Wernicke’s Encephalopathy in Cancer Patients: A Case Series from MD Anderson Cancer Center

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Introduction

- Wernicke’s encephalopathy is a neurological emergency and thiamine supplementation can prevent permanent neurological damage and death.
- Classical Wernicke’s encephalopathy symptoms include global confusion, ataxia, and ophthalmoplegia.
- Alcoholism, gastrointestinal bypass surgery, chronic malnutrition, and systemic illnesses are risk factors for Wernicke’s encephalopathy.
- 25% of hospitalized cancer patients would have altered mental status due to infection and metabolic disturbances, organ failure, medication, or metastatic disease, and a serum thiamine level should be considered as the diagnostic algorithm.
- Cancer patients are especially at risk for Wernicke’s encephalopathy because of poor nutritional status, chronic nausea, and consumption of thiamine by rapid growing cancer.

Case 1

A 63 year-old woman with uterine leiomyosarcoma status post total abdominal hysterectomy, bilateral pelvic lymph node dissection, anastomosis, synuclein, and transverse colon resection. She was treated with the first course of ifosfamide and doxorubicin with transient confusion and lethargy which resolved spontaneously.

- The patient subsequently developed seizure. On neurological exam, the patient had disorientation and confusion without diplopia or ataxia.
- MRI revealed bilateral FLAIR hyperintensity in the frontal cortex, subcortical area, mental aspect of the thalamus, and superior central vermis (Figure 1A-C).
- EEG showed no prior dominant rhythm and generalized 3-Hz delta activity.
- The patient then went into coma. CT of the brain demonstrated herniation in the fourth ventricle with obstructive hydrocephalus (Figure 2).
- She developed chronic nausea, vomiting, and diarrhea, and, one month later, she was admitted for confusion and bilateral pneumonia. She was adequately treated for pneumonia but her mental status remained poor and she developed generalized tonic-clonic seizures.
- MRI of the brain showed T2 hyperintensity in the dorsal midbrain and in the periaqueductal gray. She died several days later and autopsy findings showed microhemorrhages in the thalamus and brainstem (Figure 3E). She had chronic nausea, vomiting, diarrhea, and asthenia. Ophthalmological symptoms including sixth nerve palsy, hypotonia, and ataxia were also observed (Figure 3E).

Case 2

A 45-year-old woman with AML achieved complete remission after treatment with cytarabine and daunorubicin. She received a course of chemotherapy followed by allogenic BMT.

- She developed chronic nausea, vomiting, and diarrhea. The patient died and autopsy findings showed microhemorrhages in the thalamus and brainstem (Figure 3E) with external evidence of encephalopathy.
- She was treated empirically with thiamine while undergoing evaluation for other potential causes of altered mental status.

Case 3

A 65-year-old woman with stage IIIb inflammatory breast cancer received neoadjuvant 5-fluorouracil, docetaxel, and cyclophosphamide followed by lymph node dissection and treatment with cyclophosphamide, etoposide, and cisplatin.

- She developed chronic nausea, vomiting, and diarrhea, and, one month later, she was admitted for confusion and bilateral pneumonia. She was adequately treated for pneumonia but her mental status remained poor and she developed generalized tonic-clonic seizures.
- MRI of the brain showed T2 hyperintensity in the dorsal midbrain and in the periaqueductal gray. She died several days later and autopsy findings showed microhemorrhages in the thalamus and brainstem (Figure 3E) with external evidence of encephalopathy.
- She was treated empirically with thiamine while undergoing evaluation for other potential causes of altered mental status.

Table 1: Clinical presentations and risk factors for Wernicke’s encephalopathy

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Cancer type</th>
<th>MRI findings</th>
<th>Pathology findings</th>
<th>Treatment</th>
<th>Coma on admission</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>63</td>
<td>Uterine leiomyosarcoma</td>
<td>FLAIR hyperintensity in the frontal cortex</td>
<td>N/A</td>
<td>Yes</td>
<td>Improved mental status</td>
<td>Mortality</td>
</tr>
<tr>
<td>2</td>
<td>45</td>
<td>AML</td>
<td>FLAIR hyperintensity in the frontal cortex</td>
<td>N/A</td>
<td>Yes</td>
<td>Improved mental status</td>
<td>Mortality</td>
</tr>
</tbody>
</table>

Discussion

- Wernicke’s encephalopathy is a neurological emergency associated with a high mortality rate. The classical symptoms comprising confusion, ataxia, and ophthalmoplegia rarely occur concurrently, creating diagnostic dilemmas.
- Confusion occurs in 80% of cases. Abnormal extra-ocular movement was observed in only half of the cases. Only 18% had ataxia. Other symptoms include quadriplegia, tremor, hypotonia, and obtundation. Bilateral vision loss can also occur.
- Although the major risk factor for WE is alcoholism, which can account for as many as 90% of cases, poor nutritional status, gastric bypass surgery, chronic nausea and vomiting, systemic illness, and malnutrition are also important.
- Patients with cancer actively undergoing treatment with chemotherapy may be particularly vulnerable. Hematological malignancies and cancers are rapidly growing tumors that may deplete thiamine stores. Chronic nausea and vomiting further exacerbates underlying poor nutritional status. Individually or in combination, these factors may precipitate Wernicke’s encephalopathy in patients with chronic cancers who are unable to maintain adequate intake.
- We found previous 24 reported cases of Wernicke’s encephalopathy associated with cancer in the literature. 13 patients had a primary hematological malignancy, 5 had gastrointestinal cancers, and 1 had non-gastrointestinal carcinoma. Other cancers that have been reported are melanoma, lung cancer, and breast cancer. Confusion, shaper, and coma occurred in 75% patients. Ophthalmological symptoms including slurred speech, nystagmus, and ptosis were also present in 75% patients. Astasia was less commonly seen (23%). Imaging studies showing characteristic findings only in 31% patients. Only14 patients (58%) were treated with thiamine, and among those, 13 patients showed clinical improvement (92%). The remaining 10 patients did not receive thiamine and died (100% mortality).
- We propose that in cancer patients with confusion be treated empirically with thiamine while undergoing evaluation for other potential causes of altered mental status.