

PALLIATIVE PEARLS

BY ENCLARA PHARMACIA

Symptom Management of Brain Metastases

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PATIENT CASE

TB is a 65 year-old with stage IV small cell lung cancer metastatic to the liver and bones. Lately, he is experiencing severe headaches that seem to worsen when he coughs or bends. The headaches are frequently accompanied by nausea and vomiting. TB is also having balance problems and leg and arm weakness. During your home visit, TB suddenly falls silent and starts to shake. The seizure lasts for approximately 30 seconds, when TB regains consciousness.

A review of his progress notes indicate that brain metastases are suspected but not officially diagnosed. TB wants to remain home and not undergo additional diagnostic testing. What is the best way to manage his symptoms?

COMMON SYMPTOMS IN PATIENTS WITH PRIMARY OR METASTATIC BRAIN CANCER¹

- Drowsiness
- Headaches
- Nausea and/or vomiting
- Focal neurological symptoms
- Cognitive, behavioral and emotional changes
- Seizures
- Delirium
- Dysphagia

Approximately 10% of cancers metastasize to the brain, with the highest rates occurring in those with melanoma, lung, breast, or kidney cancer. As brain tumors grow, the blood-brain barrier breaks down and fluid accumulates in the extracellular space, leading to raised intracranial pressure (ICP), contributing to symptoms.²

Some patients may have several of the above symptoms, while others have none. Factors that influence the presence and severity of symptoms include the tumor's location and size, rate of growth, and associated edema. Patients with brain metastasis tend to develop significant and progressive neurological symptoms in the final weeks of life.¹

MEDICATIONS TO MANAGE SYMPTOMS

During the initial stages, headaches may be managed with over-the-counter acetaminophen and/or NSAIDs or opioids, however, corticosteroid and anticonvulsant medications are the mainstays for progressive symptoms. Cognitive, behavioral and emotional changes are managed with sleep aids/hypnotics (insomnia) and psychotropics (anxiety, agitation, depression). Whole brain radiotherapy

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is frequently used for palliation, but in TB's case, it is not in keeping with his goal to remain at home and avoid further treatment except for supportive care.¹

Corticosteroids

Corticosteroids cross the blood–brain barrier and improve symptoms associated with increased ICP by decreasing inflammation and reducing tissue edema. These symptoms include nausea, vomiting, and headache, as well as focal neurological deficits such as weakness and language dysfunction.¹

While any corticosteroid can be used to treat cerebral edema, dexamethasone is the drug of choice due to its duration of action, minimal sodium and water retention side effects compared to other corticosteroids, and low incidence of steroid-induced psychosis and infection.³ Up to 75% of patients initiated on dexamethasone show improvement within one to three days.⁴ Starting doses range from 4 to 8mg per day in one or two divided doses with titration to higher doses in patients with more severe symptoms or those who do not respond within 48 hours.⁵

Like other steroids, dexamethasone has potential side effects such as weight gain due to increased appetite, hyperglycemia, GI upset, and insomnia. Common dermatological side effects include acne and thinning of the skin, leading to bruising and discoloration. If the patient cannot tolerate the steroid due to adverse effects or if there is no improvement in symptom management after a week, dexamethasone should be slowly tapered by decreasing the dose by 50% every 4 days to avoid symptoms of steroid withdrawal.¹

Administer corticosteroid doses no later than 2 PM in order to minimize insomnia and restlessness and to maximize analgesia, daytime alertness, and improvements in appetite.¹ Dexamethasone tablets and compounded suppositories are absorbed rectally, which may be helpful for patients with difficulty swallowing.

Anticonvulsants

Up to 40% of patients with brain tumors have a seizure at the time of diagnosis and another 20% develop seizures during the course of the illness.⁶ In the past, anticonvulsants were commonly initiated at the time of a brain tumor diagnosis, however they do not prevent the development of seizures and guidelines published by the American Academy of Neurology do not support their use prophylactically.⁷ Based on the lack of evidence for benefit, **anticonvulsants can be safely discontinued in patients with brain tumors who have never had a seizure.**^{6,7,8}

For patients with a history of seizures, the second-generation anticonvulsant levetiracetam (Keppra®) is a favorable option for maintenance therapy due to low incidence of drug-drug interactions and adverse drug reactions compared to other anticonvulsants.⁹ Levetiracetam does not require routine lab monitoring and is available as immediate-release tablets, extended-release tablets and liquid. There is

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some evidence to suggest that immediate-release levetiracetam tablets and compounded suppositories are absorbed rectally for those with difficulty swallowing.¹⁰

Cost-effective first generation anticonvulsants, including phenytoin (Dilantin®), carbamazepine (Tegretol®), divalproex (Depakote®) and valproic acid (Depakene®), are also frequently used to manage seizures due to brain metastases, either as monotherapy or in combination with levetiracetam or gabapentin (Neurontin®) for refractory seizures. Carbamazepine and valproic acid rectal suppositories can be compounded and are well absorbed rectally, representing a possible option for patients who have difficulty swallowing. If rectal administration of medications is not possible, scheduled doses of oral lorazepam or diazepam concentrated solutions can be given to decrease the likelihood of seizure activity when the patient is no longer able to swallow. Benzodiazepines therapy is typically reserved for acute seizures lasting longer than 1 minute.¹ Compounded diazepam rectal suppositories or commercial diazepam rectal gel (Diastat®) should be readily available for initial control.

ASSESSMENT & MANAGEMENT - PATIENT CASE:

Based on his symptoms and type of cancer, TB likely has brain metastases. His medication list does not include corticosteroids or anticonvulsants. The following are recommended:

- Levetiracetam 500mg; 1 tablet by mouth twice a day for seizure prevention
May titrate by 500mg/dose every 2 weeks to a maximum recommended daily dose of 3000 mg. Doses greater than 3000 mg/day show no additional benefit.
- Dexamethasone 4mg; 1 tablet by mouth twice a day (morning and 2pm) for cerebral edema
- Diazepam 10mg suppository; Insert 1 suppository rectally every 15 minutes as needed for acute seizures until seizure activity stops, up to a maximum of 3 doses

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