PUZZLING PAIR OF LESIONS : A PAEDIATRIC DIAGNOSTIC DILEMMA

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- A 7 years 3 months old boy
- Resident of Gudlavalleru
- Born out of non consanguineous marriage
- 1st in birth order
- Admitted on 31st of January 2025 with chief complaints of
- involuntary movements of right upper limb and lower limb since 5 months

History of present illness

- Child was apparently normal 5 months ago ,when he had an episode of high grade fever which lasted for 24 hours during which he had an episode of seizure like activity of right upper limb and lower limb with deviation of angle of mouth towards right side which lasted for 2 minutes associated with involuntary passage of urine.

- No h/o loss of consciousness or post ictal drowsiness

- Child was then treated at outside hospital in Machilipatnam as Viral meningoencephalitis with GTCS and was started on AEDs (Leviteracetam and Phenytoin) and Acyclovir.

- Child was asymptomatic for 1 month , later he had an episode of sudden jerky involuntary movement involving entire right upper limb and lower limb lasting for few seconds associated with fall towards his right without impairment of consciousness.

- Later child was again asymptomatic for one more month after he had multiple similar episodes which are progressive, gradually increased in frequency (7-8 times/day) over the next 3 months and these episodes are mostly associated with involuntary micturition.

- These episodes were treated as Right focal seizures with preserved consciousness with multiple AEDs at outside hospitals but there is no decrease in the frequency of these episodes.

- MRI BRAIN (20/11/2024) was performed outside prior to admission reported as “ **Bulky & hyperintense bilateral thalami and Basal ganglia -S/O ?Metabolic encephalopathy.”**

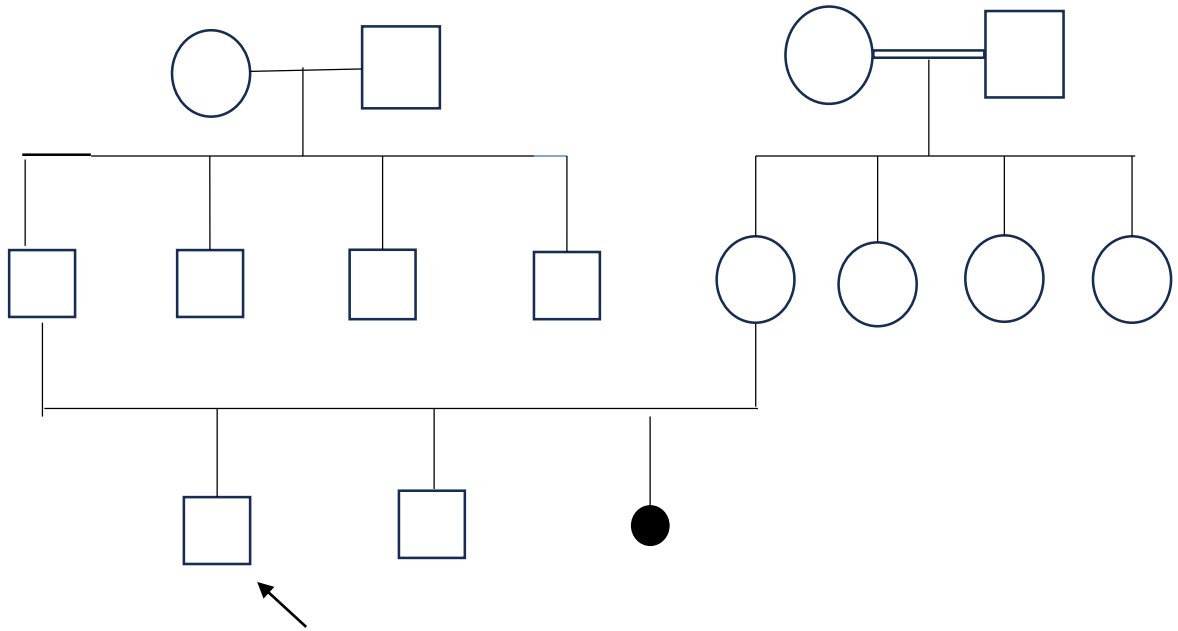
Later child had h/o fine involuntary movements of right hand while approaching an object noticed 1 month prior to admission and h/o squint noticed by mother and h/o complaint of double vision by the child 15 days prior to admission.

- H/o cautious walking present
- H/o sustaining multiple injuries on right side due to frequent falls
- H/o decrease in scholastic performance noticed since 3 months prior to admission

- No h/o any vomiting / weakness / preceeding head trauma
- No h/o jaundice

- No h/o dog bite or prior vaccination
- No significant history of cranial nerve involvement except for double vision.
- No history s/o sensory disturbances
- No h/o drug intake/toxin exposure
- No h/o TB contact

- Perinatal history was uneventful
- No significant family history
- Siblings : Younger brother - 4 years (Active, Healthy, Immunized)



- **Developmental history:** Attained milestones as per age. Studying 3rd class.

- **Immunization history:** Immunized according to National Immunization Schedule , BCG scar present ,last vaccinated at 5 years of age.

- **Socioeconomic status:** Lower middle class

- **Nutritional history:** Total Calorie intake : 2100 kcal/day

  Total Protein intake : 21 g/day

Summary

- A 7 year 3 months old boy , born out of non consanguineous marriage with
- h/o sudden jerky involuntary movements of right upperlimb and lower limb associated with fall and involuntary micturition since 5 months ,
- decreased scholastic performance since 3 months ,
- intentional tremors of right hand since 1 month ,
- left eye squint and double vision since 15 days.
- No significant past history , family history and developmental history.

- Based on the history our probable causes :

    1)Wilsons disease

    2)PANDAS (Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal infections)

    3)Metabolic encephalopathy

    4)Striatal encephalitis (?secondary to autoimmune encephalitis)

ON EXAMINATION

- Child conscious , interacting well
- Left eye convergent squint present
- Multiple scars present over right upperlimb and right side of the head (due to frequent falls towards right)

ANTHROPOMETRY

- Height-125cm(50-75th percentile)
- Weight-29kgs (75-90th percentile)
- BMI 18.56 kg/m2 (above obese percentile)

VITALS

- HR-98/min
- RR-22/min
- Spo2-98% on Room air
- TEMP- 98.5◦F
- BP-101/63 mm hg(50 – 90th centile)

CNS EXAMINATION

- **HMF -**conscious and oriented to time ,place and person
- **Speech – staccato type**
- **Cognition-** normal
- **On Cranial nerve examination**
- **III,IV,VI -**Extraocular movements normal

  Left eye convergent squint , No head tilt

  Accommodation reflex present

Other cranial nerves examination was normal

Motor system

- **Bulk -**Bilaterally symmetrical in both upperlimb and lowerlimb.

- **Tone:**

	RIGHT	LEFT
UPPER LIMB	Normal	Normal
LOWER LIMB	Normal	Normal

- **Power**

	RIGHT	LEFT
ELBOW	5/5	5/5
WRIST	5/5	5/5
SHOULDER	5/5	5/5
TRUNK	5/5	5/5
HIP	5/5	5/5
KNEE	5/5	5/5
ANKLE	5/5	5/5

REFLEXES	RIGHT	LEFT
BICEPS	2+	2+
TRICEPS	2+	2+
KNEE	2+	2+
ANKLE	2+	2+
Plantar	flexor	flexor

Sensory system : able to perceive touch and pain , able to perceive cold and hot temperatures equally on both sides.

Cerebellar signs :

- **Finger nose test positive (right side>left side)**
- **Dysdiadochokinesia , dysmetria , action tremors present on right side**
- **Hemiballistic movements only on right side**

- No signs of meningeal irritation
- No signs of raised intracranial pressure
- Spine examination and skull examination - Normal
- Gait- normal except for absent swaying movements on right with cautious walking

- CVS- S1 S2 heard, no murmurs, all peripheral & central pulses felt
- R/S- Bilateral normal vesicular breath sounds heard, no added sounds
- P/A – Soft, no organomegaly
- Musculoskeletal : No bony deformities noted, no restriction of movements

Case Summary

- A 7 year 3 months old boy ,born out of non consanguineous marriage with
- h/o sudden jerky involuntary movements of right upper limb and lower limb associated with fall (7-8 episodes/day) , involuntary micturition since 5 months,
- intentional tremors of right hand since 1 month and
- left eye squint , double vision since 15 days.
- No significant past history , family history and developmental history.
- On examination ,left eye convergent squint present with intact sensory , motor system and positive cerebellar signs , extra-pyramidal movements on right side and other systemic examination normal.

Probable diagnoses:

- Wilsons disease
- Striatal encephalitis (?secondary to autoimmune encephalitis)
- Space occupying lesion
- Metabolic encephalopathy
- PANDAS (Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal infections)

- **INVESTIGATIONS :**

CBP, LFT, RFT , SR CALCIUM, TFT- within normal limits

EEG – **Mild to moderate diffuse cerebral dysfunction (left>right)**

MRI BRAIN PLAIN & CONTRAST

- Reported as **“ill defined T2 and FLAIR hyperintensities involving bilateral thalami , left lentiform nucleus, left insular cortex, B/L Hippocampi, B/L Basifrontal lobes and periaqueductal grey matter along with swollen appearance of these structures with resultant mild mass effect as described. No diffusion restriction, no contrast enhancement- ? AUTO IMMUNE ENCEPHALITIS**.”

Other less likely possibilities are:

Neoplastic etiology

Mitochondrial disease

CSF ANALYSIS:

- Total cells-01
- Differential cells : 100% lymphocytes
- Proteins-65 mg/dl
- Glucose-60 mg/dl
- Chloride-122 mmol/L
- ADA-2.1 U/L
- Culture, Gram stain, AFB stain – negative

ECG and 2D ECHO were normal.

ASO titres were within the normal limits.

OPHTHALMOLOGY EXAMINATION : NO KF ring

NO papilledema

NO paralytic squint

Left eye convergent squint +

Diplopia+

Sr Ceruloplasmin- 24mg/dl (15-58)

24 hours urinary copper levels : 54 mcg/24 hours (15-70)

To rule out metabolic encephalopathy :

- ABG- ph-7.38, hco3-26.5, lactate-0.9 Base excess 3.9
- Sr Ammonia- 85 mcg/dl (30 – 150)
- Urine GCMS and TMS studies done – no abnormality noted.
- Whole exome sequencing along with mitochondrial gene study normal

- Sr Ferritin- 18.35ng/ml (13-400) – to rule out neuroferritinopathy
- Intact PTH-25.95pg/dl (15-65) to rule out chronic hypocalcemia

- CSF & Serum – IgG auto antibodies i/v/o suspicion of autoimmune encephalitis were sent

- Anti NMO/Aquaporin -4 –Negative
- Anti MOG - Negative
- Anti NMDAR IgG antibody- negative
- Anti neuronal antibodies (specific for striatal encephalitis): anti-CV2 (anti-CRMP 5) negative

Management:

- After the initial workup after ruling out neuroinfections,metabolic encephalopathies based on clinical suspicion of autoimmune encephalitis (striatal encephalitis) and neuroimaging findings, antibodies for autoimmune panel were sent and child was started on pulse therapy with iv methylprednisolone.Antiepileptic drugs were continued as EEG was abnormal.

- After pulse steroid therapy , there was a transient improvement in tremors and diplopia which again progressed gradually.

- In view of poor response to pulse steroid therapy, repeat imaging was performed along with MR spectroscopy which showed elevated choline and creatinine peak with bulky bilateral thalamic , caudate , midbrain with temporal lobe s/o **Bithalamic glioma**.

Child was referred to higher center for confirmational stereotactic biopsy , i/v/o financial constraints and poor prognostic outcomes parents deferred further evaluation and management.

Discussion

- Thalamic gliomas are rare, forming 1–1.5% of pediatric brain tumors; bithalamic variants are even rarer and carry a worse prognosis.
- So far in the literature 70 cases of bithalamic gliomas have been reported worldwide among all age groups ,in pediatric age group only 15 cases have been reported.
- Most commonly a variant of diffuse glioma; often low-grade.

Clinical Presentation

- Features of **raised intracranial pressure**: Headache, nausea, vomiting, papilledema.
- **Neurologic deficits**: Hemiparesis, altered consciousness, behavioral changes.
- **Cognitive decline** if hypothalamus is involved

Pathology & Molecular Markers

Histology: Often **diffuse astrocytoma** or **glioblastoma**.

Molecular features:

- H3K27M mutation: rare in bithalamic gliomas (common in unilateral).
- EGFR exon 20 insertions: frequently seen
- H3-wild type often seen in bithalamic midline gliomas.

Imaging (MRI Findings)

- Bilateral thalamic enlargement
- T2/FLAIR hyperintensity ± contrast enhancement.
- Often **non- resectable** due to deep location and bilateral spread.

Differential Diagnosis

- **Germinoma** (midline with calcification, CSF tumor markers).
- **Metabolic encephalopathies** (bilateral thalamic signal change, reversible)
- **Infectious**: Japanese encephalitis, viral encephalitis.

Management Strategy

Biopsy: essential for diagnosis & molecular testing.

Surgical resection: usually not feasible.

Radiotherapy: primary treatment.

Chemotherapy: adjunctive; evolving role with molecular targets (e.g., EGFR inhibitors).

Prognosis :

- Low-grade bithalamic glioma: poor prognosis, ~0% 4-year OS (compared to ~85% in unilateral).
- High-grade gliomas: universally poor outcome.

References:

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Thank you