Introduction:
- Papilledema, which refers exclusively to bilateral optic disc edema associated with increased intracranial pressure, is a rare clinical manifestation of meningitis, with a reported frequency of 2.5% of meningitis cases.
- In patients with atypical new onset headaches or meningitis-like symptoms, papilledema may be the only key differentiating sign of increased intracranial pressure.
- There is limited research describing the medical management of acute and chronic phases of increased intracranial pressure secondary to aseptic meningitis when the etiology is unknown.

I. Case History
- Patient demographics: AW 24 y/o NAF
- Chief complaint: double vision
- Onset: 1.5 weeks ago
- Location: horizontal
- Frequency: constant
- Treatment: none
- Associated symptoms: spots of blurred vision started 1 day ago, left eye, constant, glasses don’t help
- Ocular history: currently wears glasses, otherwise unremarkable
- Medical history: lower back surgery three years ago
- Medications: topiramate
- Other salient information:
  - The patient reports experiencing symptoms of headache x3 weeks accompanied by nausea, dizziness, chills, neck pain, bilateral paresthesia and numbness of hands and forearms.
  - The patient was seen one day prior to in the hospital emergency department for her headache and associated symptoms. A complete blood count showed elevated white blood cells. The diagnosis was complex migraine, and she was prescribed topiramate.
  - She was previously seen at two hospitals in Hawaii, where she was attending school, for these same symptoms. The workup included MR imaging, which was reported to be negative for masses and hemorrhages. Her diagnosis was altitude sickness, and she was given Zofran and Flexeril.

II. Pertinent findings
Clinical:
- Visual acuities: PH 20/20 OU
- Pupils: equally round, reactive to light (-)APD OU
- Confrontations: full OU
- IOP: 12mmHg OU
- EOM's: full OU, but on gross observation her eyes appeared simultaneously turned inwards (-)restrictions OU
- Cover Test: intermittent diplopia was reported, however no eye movement was observed on unilateral or alternating cover test, (-)phoria, (-)strabismus OU
- Hirschberg/Kappa: reflexes were centered OU, no movement of either eye on unilateral cover test
- Maddox rod: patient reported uncrossed diplopia; diplopia was neutralized with 10BO prism, upon neutralization two white dots were reported
- Amsler grid: visual disturbance inferior to fixation OS, described as “gray blur”
- Anterior segment: unremarkable
- Posterior segment: unremarkable except severe bilateral disc edema with associated hemorrhages; the macula and fovea were intact OU

Physical:
- Blood pressure: 124/81
- Pulse: 88 bpm
- Respiration: 16
- Oral temperature: 96.5 F

Laboratory studies:
- CBC: WBC 16,000 (elevated, predominance of monocytes)
- Lumbar puncture: opening pressure 530mm of water
- HSV-1 and HSV-2 DNA: negative
- CSF analysis:
  - COLOR: colorless
  - TURBIDITY: clear
  - WBC: 117
  - RBC: 10
  - Mononucleocytes: 100
  - Segs: 0
  - Interpretation: predominant mononuclear WBC, high protein, low glucose, gram stain (-)
- Additional CSF studies:
  - Coxsackie titer (results received after patient care was transferred to another facility)
    - A7, A9, A16, A24 IgG results: 1:1600 (NEG <1:100)
    - A7, A9, A16, A24 IgM results: negative (NEG <1:10)
  - HSV PCR (ordered, results not yet received)
  - Acid Fast Bacteria (AFB) culture and smear (ordered, results not yet received)

Radiology studies:
- MRI: reported by patient to be negative for masses and hemorrhaging
- CT head (done prior to lumbar puncture): negative

Other:
- Fundus photography: documentation of bilateral disc edema
- OCT 5 Line Raster of ONH: showed gross thickening of RNFL with some subretinal fluid, (-)drusen OU

III. Differential diagnosis
- Primary/leading: papilledema secondary to increased intracranial pressure
- Others: infectious/infiltrative optic disc edema, toxic neuropathy, malignant hypertension

IV. Diagnosis and discussion
Elaborate on the condition: Papilledema
- The term papilledema is most correctly used to describe bilateral optic disc edema secondary to increased intracranial pressure.
- Papilledema is commonly thought of in correlation with idiopathic intracranial hypertension (IIH), otherwise known as pseudotumor cerebri (PTC). However, a true IIH diagnosis is one of exclusion, and therefore a systematic systemic and neuro-ophthalmologic workup is needed in order to identify or rule out the underlying cause of increased intracranial pressure.
- In any case of papilledema, vital signs should be taken and a complete blood count and complete metabolic panel should be ordered to establish the patient’s immunologic state.
- The composition of elevated white blood cells give clues to an underlying infectious etiology. Neutrophilia is associated with acute bacterial infections, whereas monocytosis is associated with chronic bacterial infections. Lymphocytosis is indicative of an acute viral infection.
Magnetic resonance imaging should be performed in order to detect or rule out the presence of mass lesions and hemorrhages within the brain.

More recently, magnetic resonance venograms are also being recommended as part of the initial neuroimaging workup in order to rule out thrombotic obstruction or stenosis of the intracranial venous sinuses.

If MRI is negative for mass lesions, and no other etiology of increased intracranial pressure has been identified via MRI, MRV or serology testing, a lumbar puncture and CSF analysis are indicated.

If an infectious etiology is suspected, CSF studies can be tailored to investigate specific organisms.

Expound on unique features: Aseptic Meningitis

- Aseptic meningitis refers to patients who present clinically with signs of meningitis, have laboratory evidence supporting the diagnosis of meningeal inflammation, but have negative results on routine gram stain bacterial cultures, i.e. *N. meningitidis*, *S. pneumoniae*, and *H. influenzae*.

- Enteroviruses and HSV-2 are considered to be the leading causes of aseptic meningitis in adults, although there are many other possible infectious and drug-induced etiologies.

- Common symptoms in adults with aseptic meningitis are fever, headache, stiff neck, photophobia, nausea, vomiting, loss of appetite, and lethargy.

- Typically, aseptic meningitis does not require hospitalization and treatment, and resolves on its own in seven to ten days.

- Serology and CSF studies are needed to definitively determine the causative offending agent, but are not always necessary in self-resolving cases of aseptic meningitis.

V. Treatment, management

Treatment and response to treatment:

- AW was admitted to the adult care unit for observation and treatment. Intravenous ceftriaxone was initiated immediately, and intravenous acyclovir was started soon after, while results of the initial CSF study were pending (24-48 hours).

- Acetazolamide 500mg BID was initiated less than 24 hours after admittance in order to manage intracranial pressure.

- Despite the lack of clinical evidence, it was determined that there were no contraindications to treatment with acetazolamide as the patient was young and healthy with normal kidney function, and taking into account the chronicity of symptoms over the past three weeks, along with the potential for reduced morbidity and improved visual prognosis by lowering intracranial pressure, it was decided that treatment with acetazolamide was indicated.

- Kidney function and creatinine levels were monitored daily.

- An outside neurologist was contacted, who confirmed management decisions regarding the initiation of acetazolamide. An MRV and additional CSF studies were encouraged at this time.

- A coxsackie titer, acid-fast bacteria culture and smear, and herpes simplex virus PCR were ordered.

- AW was in adult care unit at for two and a half days where her condition remained stable with no improvement. By the end of the third day, she was transferred to Banner University Medical Center Tucson at the University of Arizona for further treatment.

VI. Conclusion

Clinical pearls, take away points if indicated

- The Frisen Scale of Papilledema is a standardized scale clinicians use to quantitatively describe papilledema.

- Kinetic perimetry should be performed if possible, in order to quantify visual impact of papilledema.
Visual prognosis of patients with papilledema is guarded, and depends on various conditional factors such as severity, duration of condition prior to diagnosis and treatment, rapid or progressive onset, and time to resolution. Overall, chronicity and severity are correlated with worse visual outcomes¹.

References