



Bilateral Hypertrophic Olivary Degeneration in a Patient with Prior Brainstem Hemorrhage: An Interesting case

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Purpose

- To illustrate the normal function of the Triangle of Guillain and Mollaret and how interruption of this pathway results Hypertrophic Olivary Degeneration (HOD)
- Describe the etiology, clinical manifestations and imaging appearance of HOD
- Present a case of Bilateral HOD, as well as provide brief summaries of recent cases in the literature
- Intended for radiologists and radiologist in training with an interest in neuroradiology

Triangle of Guillain and Mollaret

- Triangle of Guillain and Mollaret: Connection between the **red nucleus**, ipsilateral **Inferior Olivary Nucleus (ION)** and the contralateral **dentate nucleus** forming the **dentato-rubro-olivary pathway** and also known as the **Myoclonic triangle**.(Figure 1)
- ION Function – Fine motor control and coordination
 - Efferent signal to the ION is inhibitory via GABAergic signals

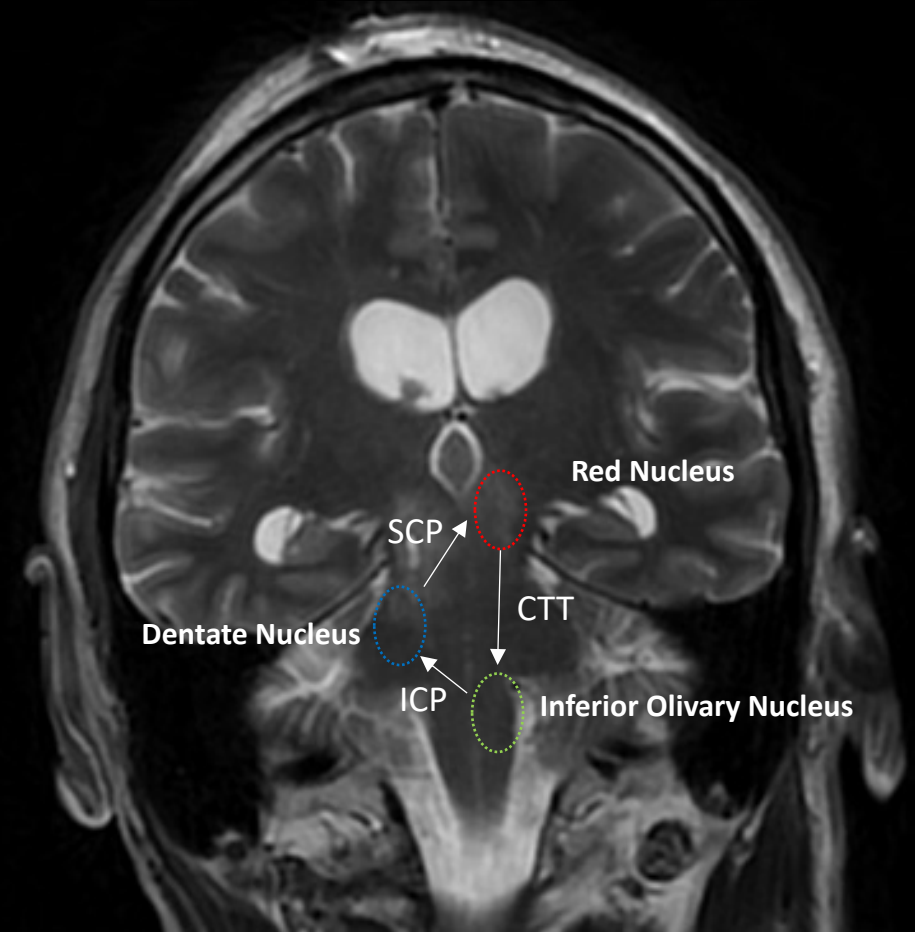


Figure 1: Coronal T2 images from our case illustrating the Triangle of Guillain and Mollaret.
SCP: Superior Cerebellar Peduncle; ICP: Inferior Cerebellar Peduncle; CTT: Central Tegmental Tract

Hypertrophic Olivary Degeneration: Pathophysiology

- HOD occurs when there is trans-synaptic degeneration resulting in hypertrophy of the Inferior olivary nucleus (ION) secondary to an insult affecting the Triangle of Guillain and Mollaret (TGM)
- Histologically, trans-synaptic degeneration results in vacuolization of the ION with an increased number of glial cells
- Interruption of this **inhibitory signal** whether occurring at the ipsilateral red nucleus or contralateral dentate nucleus results in typical clinical symptoms and radiologic/histologic manifestations

Hypertrophic Olivary Degeneration: Clinical manifestations/Etiology

- **Etiology**

- Brainstem lesions
- Infarct
- Hemorrhage
- Idiopathic

- **Clinical manifestations**

- Palatal myoclonus
- Ocular nystagmus
- Upper extremity tremors
- Oscillopsia
- Other less common manifestations
 - Dystonia
 - Peduncular hallucinosis

Hypertrophic Olivary Degeneration: Imaging

- Unilateral is more common; Bilateral HOD can also occur depending on the extent and location of initial insult
- T2-weighted and FLAIR images will show a temporal evolution of increasing signal intensity and expansion of the ION occurring in 3 distinct stages:
 1. Increasing T2 signal without hypertrophy (within a couple months following initial insult)
 2. Increased T2 signal and hypertrophy (typically 10 to 18 months but can be as early as 6 months)
 3. Hypertrophy resolves by 3 to 4 years but increased T2 signal persists indefinitely
- Abreu-Silveira et al. suggested using the “Pac-Man Ghost” sign as a learning tool to identify HOD due to its resemblance to the well-known video game character:
 - The body of the medulla represents the body of Pac-Man Ghost and the hypertrophied/hyperintense ION resemble its eyes. (Figure 2)

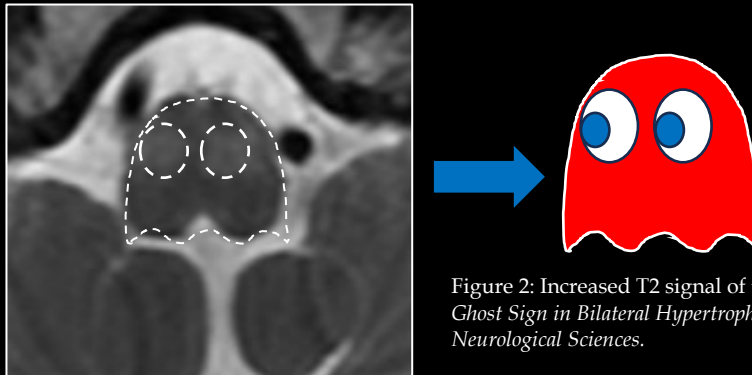


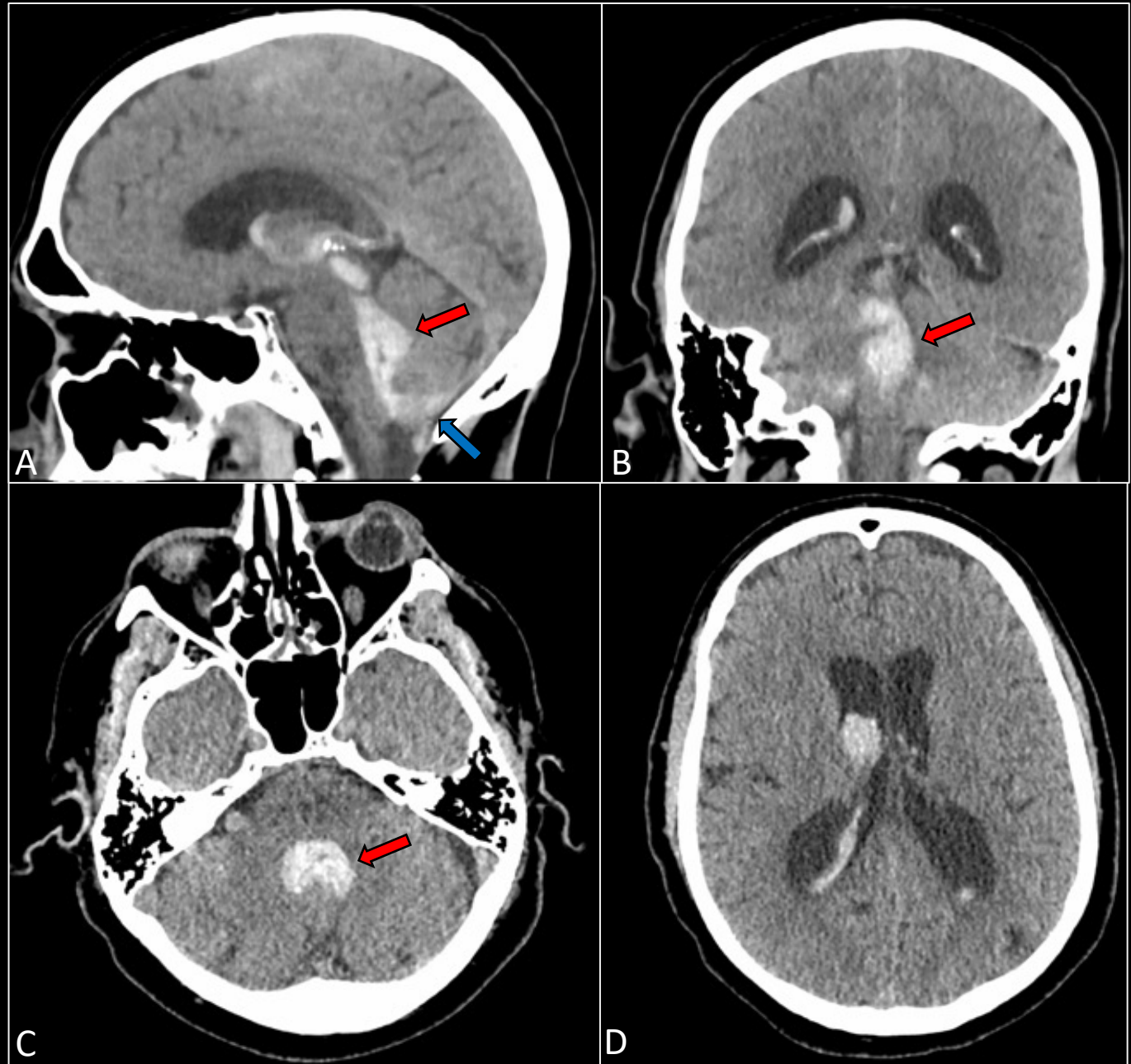
Figure 2: Increased T2 signal of the bilateral ION resembling the Pac-Man Ghost. Adapted from “Pac-Man Ghost Sign in Bilateral Hypertrophic Olivary Degeneration” by Abreu-Silveira et al, 2023, Canadian Journal of Neurological Sciences.

Case - Clinical Presentation

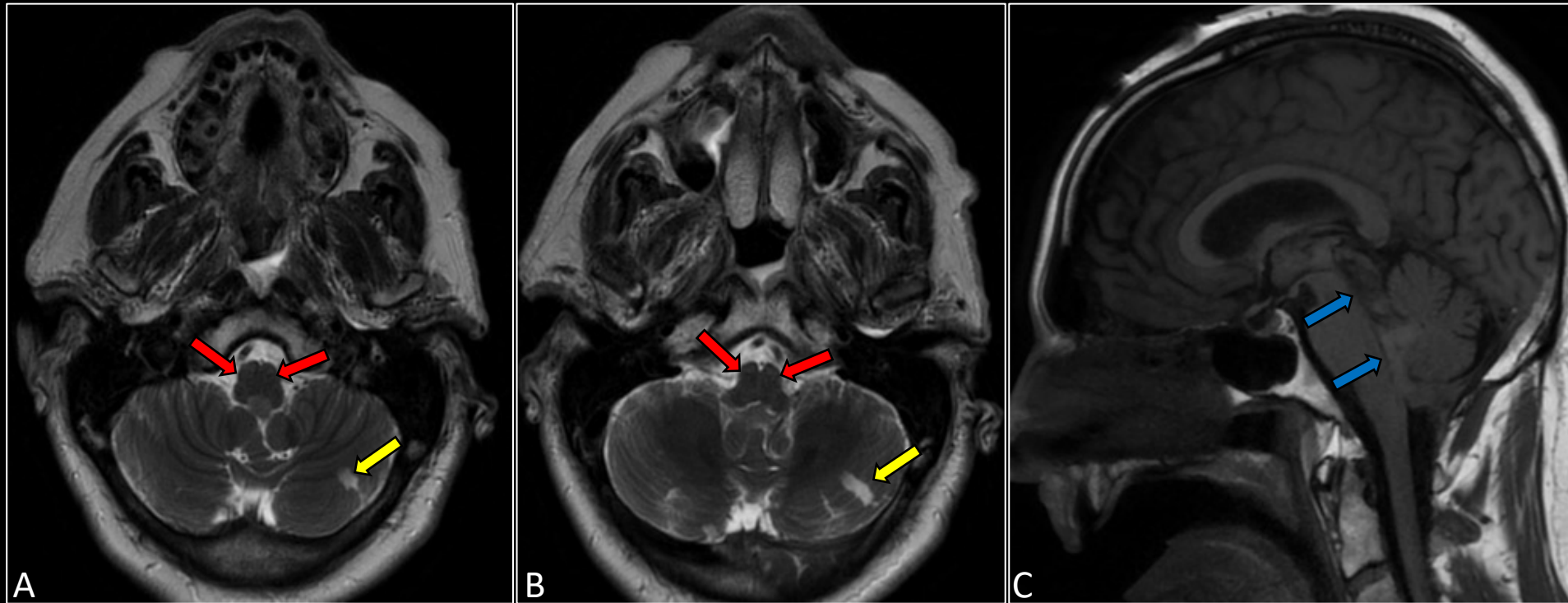
- 62-year-old male with past medical history of hypertension, hyperlipidemia who initially presented via EMS with sudden onset altered mental status, and right upper extremity weakness; presents to ED as “stroke alert”
- Initial CT head showed hemorrhage in the dorsal midbrain and pons with intraventricular blood products resulting in obstructive hydrocephalus for which an emergent external ventricular drain (EVD) was placed

Initial CT

(A-D) Sagittal, Coronal and Axial CT images show extensive hemorrhage filling the ventricles, most prominent within the 4th ventricle (**red arrows**) with extension into the subarachnoid cisterns (**blue arrow**) resulting in obstructive hydrocephalus.

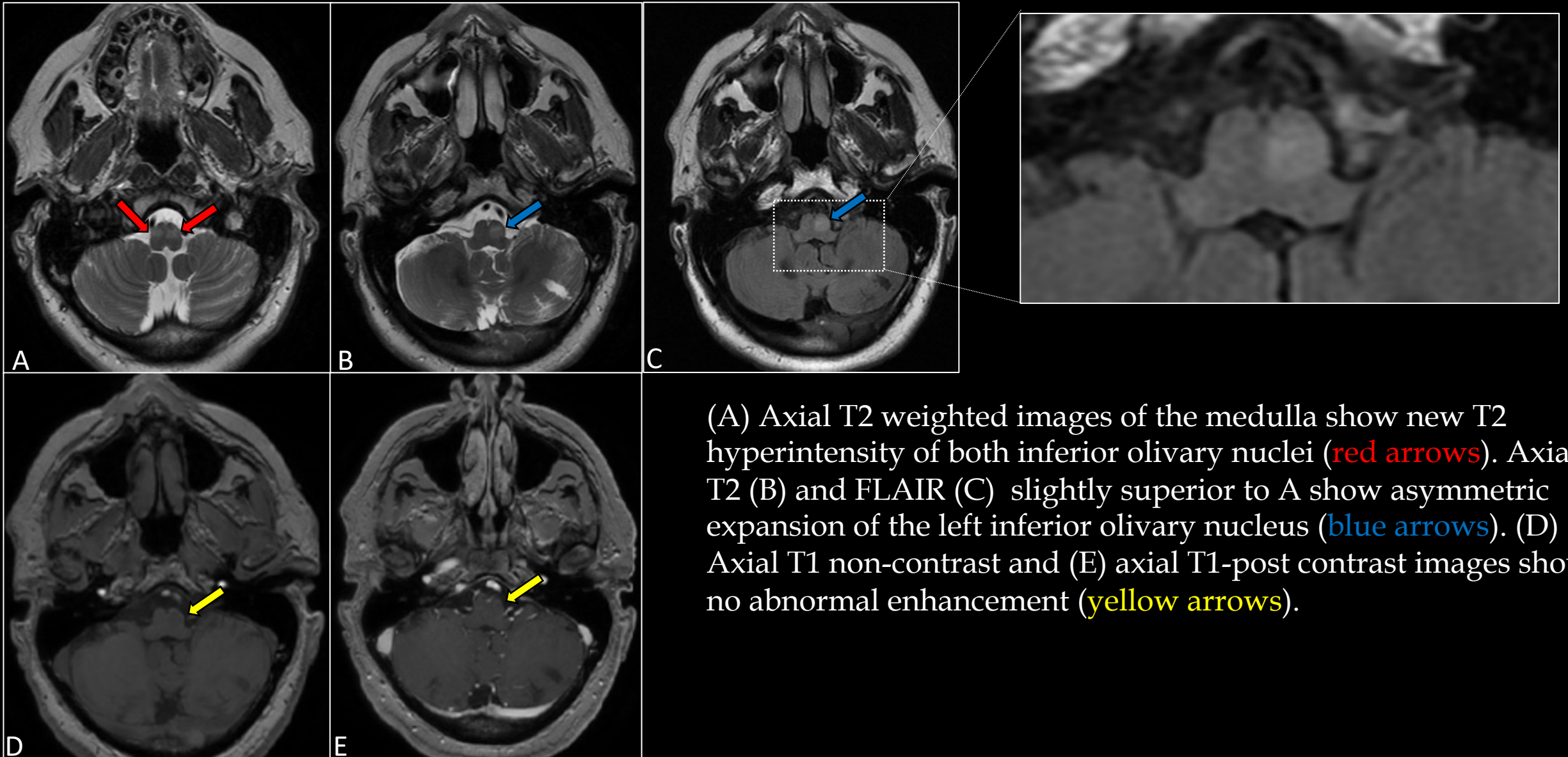


Next day MRI



(A,B) Sequential axial T2 weighted images at the level of the medulla show normal medulla, specifically normal bilateral inferior olivary nuclei (**red arrows**). Incidental remote left cerebellar infarct (**yellow arrows**) (C) Sagittal T1 weighted image shows extensive intraventricular hemorrhage throughout the ventricular system (**blue arrows**).

5 month follow up MRI



(A) Axial T2 weighted images of the medulla show new T2 hyperintensity of both inferior olivary nuclei (**red arrows**). Axial T2 (B) and FLAIR (C) slightly superior to A show asymmetric expansion of the left inferior olivary nucleus (**blue arrows**). (D) Axial T1 non-contrast and (E) axial T1-post contrast images show no abnormal enhancement (**yellow arrows**).

Hospital Course

- Patient's EVD was replaced with a VP shunt 2 weeks after admission
- During the admission the patient participated in physical therapy; His main symptoms were right upper extremity weakness, slowed cognition and intermittent diplopia
- Currently the patient continues to endorse right upper extremity tremors/poor motor control, diplopia and difficulty swallowing liquids (excessive coughing)

Brief literature review of recent cases

- **Gao et al.** – Case series presenting 4 cases with HOD secondary to brainstem hemorrhage, brain stem ischemia, brainstem glioma resection and brainstem cavernous hemangioma resection. All patients presented with symptoms relating to fine motor skills and coordination and included: palatal nystagmus, ataxia, limb tremors and dizziness.
- **Zheng et al.** – 56-year-old female with bilateral HOD who presented with palatal myoclonus and pendular nystagmus 3 months after pontine hemorrhage.
- **Stoker** – 78-year-old male with idiopathic HOD who presented with difficulty swallowing and palatal nystagmus.
- **Choi et al.** – 56-year-old male with HOD who presented with Peduncular Hallucinosis (realistic visual hallucinations) 7 months after spontaneous pontine hemorrhage.
- **Abreu-Silveira et al.** – 27-year-old male with past medical history of Wilson’s Disease who presented with bilateral HOD 13 months after initiating treatment.
- **Geng et al.** – 52-year-old male with bilateral HOD, 5 months after brain stem hemorrhage who presented with involuntary limb tremors; Case complicated by Obstructive Sleep Apnea Hypoventilation Syndrome.
- **Lycett et al.** – 33-year-old male with bilateral HOD secondary to medulloblastoma resection who presented with bilateral vocal cord adductor dystonia.

Discussion

- Knowledge of the function and location of the Triangle of Guillain and Mollaret is essential to understanding the clinical manifestations of HOD.
- It is important for the radiologist to know the patient's prior history and query any prior insults to the brainstem. It is also equally important to be aware that HOD may be idiopathic without a known cause.
- In the setting of idiopathic HOD, familiarity with imaging and clinical findings of HOD may be the only way to establish the diagnosis.
- A brief review of recent cases in literature further highlights the typical MR appearance of HOD. Additionally, in most cases there was an identifiable insult to the triangle of Guillain and Mollaret, which resulted in symptoms relating to fine motor function and coordination and most frequently included: Upper extremity tremors, palatal nystagmus (**strongly suggestive of HOD**), ocular nystagmus, and ataxia.
- Although not well established the “**Pac-Man Ghost**” sign suggested by Abreu-Silveira et al. may prove to be a valuable addition to the thriving world of radiologic signs.

Discussion

- Our patient presented with typical history and clinical symptoms but somewhat atypical imaging findings
- Specifically, he had increased T2 signal in both ION but with hypertrophy of only the *LEFT* ION.
 - Increased signal occurs as early as one month following insult, however hypertrophy typically occurs later, as early as 6 months.
 - The imaging manifestations of HOD are temporal and hence are predictable, therefore it is reasonable to expect eventual hypertrophy of the **RIGHT** HOD based on location of the primary insult.

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