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Review Article

Secondary or Metastatic Tumors of the Central Nervous System

Updates and Advances

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Introduction

Metastatic tumors in the Central Nervous System (CNS) refer to cancerous tumors that have spread to the brain or spinal cord from other parts of the body. These tumors are also known as secondary brain tumors or brain metastases. They are more common than primary brain tumors, which originate in the brain itself.

Metastatic tumors in the CNS occur when cancer cells break away from a primary tumor elsewhere in the body, enter the bloodstream or lymphatic system, and travel to the brain or spinal cord. Common primary cancer sites that may give rise to CNS metastases include the lungs, breast, skin (melanoma), kidney, and colon, among others.

The symptoms of CNS metastases vary depending on the location and size of the tumor. They may include headaches, seizures, neurological deficits (such as weakness or numbness), changes in cognitive function, and other symptoms related to increased pressure in the brain.

Treatment options for CNS metastases typically involve a combination of surgery, radiation therapy, and chemotherapy. The specific treatment approach depends on various factors, including the number and size of the tumors, the type of primary cancer, and the overall health of the patient.

Managing metastatic tumors in the CNS can be challenging, but advances in treatment options and supportive care have improved outcomes for many patients. It's important for individuals with a history of cancer to receive regular follow-up care and inform their healthcare provider about any new or unusual symptoms that may arise.

Most frequent tumors that metastasize in the CNS

Several primary cancers are known to have a higher propensity to metastasize to the Central Nervous System (CNS). The most common types of cancer that tend to give rise to CNS metastases include:

1. Lung Cancer: Lung cancer is the leading cause of CNS metastases. Its ability to spread to the brain is relatively high, and lung cancer patients often develop brain metastases at some point during the course of the disease.

2. Breast Cancer: Breast cancer is another common primary cancer that frequently metastasizes to the CNS. It may spread to the brain years after the initial diagnosis, particularly in more advanced stages of the disease.

3. Melanoma: Melanoma, a type of skin cancer, has a high propensity for CNS metastasis. It is known for its ability to spread to distant organs, including the brain.

4. Kidney Cancer: Renal cell carcinoma, the most common type of kidney cancer, can also metastasize to the CNS. These metastases often occur after the initial diagnosis and treatment of kidney cancer.

5. Colorectal Cancer: Colorectal cancer, which primarily affects the colon or rectum, can occasionally spread to the CNS. While CNS metastases from colorectal cancer are less common compared to other sites, they can occur, particularly in advanced stages.

It's important to note that while these primary cancers are commonly associated with CNS metastases, cancer cells from any primary tumor can potentially spread to the brain or spinal cord. The likelihood of CNS metastases depends on various factors, including the specific characteristics of the primary cancer and individual patient factors.

Severity of the clinical situation

CNS metastasis is a serious condition, but it is not synonymous with immediate death. The prognosis for individuals with CNS metastases varies widely and depends on several factors, including the primary cancer type, the extent of metastatic spread, the number and size of tumors, and the overall health of the patient.

With advancements in treatment options and supportive care, many patients with CNS metastases can experience improved quality of life and extended survival. Treatment approaches such as surgery, radiation therapy, and targeted therapies have shown effectiveness in controlling and managing CNS metastases, allowing for symptom relief and potentially slowing disease progression.

It's important to note that the prognosis for CNS metastases is still generally considered to be less favorable compared to primary brain tumors. However, every individual case is unique, and it is essential to consult with healthcare professionals who can provide accurate information about prognosis, treatment options, and potential outcomes based on the specific circumstances of the patient.

Prompt diagnosis, effective treatment, and ongoing monitoring can play crucial roles in managing CNS metastases and improving long-term outcomes. Therefore, it is important for individuals with a history of cancer to receive regular medical follow-up and discuss any new or concerning symptoms with their healthcare providers.

Diagnostic algorithm

The diagnostic algorithm for CNS metastasis typically involves a combination of medical history evaluation, physical examination, imaging studies, and sometimes tissue sampling. Here's a general outline of the diagnostic process:

1. Medical History and Physical Examination: The healthcare provider will gather detailed information about the patient's medical history, including any previous cancer diagnoses or treatments. They will also perform a thorough physical examination to assess neurological function and look for any signs or symptoms that may suggest CNS metastasis.

2. Neuroimaging: Imaging studies are crucial in diagnosing CNS metastases. The most commonly used imaging modalities include magnetic resonance imaging (MRI) and computed tomography (CT) scans of the brain. These imaging techniques can help identify the presence, location, and characteristics of brain tumors.

3. Tissue Sampling: In some cases, if the imaging findings are inconclusive or if a primary cancer has not yet been identified, a biopsy may be recommended. This involves removing a small sample of the tumor tissue for further analysis, which can help determine the origin of the metastasis and guide treatment decisions.

4. Laboratory Tests: Additional laboratory tests may be conducted to evaluate the patient's overall health and assess the function of various organs. Blood tests, such as complete blood count (CBC), liver function tests, and tumor markers specific to certain types of cancer, may be performed to provide further information.

5. Molecular Testing: Molecular testing of the tumor tissue may be done to identify specific genetic mutations or biomarkers that can guide treatment decisions, such as targeted therapies or immunotherapies.

The diagnostic algorithm can vary depending on individual factors, including the patient's symptoms, medical history, and the suspected primary cancer. The process is typically coordinated by a multidisciplinary team involving oncologists, neurologists, neurosurgeons, and radiologists who collaborate to reach an accurate diagnosis and develop an appropriate treatment plan tailored to the patient's needs.

Surgical or puncture biopsy?

Biopsy procedures typically involve obtaining tissue samples from the body for examination and diagnosis, but it is typically performed in a controlled environment such as an operating room or a specialized clinic.

"Puncture with graphic tone control" is not a recognized term or procedure in medical diagnostics that I'm aware of. It's possible that you may be referring to a specific technique or technology that is not commonly used or recognized by that specific name.

In general, the choice of the best diagnostic method for obtaining tissue samples depends on various factors, including the location and accessibility of the lesion, the suspected diagnosis, and the expertise of the medical team. Biopsy techniques can include needle biopsies, excisional biopsies, endoscopic biopsies, or surgical biopsies, among others.

To determine the most appropriate diagnostic method and procedure, it is essential to consult with a qualified medical professional who can evaluate the specific clinical situation and recommend the best approach based on the individual circumstances and available resources.

Biomakers

biomarkers can play a significant role in the diagnosis and treatment of cancer, including CNS metastasis. Biomarkers are measurable substances or characteristics in the body that can indicate the presence of a disease, provide information about its progression, or predict treatment response. In the context of CNS metastasis, biomarkers can help in several ways:

1. Diagnosis and Detection: Certain biomarkers can aid in the identification and detection of CNS metastasis. For example, elevated levels of certain tumor markers in blood tests may suggest the presence of metastatic tumors in the CNS. These biomarkers can guide further diagnostic evaluations.

2. Tumor Characterization: Biomarkers can provide insights into the specific characteristics of the tumor, such as genetic mutations or alterations. Molecular profiling of the tumor tissue can help identify specific biomarkers that guide treatment decisions. For instance, the presence of certain genetic mutations may indicate eligibility for targeted therapies or immunotherapies.

3. Treatment Response and Monitoring: Biomarkers can be used to assess treatment response and monitor the progression of CNS metastasis. Changes in biomarker levels or other measurable indicators can indicate the effectiveness of the chosen treatment approach. Monitoring biomarkers over time can help determine if adjustments to the treatment plan are needed.

It's important to note that not all cancers or CNS metastases have specific biomarkers available for diagnosis or treatment decisions. The availability and utility of biomarkers can vary depending on the specific cancer type, individual patient factors, and ongoing research advancements. The use of biomarkers in clinical practice is typically determined by healthcare professionals based on the latest scientific evidence and guidelines in the field.

Surgery

When it comes to operating on metastases, there are both advantages and disadvantages to consider. Here are some points to keep in mind:

Advantages of Surgical Removal of Metastases:

1. Local Disease Control: Surgery can provide local control by removing the metastatic tumors from the affected area of the body, such as the brain in the case of CNS metastases. This can help alleviate symptoms and potentially slow down disease progression.

2. Potential for Cure: In some cases, surgical removal of metastases can lead to long-term disease-free survival or even cure, especially when combined with other treatment modalities like radiation therapy or systemic treatments.

3. Symptom Relief: Surgery can help alleviate symptoms associated with metastases, such as pain, neurological deficits, or increased intracranial pressure. By reducing the tumor burden, surgical intervention can improve the patient's quality of life.

Disadvantages and Considerations:

1. Multifocality and Recurrence: Metastases often occur as multiple tumors throughout the body, which can make complete removal challenging. Additionally, there is a risk of recurrence or development of new metastases even after successful surgery due to microscopic tumor cells that may have already spread.

2. Surgical Risks: Surgery carries inherent risks, including those associated with anesthesia, bleeding, infection, and potential damage to surrounding healthy tissues or structures. The location of metastases may also impact the feasibility and risks associated with the surgical procedure.

3. Overall Disease Burden: In cases where metastatic disease is widespread and affecting multiple organs, surgical removal of individual metastases may not significantly impact overall survival or disease control. In such situations, a comprehensive treatment plan involving systemic therapies like chemotherapy, targeted therapies, or immunotherapies may be more appropriate.

4. Individual Factors: The decision to pursue surgery for metastases is influenced by various individual factors, such as the patient's overall health, primary cancer type, extent of metastatic disease, and potential benefits versus risks. A multidisciplinary team of healthcare professionals, including surgeons, oncologists, and radiologists, collaborate to assess the patient's situation and determine the most suitable treatment approach.

It's important to note that the specific advantages and disadvantages can vary depending on the individual case and should be discussed with the healthcare team to make an informed decision about the best treatment strategy for CNS metastases.

Radiotherapy

Radiotherapy plays a crucial role in the management of CNS metastases. It is a localized treatment modality that uses high-energy radiation to target and destroy cancer cells. Here are some key aspects regarding the role and types of radiotherapy used for CNS metastases:

1. Local Control: Radiotherapy is effective in providing local disease control by targeting and eradicating cancer cells within the treated area. It can help shrink or eliminate metastatic tumors in the CNS, reducing symptoms and improving quality of life.

2. Whole-Brain Radiotherapy (WBRT): WBRT involves delivering radiation to the entire brain, treating both visible metastatic tumors and potential microscopic disease. It is commonly used when multiple metastases are present throughout the brain and when there is a risk of new metastases developing.

3. Stereotactic Radiosurgery (SRS): SRS is a precise and highly targeted form of radiotherapy that delivers a high dose of radiation to a small, well-defined metastatic tumor or tumors in the CNS. It is typically used when there are limited metastases or when surgery is not feasible due to tumor location or patient factors.

4. Fractionated Radiotherapy: Fractionated radiotherapy involves delivering radiation in smaller, divided doses over several treatment sessions. This approach is often used when treating larger metastatic tumors or when there is a need to spare nearby healthy brain tissue from excessive radiation exposure.

5. Hippocampal Sparing: In certain cases, to minimize potential cognitive side effects associated with radiation to the hippocampus, which plays a role in memory function, techniques like hippocampal sparing are employed during WBRT.

The specific type and course of radiotherapy depend on several factors, including the number, size, and location of metastases, the overall health of the patient, and the goals of treatment. A multidisciplinary team of healthcare professionals, including radiation oncologists and neurosurgeons, will evaluate individual cases and determine the most suitable radiotherapy approach.

Toxicity of immediate and long-term radiotherapy

It's important to note that radiotherapy may be used alone or in combination with surgery, systemic therapies (chemotherapy, targeted therapy, immunotherapy), or other treatment modalities, depending on the specific circumstances of the patient and the overall treatment plan.

Radiotherapy for CNS metastases, like any medical treatment, can have associated toxicities. The toxicities can be classified into immediate (acute) and long-term (chronic) effects. Here are some common toxicities:

Immediate (Acute) Toxicity:

1. Fatigue: Fatigue is a common side effect of radiation therapy, which can cause a general feeling of tiredness and lack of energy.

2. Skin Reactions: If radiation is delivered to the scalp, skin reactions such as redness, itching, dryness, and hair loss may occur. These reactions are usually temporary and resolve after treatment completion.

3. Nausea and Vomiting: When radiation involves the area near the stomach or upper abdomen, patients may experience nausea and vomiting. Medications can help manage these side effects.

4. Headache and Neurological Symptoms: In some cases, patients may experience temporary worsening of existing neurological symptoms, such as headache or seizures, shortly after radiation treatment.

Long-Term (Chronic) Toxicity:

1. Cognitive Changes: In some cases, radiotherapy to the CNS may lead to long-term cognitive changes, such as memory problems, difficulty with concentration, or decreased processing speed. The risk and severity of cognitive effects depend on various factors, including the radiation dose and volume treated, age, and individual susceptibility.

2. Radiation Necrosis: Radiation necrosis refers to the death of healthy brain tissue surrounding the treated area. It can occur months or years after radiation therapy, leading to neurological symptoms like headaches, seizures, or cognitive decline. Monitoring and follow-up imaging are important to detect and manage radiation necrosis.

3. Endocrine Dysfunction: Radiation therapy to the CNS can affect the function of the pituitary gland, leading to hormonal imbalances and various endocrine dysfunctions. Hormone replacement therapy may be necessary to manage these effects.

4. Radiation-Induced Secondary Cancers: Although rare, long-term radiation exposure increases the risk of developing secondary cancers in the irradiated area. The risk is generally outweighed by the potential benefits of treating the metastases, but it is an important consideration.

It's important to note that the specific toxicities and their severity can vary depending on various factors, including the specific treatment parameters, the dose of radiation, the patient's overall health, and individual variability. The healthcare team will closely monitor and manage any potential side effects, and the benefits and risks of radiotherapy will be weighed in each individual case to optimize the treatment approach.

Medical treatment. Role of the blood-brain barrier

1. Blood-Brain Barrier (BBB): The blood-brain barrier is a protective mechanism that limits the entry of substances, including some medications, from the bloodstream into the brain. It can pose a challenge in treating CNS metastases as it restricts the delivery of certain drugs. However, some medications can penetrate the BBB and effectively reach the metastatic tumors.

2. Targeted Therapies: Targeted therapies are designed to specifically target certain molecules or pathways that are involved in cancer growth and progression. These therapies can be effective in treating CNS metastases if the tumor has specific genetic mutations or molecular characteristics. For example, targeted therapies such as tyrosine kinase inhibitors (TKIs) may be used to inhibit specific signaling pathways in tumors that have particular mutations, such as EGFR mutations in lung cancer or BRAF mutations in melanoma.

3. Monoclonal Antibodies: Monoclonal antibodies are laboratory-produced antibodies designed to target specific proteins present on cancer cells. These antibodies can either directly attack cancer cells or stimulate the immune system to recognize and destroy cancer cells. In the context of CNS metastases, monoclonal antibodies may be used in certain cancers to target specific proteins or markers on the tumor cells.

4. Immunotherapy: Immunotherapy harnesses the body's immune system to recognize and attack cancer cells. It can include various approaches such as immune checkpoint inhibitors, adoptive cell therapies, and cancer vaccines. Immunotherapy has shown promising results in certain cancers, including melanoma, lung cancer, and kidney cancer. Its effectiveness in CNS metastases is being actively studied, and it has demonstrated some benefits in select cases.

5. Biological Therapies: Biological therapies refer to treatments that use substances produced by living organisms, such as cytokines, growth factors, or immune system components. These therapies can help modulate the immune response or target specific aspects of cancer cell growth and survival.

It's important to note that the selection and suitability of these medical treatments depend on various factors, including the specific characteristics of the tumor, individual patient factors, and ongoing research advancements. Treatment decisions are made by healthcare professionals based on the latest scientific evidence, guidelines, and the unique circumstances of each patient.

Medical treatments

1. Chemotherapy: Systemic chemotherapy is sometimes used for CNS metastases, especially when there is widespread disease or the primary cancer is sensitive to chemotherapy. The toxicities of chemotherapy can vary depending on the drugs used, but commonly include fatigue, nausea/vomiting, hair loss, immunosuppression, and peripheral neuropathy.

2. Targeted Therapies: Targeted therapies, such as tyrosine kinase inhibitors (TKIs) or other small-molecule inhibitors, are used for certain cancers with specific genetic alterations. The toxicity profile of targeted therapies varies depending on the specific agent used, but potential side effects may include rash, diarrhea, liver toxicity, cardiovascular effects, and others specific to the targeted pathway.

3. Immunotherapy: Immunotherapy, including immune checkpoint inhibitors, can be used in select cases of CNS metastases. Immunotherapy-related toxicities, known as immune-related adverse events (irAEs), can affect various organs and systems, including the skin, gastrointestinal tract, liver, lungs, and endocrine system. These toxicities range from mild to severe and require close monitoring and management.

It's important to note that the toxicity profile of each treatment modality can vary, and not all patients experience the same side effects. The healthcare team will closely monitor patients for potential toxicities, manage side effects, and tailor treatment plans to maximize benefits while minimizing risks and toxicities. Individual patient characteristics and preferences are also taken into account when determining the most appropriate treatment protocol.

Primary CNS tumors are generally more frequent than secondary (metastatic) CNS tumors. Primary CNS tumors originate within the brain or spinal cord, while secondary CNS tumors are metastases that spread from cancers in other parts of the body.

Primary versus metastatic tumors

Primary CNS tumors include a wide range of tumor types, such as gliomas (e.g., glioblastoma, astrocytoma), meningiomas, medulloblastomas, and ependymomas, among others. These tumors can be benign (non-cancerous) or malignant (cancerous).

On the other hand, secondary CNS tumors, or CNS metastases, occur when cancer cells from primary cancers in other organs, such as the lungs, breast, or colon, spread to the CNS. The most common primary cancers that metastasize to the CNS are lung cancer, breast cancer, melanoma, colorectal cancer, and renal cell carcinoma.

While primary CNS tumors are more frequent overall, the incidence of secondary CNS tumors is significant due to the high prevalence of certain primary cancers. The occurrence of secondary CNS tumors is influenced by the primary cancer type, stage, and other factors such as patient age and overall health.

It's important to note that the treatment and prognosis for primary and secondary CNS tumors can differ, and a thorough evaluation by healthcare professionals is essential to determine the appropriate diagnostic and treatment approach for each individual case.

References

1. Mehta M, Vogelbaum MA, Chang S, et al.: Neoplasms of the central nervous system. In: DeVita VT Jr, Lawrence TS, Rosenberg SA: Cancer: Principles and Practice of Oncology. 9th ed. Lippincott Williams & Wilkins, 2011, pp 1700-49.
2. American Cancer Society: Cancer Facts and Figures 2023. American Cancer Society, 2023. Available online. Last accessed January 13, 2023.
3. National Cancer Institute: SEER Cancer Stat Facts: Brain and Other Nervous System Cancer. Bethesda, Md: National Cancer Institute. Available online. Last accessed October 14, 2022.
4. Sung H, Ferlay J, Siegel RL, et al.: Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin 71 (3): 209-249, 2021. [PubMed]

5. Schabet M: Epidemiology of primary CNS lymphoma. J Neurooncol 43 (3): 199-201, 1999. [PubMed]
6. Behin A, Hoang-Xuan K, Carpentier AF, et al.: Primary brain tumours in adults. Lancet 361 (9354): 323-31, 2003. [PubMed]
7. Kleihues P, Cavenee WK, eds.: Pathology and Genetics of Tumours of the Nervous System. International Agency for Research on Cancer, 2000.
8. Cloughesy T, Selch MT, Liau L: Brain. In: Haskell CM: Cancer Treatment. 5th ed. WB Saunders Co, 2001, pp 1106-42.
9. Hutter A, Schwetye KE, Bierhals AJ, et al.: Brain neoplasms: epidemiology, diagnosis, and prospects for cost-effective imaging. Neuroimaging Clin N Am 13 (2): 237-50, x-xi, 2003. [PubMed]
10. Ricci PE: Imaging of adult brain tumors. Neuroimaging Clin N Am 9 (4): 651-69, 1999. [PubMed]
11. Baumert BG, Hegi ME, van den Bent MJ, et al.: Temozolomide chemotherapy versus radiotherapy in high-risk low-grade glioma (EORTC 22033-26033): a randomised, open-label, phase 3 intergroup study. Lancet Oncol 17 (11): 1521-1532, 2016. [PMC free article] [PubMed]
12. Reijneveld JC, Taphoorn MJ, Coens C, et al.: Health-related quality of life in patients with high-risk low-grade glioma (EORTC 22033-26033): a randomised, open-label, phase 3 intergroup study. Lancet Oncol 17 (11): 1533-1542, 2016. [PubMed]