Pearls & Oy-sters:
Transient neurologic events in a patient with leptomeningeal metastases

PEARLS

- Patients with leptomeningeal metastases (LM) may develop transient neurologic events in the setting of temporary elevations of intracranial pressure (ICP).
- Clinical manifestations previously described include change in level of alertness, posturing of the extremities, arching of the neck and back, nausea, vomiting, and incontinence.1

OY-STERS

- The exclusion of clinical or electrographic seizures is important, as these are not uncommon in patients with LM.2
- These paroxysmal events are an important neurologic differential diagnosis in patients with a history of cancer and may occur even in the absence of radiologic hydrocephalus.3

CASE REPORT

A 48-year-old woman with a 1-week history of blurry vision was transferred from an outside hospital for surgical management of a 0.8 × 1.7 × 0.7 cm pituitary tumor.

The patient had a remote history of Hodgkin lymphoma treated with radiochemotherapy, as well as controlled hypertension. The patient had been well until about 2 weeks before transfer, when abdominal pain prompted a CT of the abdomen, which was reported as diverticulitis, but could not exclude a colonic neoplasm.

Upon admission, the patient’s neurologic examination including evaluation of mental status, cranial nerves with funduscopy, motor, sensory, coordination, and gait were normal.

Subsequently, the patient developed episodes of several minutes duration of decreased alertness, which resolved spontaneously. During some of these events, the patient was noted to have papilledema on funduscopic examination, which subsequently resolved.

Video-EEG monitoring was initiated. During 48 hours of recording, a total of 22 clinical events were captured. They lasted between 5 and 10 minutes and consisted of delayed or absent verbal responses, eye rolling, staring, and alternating gaze preferences to both sides. There were no obvious clinical changes observed with head of bed elevation. Initially, levetiracetam was administered given concern for seizures, without clinical or electrophysiologic response. Subsequently, these events resolved spontaneously.

EEG recordings showed a normal background prior to the events (figure, A), a transition marked by abrupt onset of marked background slowing (figure, B), and generalized 2–3 Hz delta, mixed with some theta frequencies during the events (figure, C).

There were no seizures, epileptiform discharges, cardiac arrhythmias, or state changes. Interictal EEG was normal. A workup for metabolic causes of encephalopathy, including comprehensive metabolic profile, liver function tests, ammonia, and thyroid-stimulating hormone, was nonrevealing.

Review of outside and repeat imaging with MRI of the brain, magnetic resonance venogram of the head, and MRI of the pituitary with contrast revealed metastases to the cerebellar vermis and the leptomeninges (figure, D and E), which were present, although not reported on outside imaging. The originally reported pituitary tumor was believed to be an incidental finding. There were no radiologic signs of CSF flow obstruction or hydrocephalus. CT chest, abdomen, and pelvis demonstrated a right pleural effusion as well as colonic neoplasm. Given the above-mentioned EEG findings and radiologic diagnoses of brain and leptomeningeal metastases, a presumptive diagnosis of plateau waves due to temporary elevations in ICP was made.

Two lumbar punctures were performed. On the initial CSF examination, opening pressure was not obtained and profile was as follows: 123 leukocytes with lymphocytic predominance, 0 erythrocytes, glucose 47, and protein 48. Cytology revealed atypical cells and malignancy could not be excluded due to scant cellularity. Flow cytometry revealed a nonspecific CD45 cell population.
A subsequent lumbar puncture revealed an opening pressure of 25 cm H$_2$O, with 183 leukocytes with lymphocytic predominance, 25 erythrocytes, glucose 45, and protein 67. Cytology was positive for malignant cells, favoring an epithelial neoplasm. Pleural fluid yielded analysis was consistent with an exudate and cytology was positive for signet ring cell carcinoma.

In addition to the described transient changes in behavior, the patient subsequently complained of double vision as well as blurry vision. Funduscopic examination in consultation with ophthalmology revealed bilateral papilledema and severe loss of visual acuity (20/200 OS and 20/100 OD).

In consultation with hematology and radiation oncology, further workup with endoscopy and biopsy of the gastrointestinal tract was recommended, yet declined by the patient.

The patient underwent whole-brain radiotherapy (WBRT) for symptom control and pulse steroids were administered. There was no improvement with respect to diplopia or vision loss. In light of the patient’s overall poor prognosis, the patient’s family decided to change goals of care to comfort measures only.

**DISCUSSION** In our patient, the pathologic diagnosis of signet ring cell cancer (SRCC) was ultimately established through pleural fluid analysis. The most likely primary tumor site was the colon, based on imaging findings; however, endoscopy with biopsy was deferred as above. SRCC of the colon is a rare malignancy, accounting for less than 1% of all colorectal cancers and associated leptomeningeal spread is even less common.

LM, defined as the spread of metastatic cancer cells to the subarachnoid space, CSF, or leptomeninges, occur in 1%–8% of solid and hematologic malignancies. Increased ICP has been reported in up to 26% of patients with LM and confers a poorer prognosis. In some patients, paroxysmal neurologic events may occur due to temporary elevations in ICP. In this setting, plateau waves, also known as Lundberg A waves, may appear. These waves begin and end abruptly when ICP rises between 25% and 72% above the mean. The duration of
these ICP elevations has been reported between 5 and 20 minutes.9

The pathophysiology of these transient neurologic events is thought to be a result of reduced cerebral perfusion pressure (CPP).1 Without corresponding increases in mean arterial pressure, increases in ICP will result in reduced CPP, potentially leading to these paroxysmal events.

Clinical manifestations that have previously been described include a change in the level of alertness, posturing of the upper and lower extremities, arching of the neck and back, nausea and vomiting, and incontinence.1

In the absence of invasive ICP monitoring, plateau waves are often presumed if video-EEG monitoring documents clinical events without electrographic seizures or epileptiform patterns. The exclusion of clinical or electrographic seizures is important, as these may occur in 1 of 7 patients with LM.2

There is a paucity of clinical reports correlating video-EEG with definite or presumed plateau waves in patients with LM.10 The purpose of this report is to add to the literature of reported correlations of paroxysmal neurologic events with video-EEG monitoring in patients with LM. Further, it aims to raise awareness of this phenomenon as an important differential diagnosis of transient neurologic events in a patient with a history of cancer.

In this patient with leptomeningeal and brain metastases, the absence of electrographic seizures allowed for a presumptive diagnosis of plateau waves.

In reviewing the current literature, we found one additional report describing video-EEG correlates of presumed plateau waves in 3 patients with LM.10 The clinical events reported by Gold et al.10 included unresponsiveness, upward eye rolling, irregular mouth movements, neck and back arching, nausea and dizziness, unresponsiveness, and rigidity. Our patient had similar manifestations as displayed by delayed or absent verbal responses, eye rolling, staring, and alternating gaze preferences to both sides.

In this patient population, awareness of such transient neurologic events may serve as a marker of temporarily increased ICP before classic clinical signs develop. It may also help delineate the cause of raised ICP due to CNS metastases in a patient with a corresponding history of cancer.

When encountering a patient with a history of cancer who experiences transient neurologic events, one should keep a broad differential: EEG may help exclude seizures in the setting of brain or leptomeningeal metastases and state changes, and assess for characteristic changes seen with plateau waves due to transient ICP elevations. Cardiac arrhythmias should be ruled out with telemetry. Metabolic causes (infectious, electrolyte imbalance, toxic due to potential side effects from chemotherapy) should be reviewed.

The data reported are limited by several factors. Plateau waves were presumed but not definite in the absence of invasive ICP monitoring. Further, there is no standardized reporting of delta range slowing in the setting of plateau waves.9 We acknowledge the absence of radiologic findings such as mass lesions or CSF flow obstruction to account for increased ICP. However, the fundoscopic examination with bilateral papilledema could be seen as a clinical surrogate marker for raised ICP. Further, it has been reported that these patients may develop transient increases in ICP even in the absence of radiologic hydrocephalus.3 We could not assess for interval changes of presumed plateau waves after initiation of WBRT and steroids, given the change in goals of care.

Our clinical description of transient neurologic events in this patient adds to the current literature of paroxysmal manifestations due to raised ICP in patients with LM. There have been no reports to date that correlate these transient clinical neurologic events with both video-EEG and accurate ICP assessment through invasive monitoring. This would allow for a confirmation of definite rather than presumed plateau waves as well as observe for response to treatment if initiated for patients with LM.

REFERENCES
Pearls & Oy-sters: Transient neurologic events in a patient with leptomeningeal metastases
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