larger, more centrally located, generally solitary, and usually have little associated brain edema), but differentiation from cerebral abscesses is more difficult because of the similarities in smooth, thin margins, low-density centers, and degree of perifocal brain edema (11).

Although as recently as 1985 CT scan was considered the best diagnostic test for brain metastasis (7), contrast-enhanced MRI has been shown to be more sensitive and specific than any other imaging

technique in determining location, number, and presence or absence of metastases. It is the best single tool for radiographic evaluation. MRI has the advantages over CT of being able to detect mild degrees of brain edema, particularly when T2-weighted spin-echo sequences are used, and of depicting areas that are often imaged suboptimally by CT, such as the brain stem, cerebellum, and temporal lobe. The acknowledged disadvantages of MRI scans are that they generally take longer than CT, patient cooperation is a more critical factor, and certain patients cannot be scanned by MRI because of their emergency life support requirements or the presence of pacemakers or vascular clips (11).

The contrast agents currently being used are especially useful because they do not pass through the blood–brain barrier (BBB) except when it is disrupted. Furthermore, new contrast agents with different pharmacokinetics from those currently used in clinical practice for CT and MRI are being investigated, among which are intravascular agents that have been used to explore blood pool and perfusion properties, albumin-(Gd-DTPA) that has been used to obtain MR angiography, paramagnetic and superparamagnetic agents that can also be used to evaluate the intravascular space, and perfusion agents that potentially can measure intravascular volume (12).

TREATMENT CONSIDERATIONS

Because the majority of patients (≥50%) have uncontrollable systemic cancer (2,7), control of the metastasis for maintaining or improving quality of life, rather than survival, may be the most appropriate endpoint for analyzing the efficacy of treatment. However, results from our clinic show that when the systemic cancer has been eliminated by various therapeutic modalities, complete excision of the metastasis(es) can result in cure. Neurological palliation with corticosteroids (dexamethasone 4 mg i.v. or orally every 6 h) and radiotherapy is the main treatment modality for patients with widespread and/or uncontrolled systemic cancer. For patients with controlled systemic disease, the therapeutic modalities are similar to those for primary brain tumors, but determining the best modality is more difficult, especially for patients who are candidates for surgery. Initial considerations include factors such as tumor size, site, and histological features; the patient's age, neurological status, and general condition; the extent of the systemic cancer, as well as its past or potential response to therapy; and possible damage to other organ systems from previous treatment.

The neurological status is the most important determinant for all patients, especially for patients who are deteriorating rapidly (4). A second major consideration is the extent of the patient's systemic disease (2). For patients with a limited life expectancy, the goal is short-term palliation, which is best provided by whole brain radiotherapy (WBRT) and corticosteroids. For patients expected to survive 3–4 months or more, palliation is insufficient and they are evaluated for more aggressive therapy, namely surgery, which is usually recommended if the systemic disease is absent, minimal, or controllable for an extended period (4).

Other vital determinations are location, whether the patient has single or multiple metastases, and the hematological parameters, especially for those who have received chemotherapy. Solitary tumors located in a silent area of the brain may be surgically removed, whereas metastases in less accessible areas of the brain, such as the thalamus or brainstem, are treated nonsurgically. Metastases occur more frequently in the frontal and parietal lobes than in the occipital and temporal lobes. An overrepresentation occurs in the temporooccipital and parietooccipital areas, possibly due to a preferential location of metastases in the posterior border zone, and an overrepresentation occurs in the anterior border zone, strongly supporting the view that most brain metastases result from arterial tumoral microemboli (5).

The interval between the initial diagnosis and the diagnosis of brain metastases also plays an important role in determining the most efficacious treatment modality. Because primary tumors spread at different times in the disease course [melanoma, breast cancer, and colon cancer have a median interval of 2–3 years (13) vs. 1 year for renal cancer (9,14) and 6–9 months for lung cancer (15)], the interval often suggests whether metastases in other areas are likely, as well as the extent of the systemic disease. Patients who have undergone major lung resections or have been treated with pneumotoxic or cardiotoxic chemotherapy should be assessed for cardiopulmonary function.

TREATMENT

The management of patients with brain metastases is especially difficult because of the poor prognosis that accompanies disseminated cancer.

Initially, the most common forms of treatment were WBRT, surgery, or chemotherapy. Subsequently, combined therapies were shown to be more efficacious than single therapies, and more recently, stereotactic radiosurgery has been shown to offer some added advantages. Nevertheless, the optimum treatment of brain metastases remains controversial (1).

Radiotherapy

WBRT is effective in providing relief of symptoms in 70–90% of patients and has been the mainstay of treatment since the 1950s. One critical consideration is the end-point, which includes (a) symptom relief, such as the percent of overall symptom response rate and complete response rate, as well as promptness of and duration of symptom response; (b) failure in the brain, which involves analyzing the length of time from treatment to recurrence of the original brain metastases; or (c) quality of life, including the percent of survival time the patient spends in an improved or stable neurologic condition. Relief or improvement of symptoms can be expected in 66% of patients with serious neurologic dysfunction and 33% of patients with moderate dysfunction. Unfortunately, median survival time, which is 1 month with no treatment and 2 months with corticosteroids (16), is only moderately improved to 3–6 months with WBRT (4,17).

The standard treatment regimen is 30 Gy in 2 weeks, but appropriate treatment varies widely depending on radiotherapeutic and oncologic practices. Trials conducted by the Radiation Therapy Oncology Group (RTOG) indicated that no significant difference in neurological control of disease or length of survival is evident in doses ranging from 20 to 50 Gy, but doses of <20 Gy appear less effective. Furthermore, increased focal radiation to the tumor site reportedly has no better results than WBRT alone (18).

For patients who have undergone surgical removal of a solitary brain metastasis, 36 Gy at 3 Gy/fraction postoperative WBRT may be advised because it has been reported to have significant benefit compared with WBRT alone. Postoperative adjuvant WBRT results in a much smaller incidence of subsequent brain relapse, more frequent systemic failures, and a higher proportion of patients remaining disease free. Along with female gender, long disease-free survival, and good neurologic function before craniotomy, it is also a factor significantly associated with improved survival (19).

Complications of dose fractionation are acute, generally mild to moderate, but occasionally severe. Transient worsening of symptoms, which are treated with steroids during the therapeutic period (1), can be expected. Dry desquamation occurs early in the course of treatment and hair loss usually begins after 2 weeks of treatments. Other common complications are headaches, nausea, lethargy, and otitis media, a subacute "somnolence syndrome" of increased fatigue that may occur 1–4 months after irradiation, and myelosuppression caused by cranial irradiation that may hinder delivery of chemotherapy. More severe and debilitating late complications that may occur include brain atrophy, necrosis, and leukoencephalopathy (progressive white matter disease) with mental and neurologic deterioration and dementia (20–22).

Although one study showed 42% of patients undergoing reirradiation had improvement in symptoms and in at least one functional level (23), for the most part, only modest success has been reported for a repeat course of cranial irradiation in the event of recurrence.

Surgery

Although radiotherapy is generally considered the preferred treatment and some investigators report that surgical therapy is not an option for most patients (1), for many metastases the most effective palliation of the tumor-associated mass, whether single or multiple, is surgical removal. The causes of initial unsuccessful attempts at surgical resection of brain metastases that discouraged early pioneers such as Cushing (24) and Dandy (25) from operating on them have been overcome by modern neurosurgical techniques and perioperative care. Today, surgical resection offers increased benefits and is becoming a routine consideration (Fig. 1A and B). Surgical considerations currently are based mainly on accessibility and resectability (26), which are interrelated with the limits of surgery determined by the functional importance of the brain tissue to be traversed and the quality of survival that might be expected, a factor based on subjective determination.

Previous guidelines suggested that surgical excision should be considered only (a) for patients with relatively superficial, solitary lesions; (b) if the primary cancer could or had been treated or if the primary cancer permitted reasonably long survival; and (c) if the diagnosis of the intracranial lesion was uncertain (27). However, modern neurosurgical

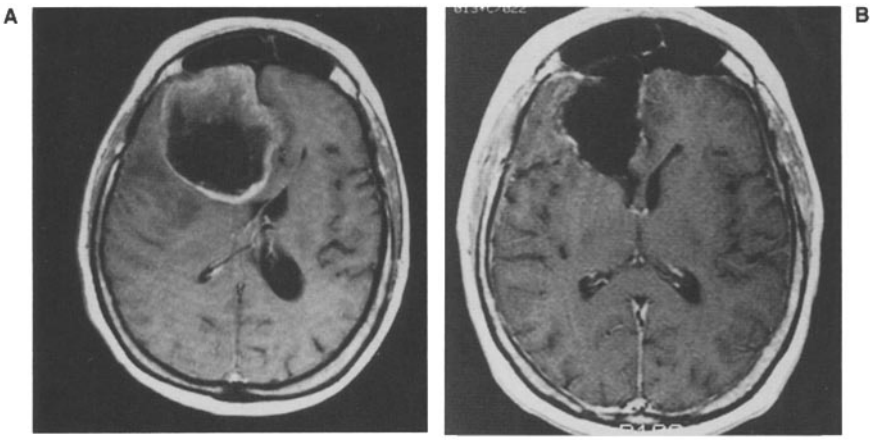

FIG. 1. A: MRI of a large right frontal metastatic tumor causing marked shift of the midline structures. B: Postoperative MRI showing gross total resection of the metastatic tumor and relief of the mass effect.

techniques have significantly increased the scope of potential surgical benefits, and today a far broader spectrum of patients, including those with multiple metastases, are routinely considered for surgical treatment. Surgical adjuncts include intraoperative ultrasound, which is widely used for tumor localization and can be used to guide aspiration of a tumor-associated cyst before resection; the surgical laser, which allows precise resection of tumors with minimal injury to surrounding tissue and, although not as effective with tumors that have a high fluid content, is useful with deep exposures and tough, fibrous tumors; the ultrasonic aspirator, which uses ultra high frequency vibrations to shatter tumor cells with sound waves while causing minimal injury to surrounding normal structures; intraoperative neurophysiologic monitoring, which assists in identifying eloquent brain areas, thereby allowing maximal tumor resection with decreased risk of postoperative neurologic deficit; and cortical mapping, which is especially valuable when normal-appearing cortex overlies a subcortical tumor. Perhaps more than any other instrument, the operating room microscope, with its precision optics and powerful illumination, has revolutionized neurosurgery, reducing morbidity and mortality. It is particularly effective when the exposure is deep or the tumor involves critical vascular or neural structures.

Among the advantages of resection are extended survival times, improved control of neurological problems, and expanded diagnostic determinations. Furthermore, although reports as late as 1986 showed operative mortality and morbidity rates of 2% and 20%, respectively (28), we have had rates of 0–3% and <10%, respectively (29). Surgery also has been shown to be beneficial in ascertaining the presence of metastases. Patchell et al. (28) noted that clinical examination of 54 patients initially entered as having brain metastases showed that six had other lesions and three had no neoplastic disorders, errors that cannot be precluded by either CT scanning or MRI and that can be detected only by microscopical examination of tissue (10). Recent retrospective series have shown that surgically treated heterogeneous groups of patients have median survival times extended to 10–14 months for patients treated for a single metastasis (1,29–31) and a recent study by Bindal et al. (29) showed that median survival extended to 14 months for patients treated surgically for multiple metastases.

In addition to showing that surgical resection combined with WBRT is more efficacious than WBRT alone (6,32,33), studies also indicate that recurrence at the original site of metastasis is significantly less frequent and functional independence is significantly longer. A 1980 report of a series of 33 patients who underwent surgical resection for solitary brain metastases and postoperative radiotherapy showed a low incidence of recurrence, a median survival of 8 months, and a 1-year survival of 44% (34). Patchell et al. (28) also found that randomly selected patients with cancer and a single brain metastasis treated with surgery followed by radiotherapy had considerably better results than those treated by radiotherapy alone: the surgical group had lower percentages of recurrence (20% vs. 52%), significantly longer median survival (40 vs. 15 weeks), and longer functional independence (38 vs. 8 weeks). Patients with lung cancer metastases to the brain have shown a 12% recurrence when treated with surgery combined with radiation versus 58% with radiation alone (31), and a retrospective study of 185 consecutive patients who under-

went resection of brain metastases for non–small cell lung carcinoma between 1974 and 1989 showed that the primary determinant of survival for these patients was complete resection (35).

Similar differences have been reported for patients with brain metastases from malignant melanoma (36). Although patients with melanoma have consistently poorer survival after surgery for brain metastases than do patients with other types of systemic cancer, patients treated with surgery have better results than do patients treated nonsurgically. For instance, Fell et al. (37) reported a difference in median survival of 5 months versus 6 weeks for patients treated with and without surgery, respectively, and a documented 87.5% immediate postoperative neurological improvement for surgical treatment versus the 39% rate reported for radiotherapy and chemotherapy. Other reports also confirm that patients treated surgically for metastases from melanoma have considerably better results than do untreated patients or patients treated with radiation or chemotherapy alone (36,38). Likewise, reviews of treatment of brain metastases from breast cancer show extended median survivals, including cases of multiple metastases (39,40). The synergistic value of combined surgery and WBRT was noted in a recent retrospective report by Skibber et al. (41). They compared 22 patients who underwent combined surgery and cranial irradiation with 12 patients who underwent surgical excision alone and found that the median survivals were 18 and 6 months, respectively, and that failure in the brain was less frequent with the addition of radiation to surgery ($p = 0.06$).

The general consensus among neurooncologists and neurosurgeons has been that surgery for multiple brain metastases is justified in only rare instances and should be limited to patients with (a) a life-threatening mass effect on the brain stem, (b) two or more lesions that can be removed through the same cranial opening (31), or (c) unknown histology. However, a recent review by Bindal et al. (29) of 56 patients who had undergone surgery for multiple brain metastases showed a median survival of 6, 14, and 14 months for patients in group A (patients who had one or more lesions remaining after surgery), group B (patients who had all lesions removed), and group C (patients matched with group B patients, but who had undergone surgery for only a single lesion), respectively, as well as a significant correspondence in recurrence or neurologic improvements between Groups B and C. These results indicated that surgery for patients with multiple metastases that are all removed was as effective as surgery for patients having a single lesion.

Finally, advances in surgery have allowed tumors in areas previously considered inaccessible to be selectively resected. In 1986, Tobler et al. (42) reported the first successful removal of a metastatic lesion to the tectum of the midbrain. A rare occurrence (1–3% of brain metastases) previously considered inoperable, the tumor was vaporized with carbon dioxide laser beam of up to 20 W and removed by a central coring technique.

Stereotactic radiosurgery

In 1951, Leksell (43) coined the term "radiosurgery" to stress the fact that the combination of mechanically directed instruments and modern radiation physics is still surgery and has little to do with radiotherapy in its conventional meaning. He suggested treating Parkinson's disease and chronic pain with radiosurgery to ablate small areas of the brain; later, radiosurgery was found to be efficacious in treating various brain lesions. Since that time, the procedure has been relatively slow in being developed, but recent advances in linear accelerators modified to perform radiosurgery have greatly expanded the availability of this technique.

Stereotactic radiosurgery proffers a noninvasive means of destroying intracranial tissues or lesions that may be inaccessible or unsuitable for open surgery. Narrow beams of single high doses of ionizing radiation can be directed using a linear accelerator (44) or a gamma knife (45) to small intracranial targets without markedly affecting the surrounding brain tissue. Other advantages of radiosurgery versus conventional radiotherapy include the ability to (a) deliver a large-fraction boost to the metastatic tumor with $<10\%$ dose to surrounding normal brain, (b) give a radiosurgical boost to multiple lesions in remote locations in one treatment session with minimal dose overlapping, (c) minimize damage to nonaffected brain when retreating previously irradiated patients, (d) provide 1-day treatment that maximizes patient convenience and minimizes patient cost, and (e) potentially improve local control as a result of high total dose and shortened treatment time (46).

In contrast to malignant primary brain tumors, metastases are particularly well suited for stereotactic radiosurgery. They are usually well circumscribed and to some extent spherical, have distinct enhancing margins on MR or CT images, and tend

to be relatively small (<3 cm) when detected. They displace normal brain parenchyma circumferentially outside the potential radiosurgical target, thereby reducing the probability of injury to normal brain tissue. They tend to be minimally invasive and easily encompassed in the radiosurgical treatment field (47).

Stereotactically delivered radiation has a reported local control of 88% (46), a considerably better rate than the 41–44% local control reported for fractionated WBRT alone (10). Radiosurgery also allows discontinuance of corticosteroid therapy, thereby reducing the morbidity of its long-term use.

Complications of radiosurgery are minimal, with the major acute complication being the transient headache experienced immediately after removal of the headframe. Acute onset of nausea and vomiting that correlated with total dose of radiation to the area postrema have also been reported (47). The risk of developing radiation necrosis is increased in patients with large (>3 cm) metastases.

The decided advantages and minimal risks of radiosurgery indicate that it proffers an important therapeutic role in the management of metastatic cerebral lesions, although in the absence of a randomized study comparing radiosurgery to surgery, no conclusions regarding which therapy is superior can be made.

Chemotherapy

Wilson and Garza (48) first reported response by cerebral metastasis to systemic chemotherapy in 1965, but until the early 1990s, chemotherapy was not considered a likely candidate for efficacious treatment of brain metastases because the BBB was thought to prevent cytotoxic drugs from penetrating into the tumor. However, recent studies indicate that chemotherapy may be especially efficacious for metastases from chemosensitive tumors such as small cell lung cancer (SCLC) or breast cancer. In the late 1980s, studies designed to assess the response rate of patients with cerebral metastases from SCLC who received chemotherapy alone showed that the overall response rate was 56%. Furthermore, the patients who responded showed rapid neurological improvement and objective responses apparent on CT as early as 3 weeks after the first cycle of treatment (49). Similarly, tests with patients with breast cancer showed a 50% response for cerebral metastases (50). Twelves and Souhami recently suggested several advantages of chemotherapy over irradiation in treating cerebral metastases from chemosensitive tumors: (a) immediate administration without prolonged hospital admission or repeat trips to the hospital, (b) simultaneous treatment of the cerebral metastases and the extracranial disease, and (c) response monitoring by CT scan that allows irradiation to be started if results indicate no improvement (51).

Unfortunately, most candidates for chemotherapy will require corticosteroids, which relieve neurological symptoms but also have the adverse effects of systemic complications and diminish efficacy of the chemotherapy by rebuilding the BBB. Other complications of chemotherapy include permanent functional damage or even a fatal outcome, and the regimens are physically and mentally demanding, often requiring multiple treatments. Nevertheless, chemotherapy offers an attractive primary treatment for some patients with brain metastases by providing simultaneous treatment of cranial and extracranial disease, reducing the risk of late neurological side effects and using an outpatient setting that is cost effective.

RECURRENCE

Recurrence is a difficult clinical problem, one that is usually complicated by an accompanying extensive systemic disease. For recurrence after surgical resection and radiotherapy, therapy options are limited and must be carefully considered. A patient with a previous single metastasis treated by surgery alone has all the same options as a patient with a newly diagnosed tumor; patients who have already received radiotherapy are usually limited to 15–20 Gy as a safe dosage, but one that is usually too low to control the tumor. Surgical treatment may be an option for a select group of patients. In 1988, Sundaresan et al. (32) found that reextirpation resulted in neurologic improvement in 66% of the patients, and a median duration of 6 months, with no mortality and only one instance (5%) of increased deficit. They recommended that repeat resection be considered in symptomatic patients with accessible lesions before using other experimental treatments. Young and Patchell (52) recommended repeat resection if the lesion was single and radioresistant, the patient's Karnofsky rating >60, and the systemic disease under control.

CONCLUSION

Brain metastasis is a widely prevalent condition that occurs frequently in the setting of advanced

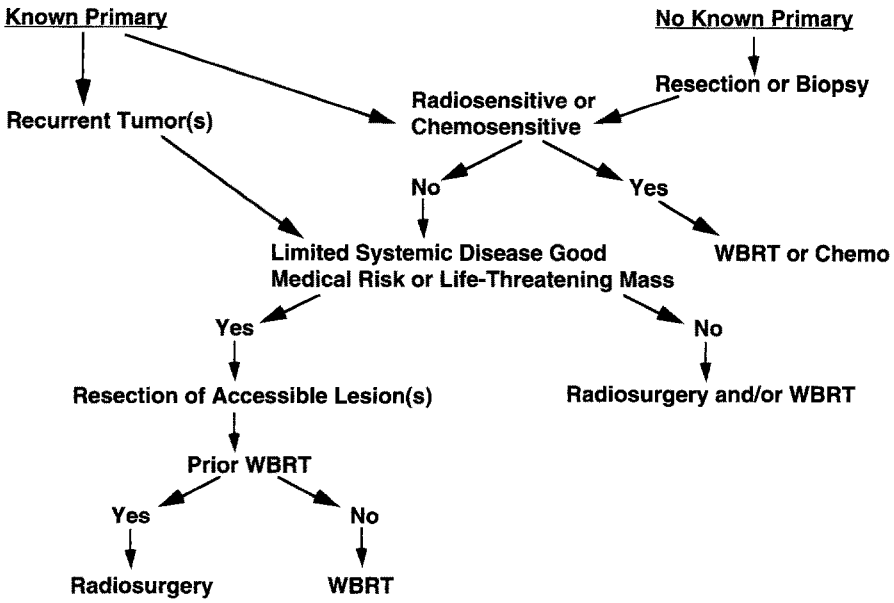

FIG. 2. Management of brain metastasis.

systemic disease. The need to effectively treat brain metastasis is becoming increasingly important because of the greater number of patients who are benefiting from the advances made in treating their primary cancers.

Several treatment options exist and, although each is limited in its effectiveness by the eventual progression of the systemic illness, considerable strides have been made to provide patients with palliation or cure of the lesion and/or its accompanying symptoms. Patients with previously known or newly diagnosed cancer, who represent the majority of patients with brain metastasis, are first evaluated to determine the specific radio- or chemosensitivity of the tumor. Tumors that are especially radio- or chemosensitive are generally treated with the respective modality. WBRT and/or chemotherapy usually provides good results, but surgical excision is performed if there is reason to believe that the lesion may not respond to these treatments or if the recurrent lesion has been treated previously with these modalities. Patients who have metastases that are not especially radio- or chemosensitive are evaluated for the status of the systemic disease, a crucial consideration in determining the appropriate therapy. The treatment goal for patients with a limited life expectancy is short-term palliation, and they are treated with WBRT and corticosteroids, which usually provide adequate relief from symptoms. Patients with controlled or limited disease are evaluated for more aggressive therapy, namely surgery, because palliation is unlikely to provide adequate relief for the patient's life and more aggressive therapy may even significantly prolong life. If the metastasis is single and accessible, surgery is a definite consideration, as it is for certain multiple metastases; if the metastasis is not surgically accessible, the patient is evaluated for stereotactic radiosurgery. Lesions that are immediately life threatening and accessible should be removed. Multiple metastases require more extensive evaluation. If the metastases can all be removed, surgery is still an option, as it is for patients who have some metastases that are not easily accessible. WBRT should follow to possibly eradicate any remaining tumors. Patients with too many lesions to be removed surgically are usually treated with WBRT alone (Fig. 2).

Radiotherapy remains the main therapeutic modality. However, surgical excision has increasingly shown substantial advantages in the appropriate settings of accessibility and resectability, even in patients with multiple brain metastases. Radiosurgery as an effective therapeutic modality offers clear advantages, particularly for those patients who have locally failed prior therapies. Its role in the treatment of newly diagnosed brain metastasis is still being evaluated.

Clearly, these significant advances in providing efficacious therapeutic options for patients with brain metastases portend a more hopeful future for patients than was once considered possible.

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