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Cushing's Reflex and Bradycardic Arrest in Cryptococcal Meningitis

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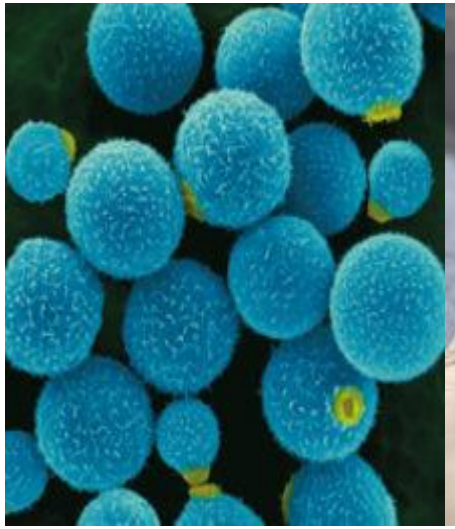
Abstract:
Cushing's reflex is a physiologic response to maintain cerebral perfusion pressure with elevated systolic blood pressure, widened pulse pressure, and bradycardia occurring in the setting of elevated intracranial pressure (ICP). The proposed mechanisms for reflexive bradycardia include ischemia to medullary brain tissue and compression of the intracranial segment of the vagus nerve leading to parasympathetic activation. (1) In acutely elevated ICP, bradycardia is a late finding of worsening intracranial pathology suggestive of impending herniation and cardiovascular collapse.

Cryptococcal meningitis has been identified by Infectious Disease Society of America for its association with elevated ICP. (2) Variety of pathogenic mechanisms occurring in meningitis predispose to ICP including toxin mediated injuries and inflammatory host response leading to cytotoxic, vasogenic and interstitial edema with hydrocephalus and venous congestion. (3) Previous studies of cryptococcal meningitis have shown a mortality benefit from therapeutic lumbar puncture (LP) with CSF removal to reduce ICP. (4)

Case Report
51 year old male with past medical history of HIV and hypertension presented to the Emergency Department with altered mental status. The patient has been non-compliant with his medications and reportedly "cured of HIV" so has not been on anti-retroviral therapy since 2016. His initial work up included a CT head that showed periventricular edema and hydrocephalus, CTA head with heterogenous enhancement of distal small caliber left MCA and PCA consistent with vasculitis or inflammatory process, as well as prominent superior ophthalmic veins.

LP initial opening pressure of >55 cmH20, WBC 65, glucose <10, protein 82. CSF studies returned positive for cryptococcus neoformans by PCR. Amphotericin B and flucytosine were started and the patient was admitted to the ICU.

While in the ICU, the patient became tachycardic to 130 bpm and hypertensive 250/140 mmHg. Due to suspicion for elevated ICP, while setting up for therapeutic LP the patient became bradycardic to 20 bpm with third degree block and lost pulses. CPR was initiated, he was given 1 round of epinephrine, calcium gluconate, and mannitol with ROSC after 3 minutes followed by transcutaneous pacing. LP was performed with opening pressure >55 cmH20 and 35-40cc CSF drained with closing pressure of 12 cmH20. Vital signs including heart rate and blood pressure improved following LP and patient was transferred for Neurosurgical intervention with ICP monitoring.



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Discussion
Therapeutic LP with CSF drainage is an important strategy to consider for decreasing ICP. Studies on CSF drainage, ICP and cerebral perfusion pressure in traumatic brain injuries have shown drainage of 3mL of CSF resulted in 10.1% decrease in ICP and 2.2% increase in cerebral perfusion pressure for at least 10 minutes. (5) Serial LP with therapeutic CSF drainage is a potential strategy to manage ICP when Neurosurgical intervention with a ventricular or lumbar drain is not available. However, it is difficult to determine when the ICP is becoming elevated between procedures without monitoring and vital sign abnormalities such as Cushing's reflex are often a late sign of severe elevations. Daily LP with CSF drainage until opening pressure decreased by 50% or <20 cmH20 has been recommended in cases of persistently elevated ICP. (2)

Due to the loss of cerebral autoregulation, the cerebral perfusion pressure is a function of the mean arterial pressure and intracranial pressure. LP opening pressure has been shown to accurately estimate ICP and aggressive blood pressure management can be utilized to maintain cerebral perfusion. (6)

Conclusions
Elevated ICP is a concerning feature of meningitis, particularly in Cryptococcal meningitis, due to various mechanisms. Cushing's reflex with widened pulse pressure, elevated systolic blood pressure and ultimately bradycardia are indicators of severely elevated ICP. Therapeutic LP with large volume CSF drainage can be performed to rapidly decrease ICP and maintain cerebral perfusion.

References
1. Sebening C., Hagl C., Szabo G., et al. Cardiocirculatory effects of acutely increased intracranial pressure and subsequent brain death. *European Journal of Cardio-Thoracic Surgery. 1995;**9**(7):360–372. doi: 10.1016/S1010-7940(05)80168-X.*
2. Perfect J., Dismukes W., Dromer F., et al. Clinical Practice Guidelines for the Management of Cryptococcal Disease: 2010 Update by the Infectious Diseases Society of America, Clinical Infectious Diseases, Volume 50, Issue 3, 1 February 2010, Pages 291–322, https://doi.org/10.1086/649858
3. Tariq, A., Aguilar-Salinas, P., Hanel, R. A., Naval, N., & Chmayssani, M. (2017). The role of ICP monitoring in meningitis, Neurosurgical Focus FOC, 43(5), E7. Retrieved Mar 15, 2021, from https://thejns.org/focus/view/journals/neurosurg-focus/43/5/article-pE7.xml
4. Rolfes M., Mullseik K., Rhein J., et al., The Effect of Therapeutic Lumbar Punctures on Acute Mortality From Cryptococcal Meningitis, Clinical Infectious Diseases, Volume 59, Issue 11, 1 December 2014, Pages 1607–1614, https://doi.org/10.1093/cid/ciu596
5. Kerr ME, Weber BB, Sereika SM, Wilberger J, Marion DW. Dose response to cerebrospinal fluid drainage on cerebral perfusion in traumatic brain-injured adults. Neurosurg Focus. 2001 Oct 15;11(4):E1. doi: 10.3171/foc.2001.11.4.2. PMID: 16519419.
6. Lenfeldt N, Koskinen LO, Bergenheim AT, Malm J, Eklund A. CSF pressure assessed by lumbar puncture agrees with intracranial pressure. Neurology. 2007 Jan 9;68(2):155-8. doi: 10.1212/01.wnl.0000250270.54587.71. PMID: 17210899.