CASE STUDIES IN METASTATIC CANCER

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Introduction: Building on principles and evidence detailed in earlier parts of this consultations course, we will analyze 5 case studies in metastatic cancer, emphasizing those metastatic tumors most commonly seen by neurologic consultants (melanoma, breast cancer and lung cancer) and encouraging audience participation. Please note: in order to make the cases more diagnostically realistic and challenging and in order not to bias your clinical reasoning, this syllabus background material is NOT presented in order of presentation during the live session. For similar reasons, reference list is alphabetized.

For each case, where relevant, we will summarize:

1) state of the art treatment and its evidence base
2) novel presentations or differential diagnostic dilemmas (for example, when is what appears to be a tumor in a patient with known cancer NOT a tumor)
3) cost-effective diagnoses (short of biopsy)
4) newer therapies

Case 1: Non Small Cell Lung Cancer in the Era of Personalized Diagnostics

A 72 year old man with recently diagnosed stage IV non-small cell lung cancer presents with gait ataxia and episodes of sometimes painful clenching of his left hand. MRI shows an isolated 3X2X2 cm lesion in the right motor cortex. There is also considerable white matter disease consistent with small vessel ischemic disease. He has just completed radiation therapy to the lung and is receiving erlotinib based on the actionable mutation in his primary tumor tissue. What is the best treatment for his CNS disease?

Clinical Points:
A) Seizures: what is the best anti-epileptic drug? B) Diagnosis: Should he be advised to have biopsy (is the metastatic tumor the same as the associated primary cancer?) C) Prognosis: estimating survival in patients with cerebral metastases; D) Treatment of solitary or oligometastatic CNS disease- stereotactic radiosurgery (SRS), whole brain radiation therapy, response of CNS disease to tyrosine kinase inhibitor therapy, risks of combining SRS and targeted therapies.

Case 2: Longitudinally extensive transverse myelitis in a patient with known breast cancer

A 48 year old woman with known stage IV breast cancer complicated by positive cytology for adenocarcinoma 8 months ago has received 12 doses of intrathecal methotrexate via Ommaya reservoir. Drug was discontinued when patient became confused and an MRI scan (to be shown) was found to be abnormal. Despite the extensive white matter disease on MRI, she has been cognitive stable. Five months after the diagnosis of leptomeningeal metastases, she developed localized back pain and was found to have a compression fracture at T10. She underwent posterior spinal fixation T9-T11 four months ago and now presents with decreased rectal tone, difficulty urinating, and right lower extremity numbness. Her MRI scan of the brain shows diffuse leukoencephalopathy and her MRI scan of the thoracic spine shows a lesion that is longitudinally extensive from T2 through the conus. Enhancement of the cord is seen from T8 to T10.

Clinical Points: A) Extensive differential diagnosis of longitudinally extensive transverse myelitis, each item of which would dictate very different therapy. B) Altered timing and appearance of toxicity from conventional radiation dosing when coupled with new targeted therapies C) Palliative care

Case 3: Melanoma: what's new—can we replicate the success of medical oncology?

We will discuss several examples of melanoma behavior in the CNS, including
1) multiple hemorrhagic metastases and their palliation,
2) small frontal metastases and a clinical examination that does not fit with the MRI

3) newer treatment strategies including BRAF inhibitors and immune checkpoint inhibitors that have dramatically altered prognosis of melanoma cerebral metastases, but also have led to some novel neurological complications including subacute neuropathies and altered presentation of recurrent cerebral metastatic disease

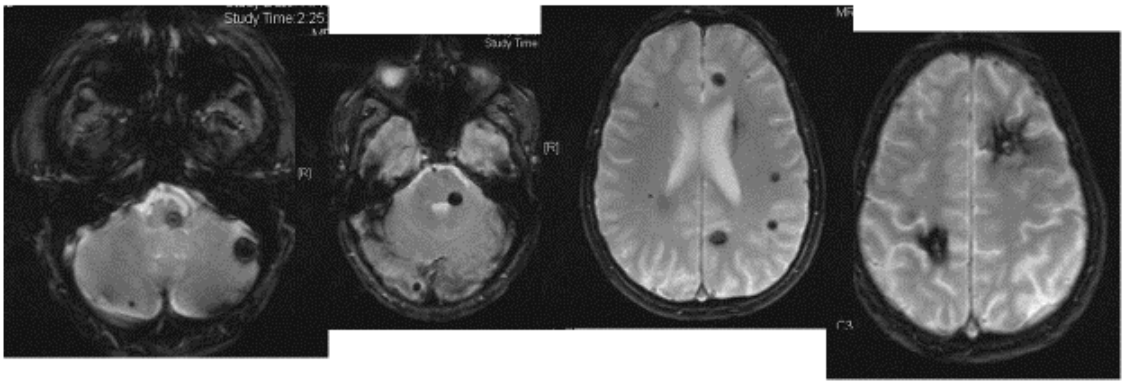
Case 4: The confused oncology patient: failure to thrive with brainstem signs

A 63 year old woman has been treated for uterine leiomyosarcoma and is
s/p multiple procedures-- TAH, BSO, rectosigmoid resection, nephrostomy. She has had progressive systemic disease and has sustained a recent (three months) 40 pound weight loss. She has received 2 doses ifosfamide, doxorubicin with transient confusion. Over next 2 weeks, has fluctuating arousal, tremor, diplopia.

Clinical Points:
Differential Diagnosis: The usual culprits: direct involvement of CNS, indirect (paraneoplastic?), seizures, infections with tropism for brainstem, osmotic demyelination,
A specific treatable culprit
Which oncology patients are at greatest risk for this complication?

Case 5: Chemobrain: "Is the brain the new bone marrow?"

A 44 year old nurse was treated at age 3 for ALL. He received 2400 cGy brain radiation as part of his conditioning regimen. Now after twenty years in nursing practice he is beginning to question his clinical acumen and worries that he will not be able to continue in his profession. He has had several episodes of sudden unsteadiness followed by a posterior headache as well as recurring episodes of up to three hours of left arm numbness, again followed by a mild headache. MRIs are shown below:



Clinical Points: We will discuss A) the nature and significance of the above findings; B) stroke-like migraines after radiation therapy; C) the evolving understanding of "chemobrain"; D) the spectrum of long-term complications of childhood cancer treatment, providing a check list for consultants who may work as part of a multi-disciplinary team to support cancer survivors.

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