

2014年6月19日-21日

# 第34回神経放射線ワークショップ

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# Case: 15 year-old female

The patient was born to healthy and unrelated parents after an uneventful delivery.

Early development was normal.

She walked unsteadily from the time she began to walk, and at 4 year-old, on the arrival at our hospital, she had ataxic gait, dysarthria, intention tremor, and dysmetria.

She had also had mild spasticity and intellectual disability.

She displayed slow, progressive, and mild clinical course.

## <General findings>

a short stature

(- 2.0SD : at birth → - 3.0SD : 11 year-old)

normal head circumference, normal teeth,  
lack of cataract

## <Laboratry findings>

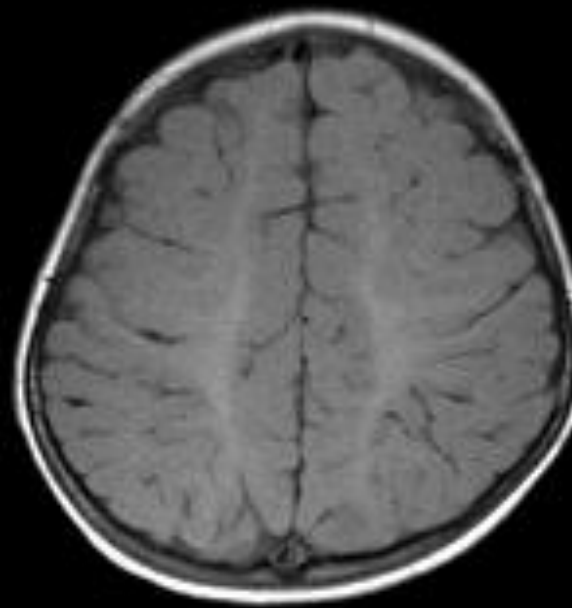
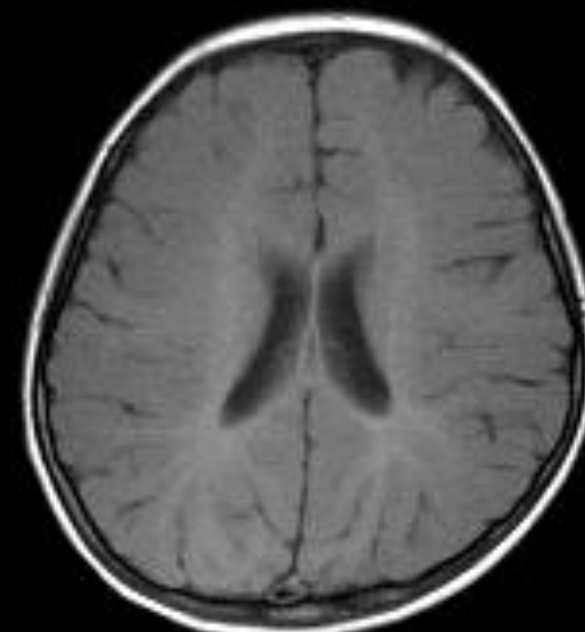
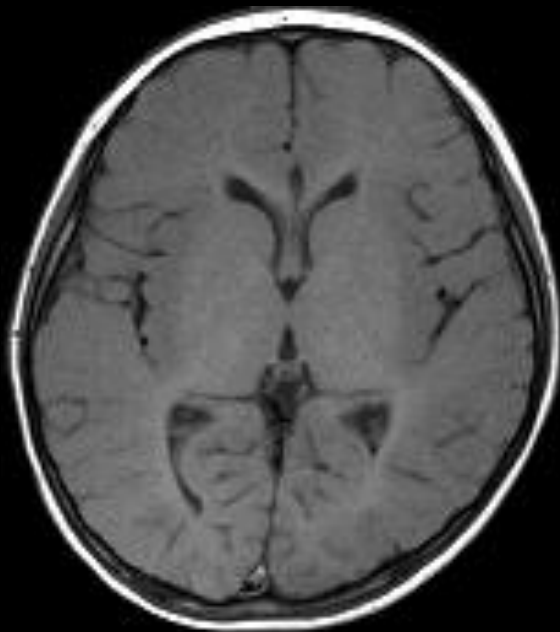
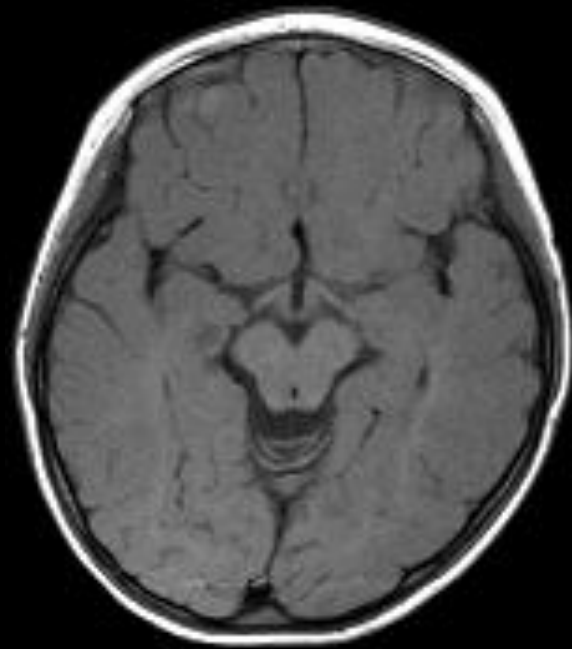
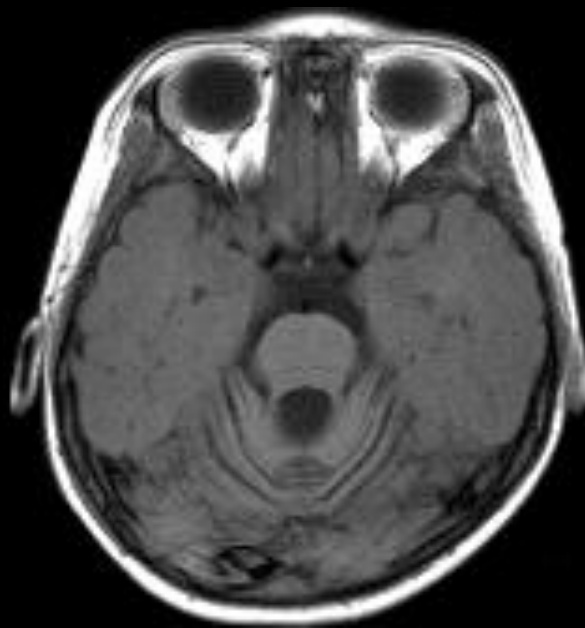
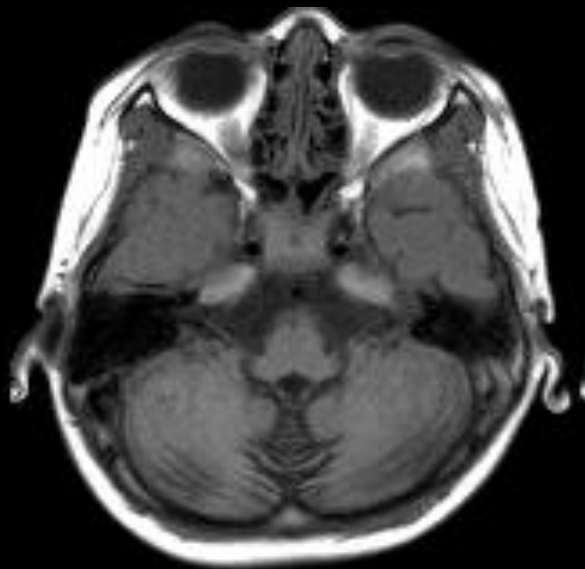
blood gonadotropin level : normal

## <Other examination>

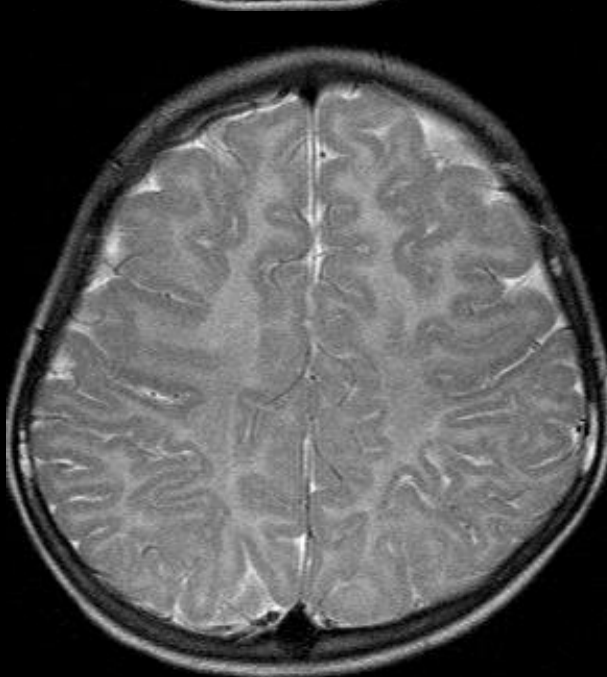
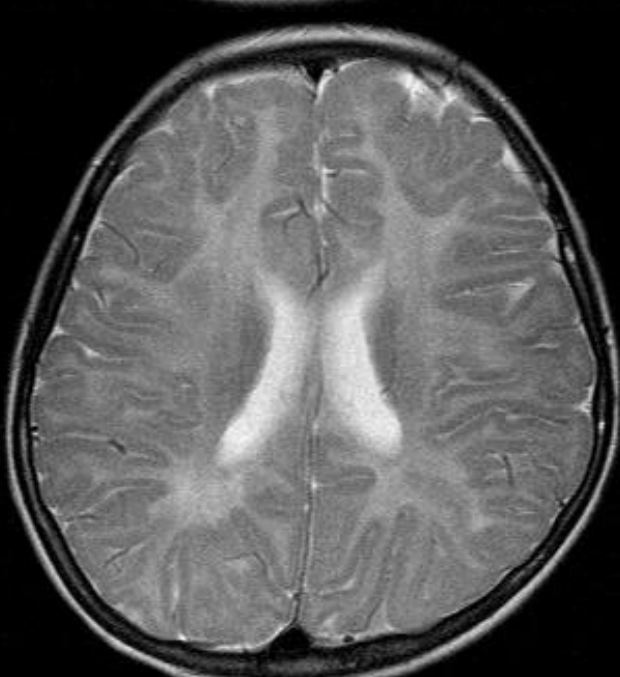
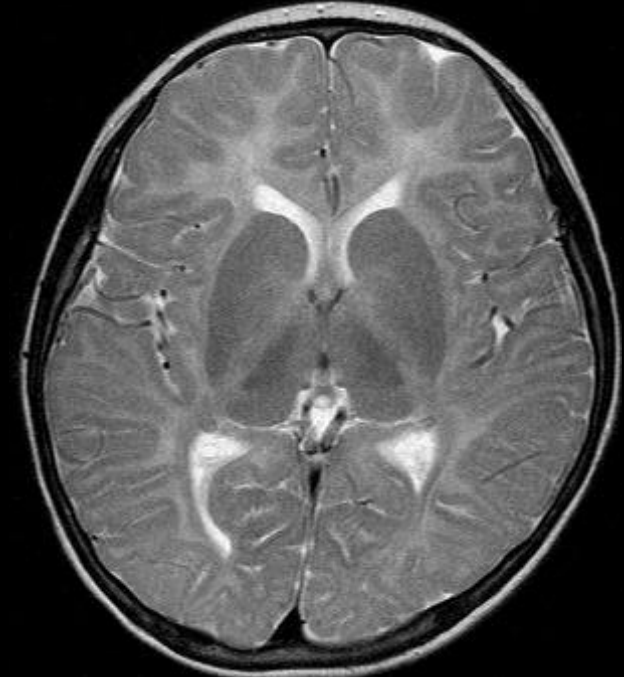
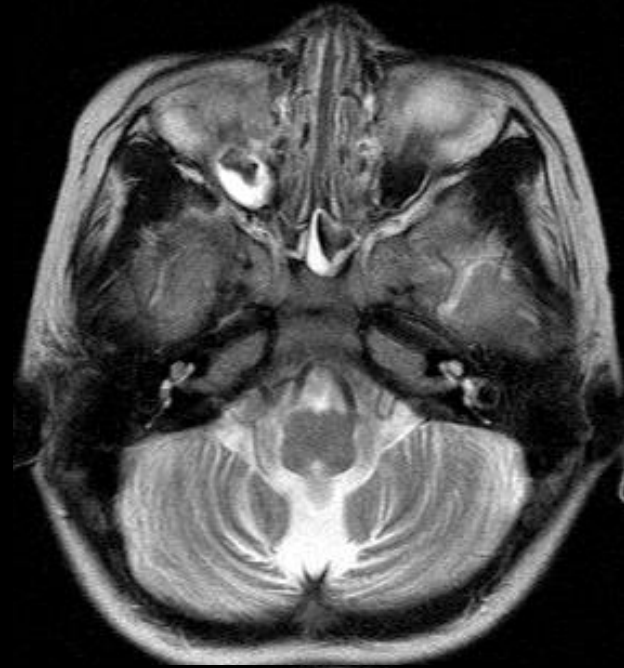
Auditory brainstem responses : normal

Nerve conduction studies : normal

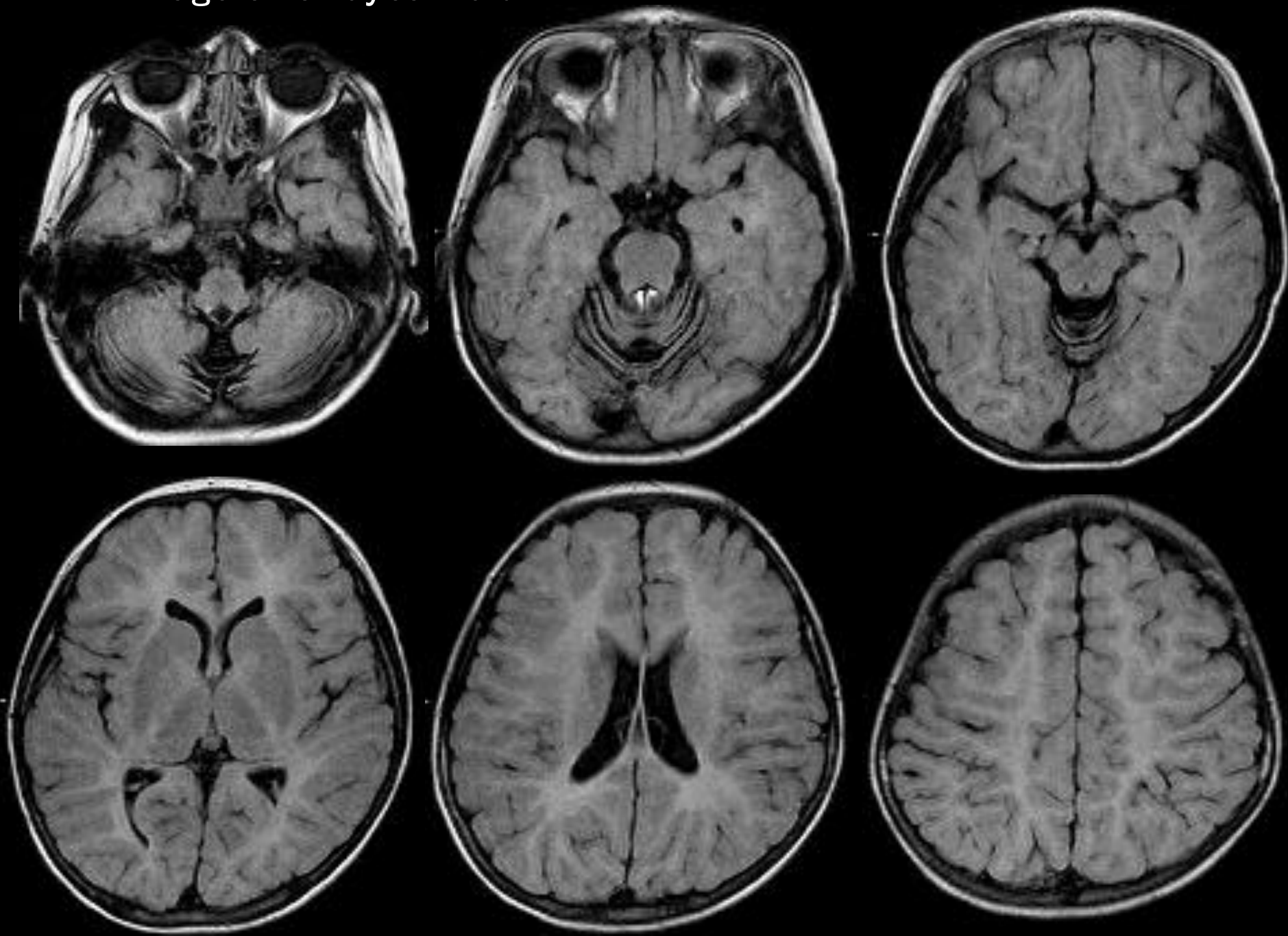
T1WI axial 5 year-old



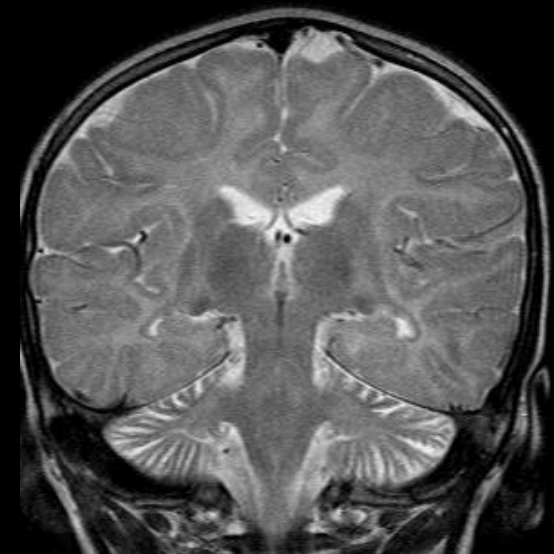
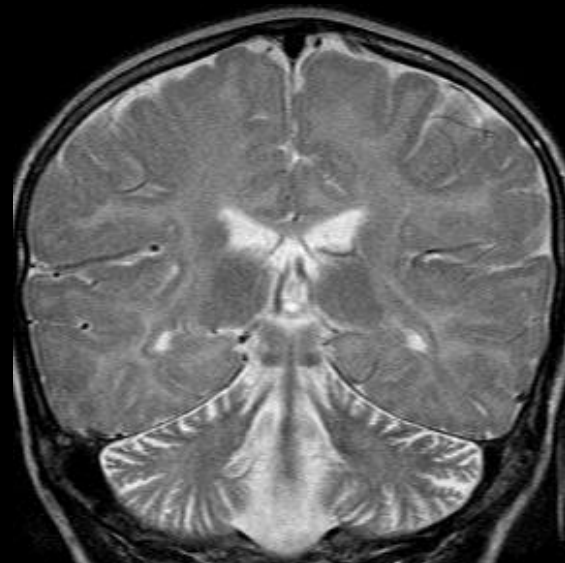
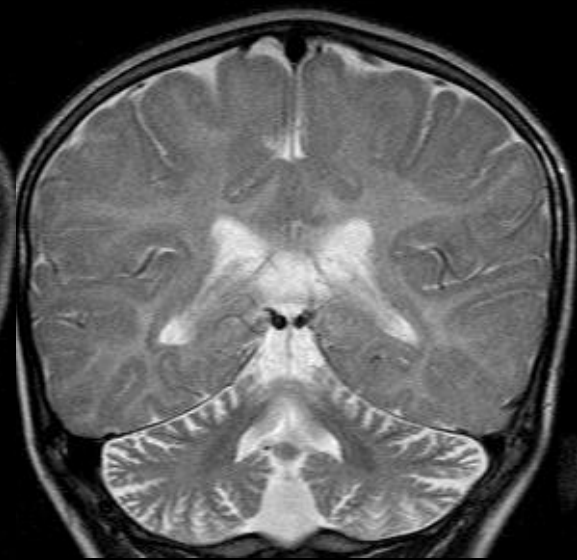
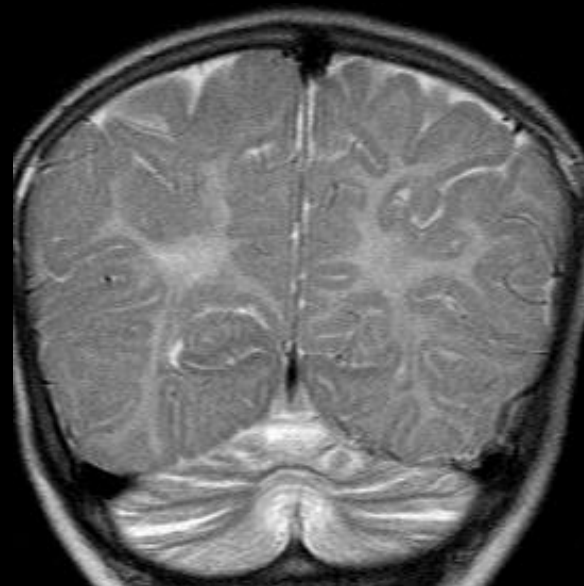
T2WI axial 5year-old



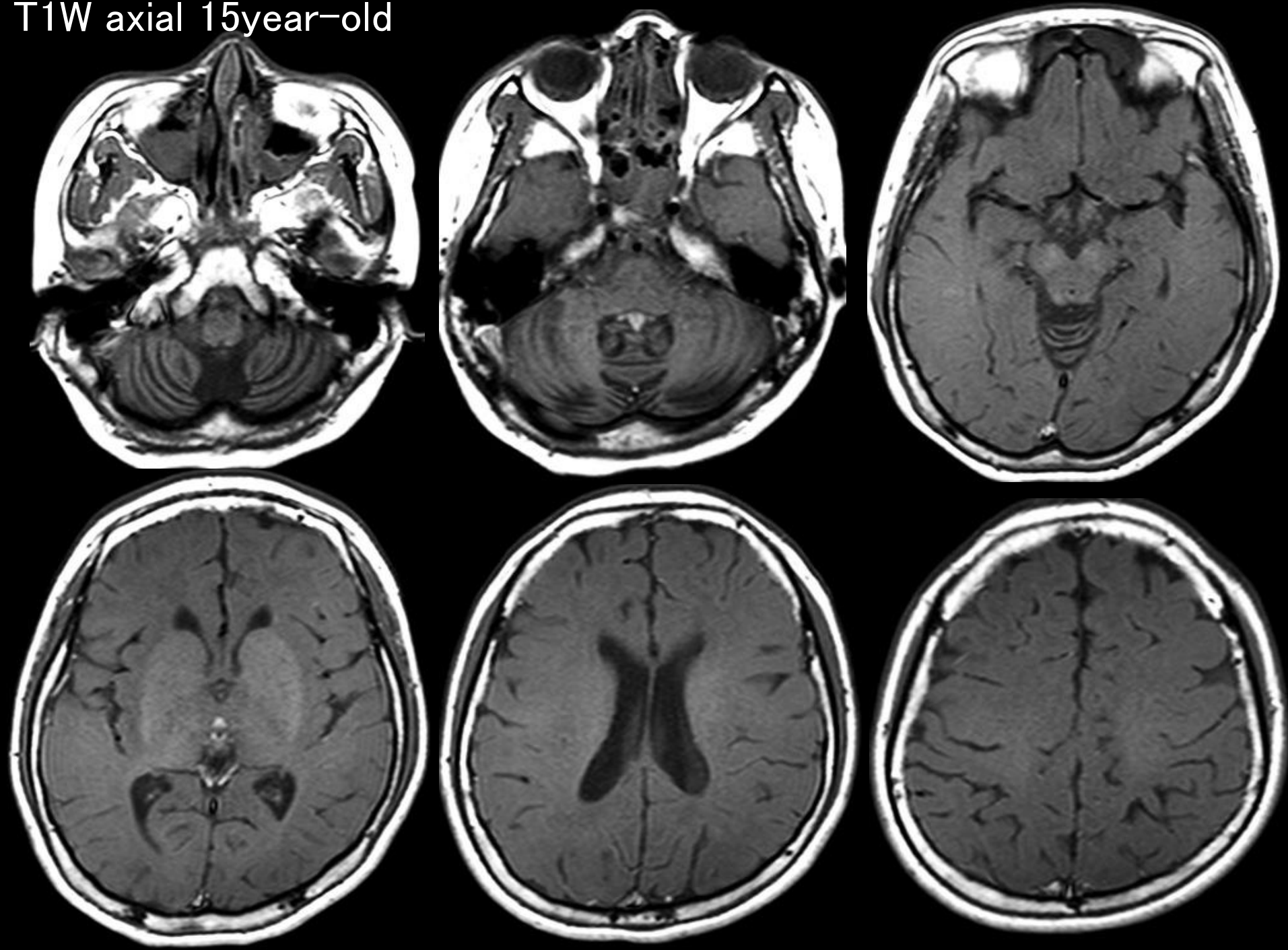
FLAIR image axial 5year-old



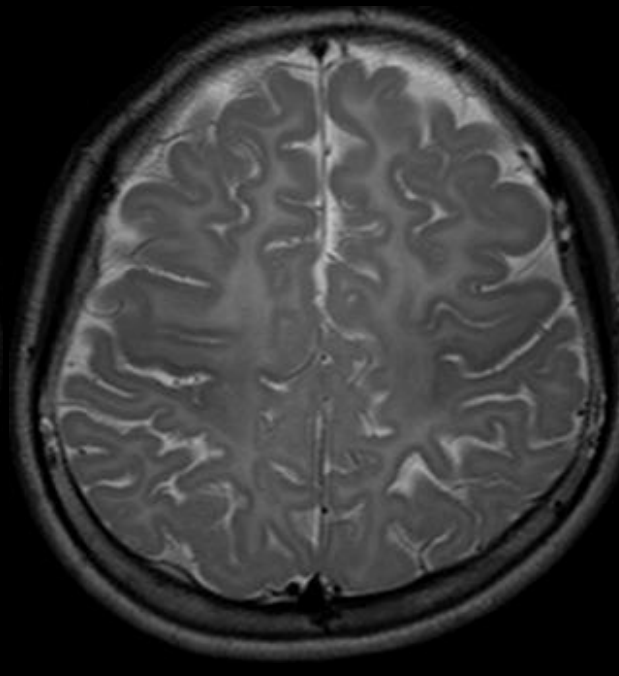
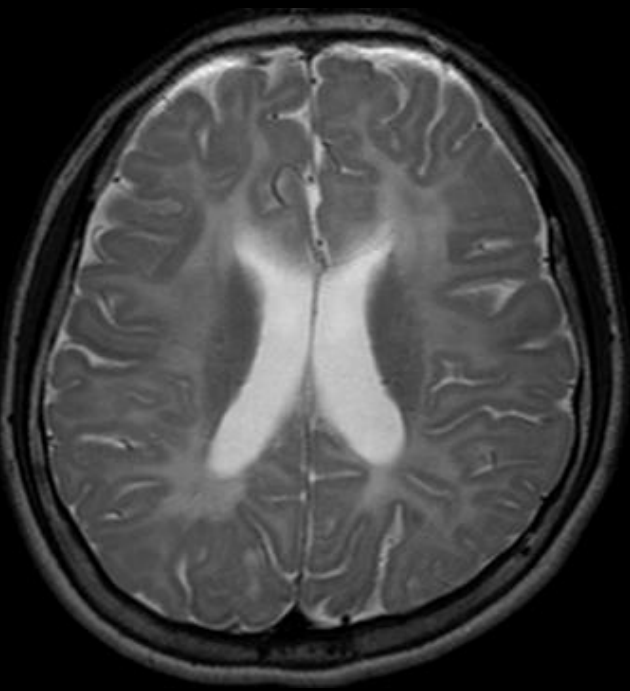
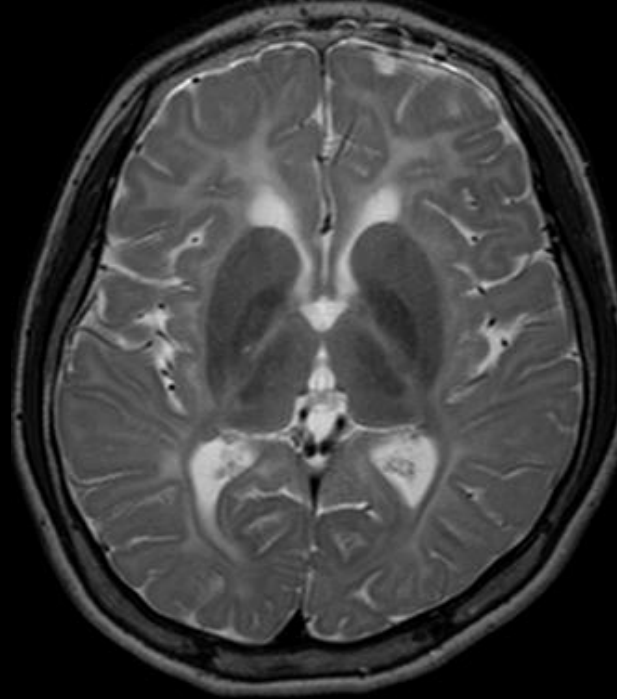
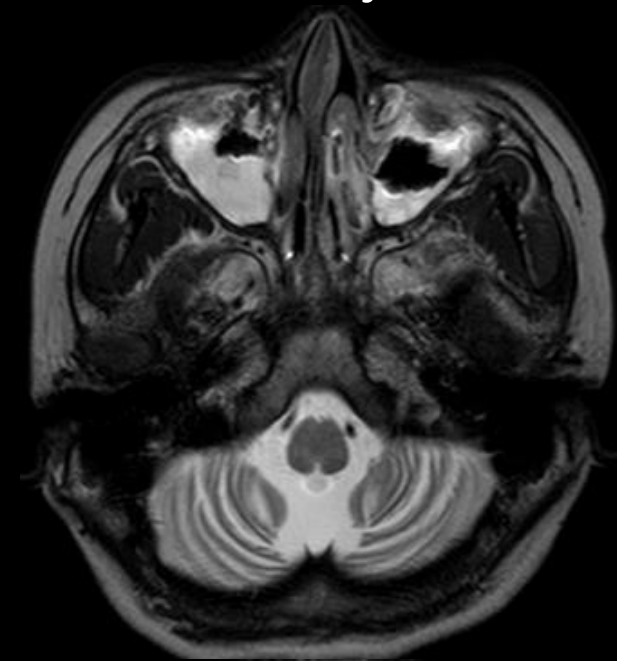
T2WI sagittal/coronal 5year-old



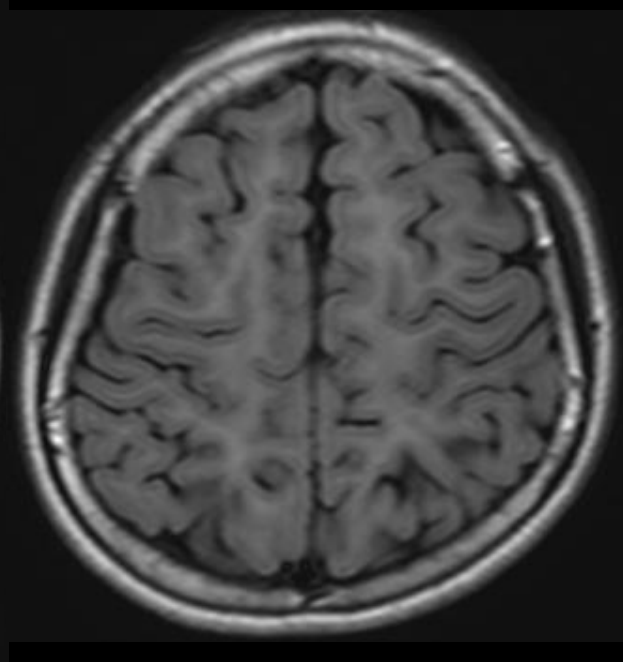
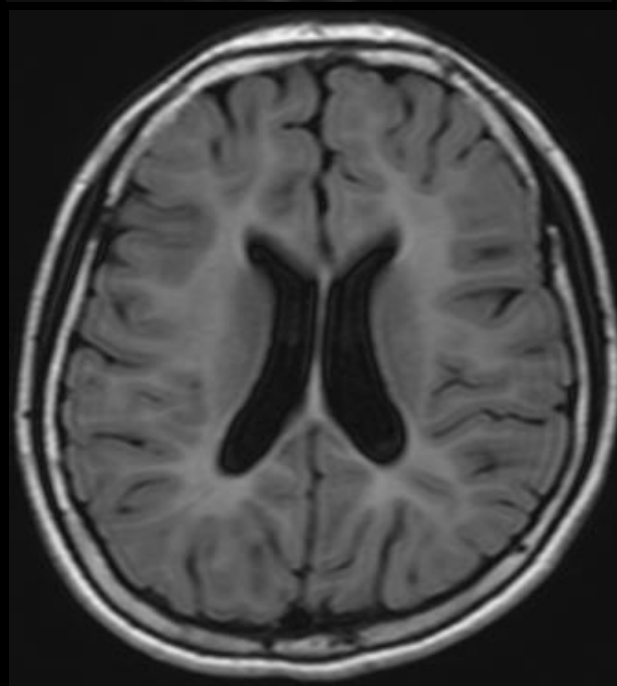
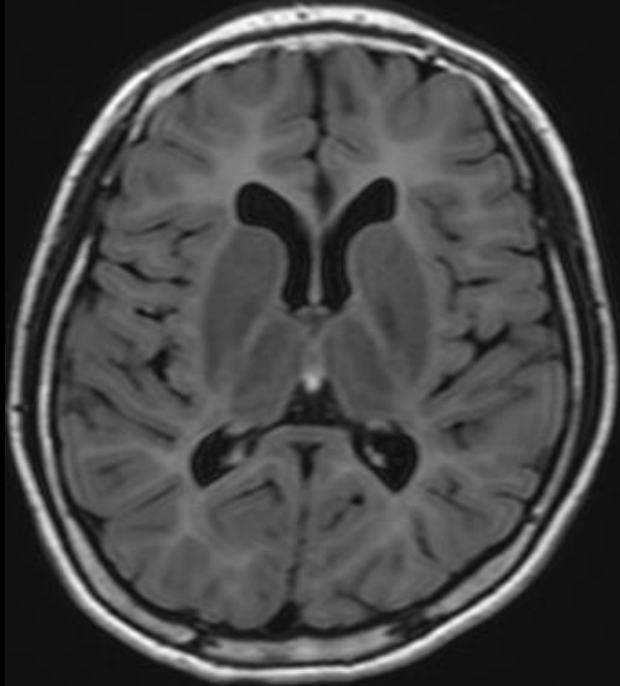
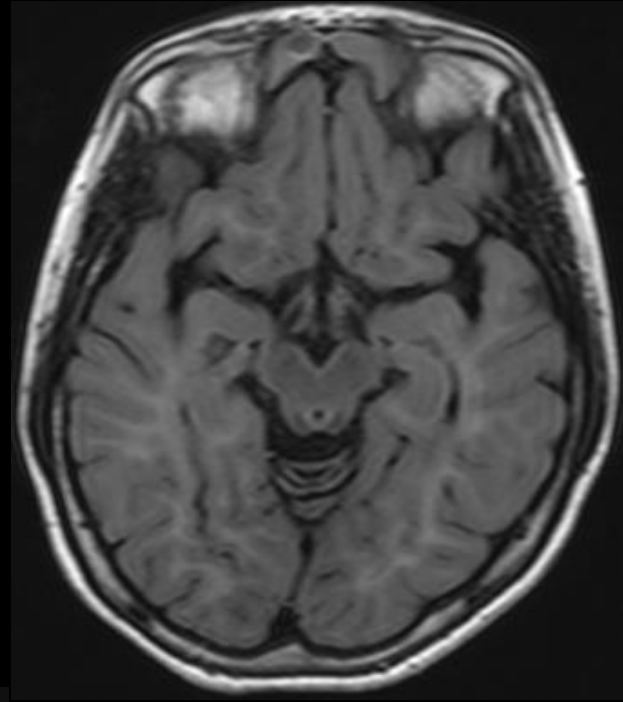
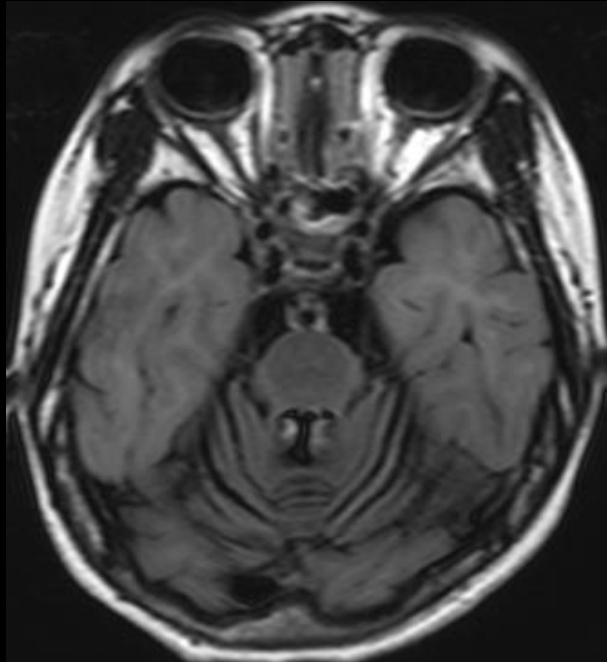
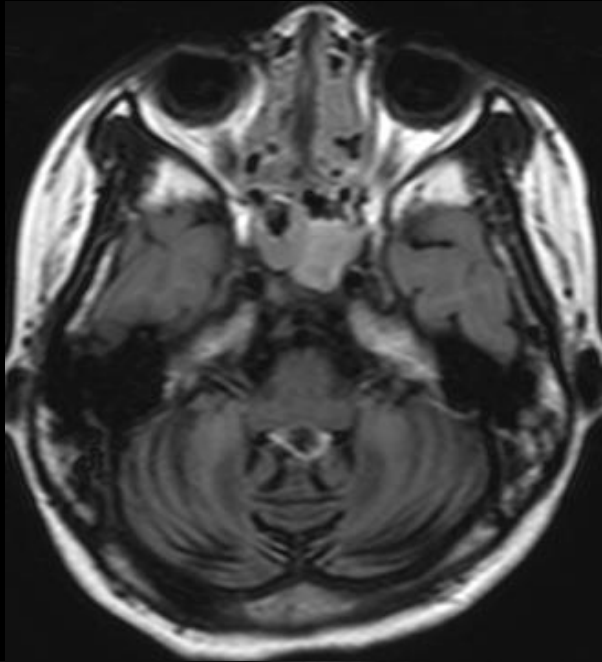
T1W axial 15year-old



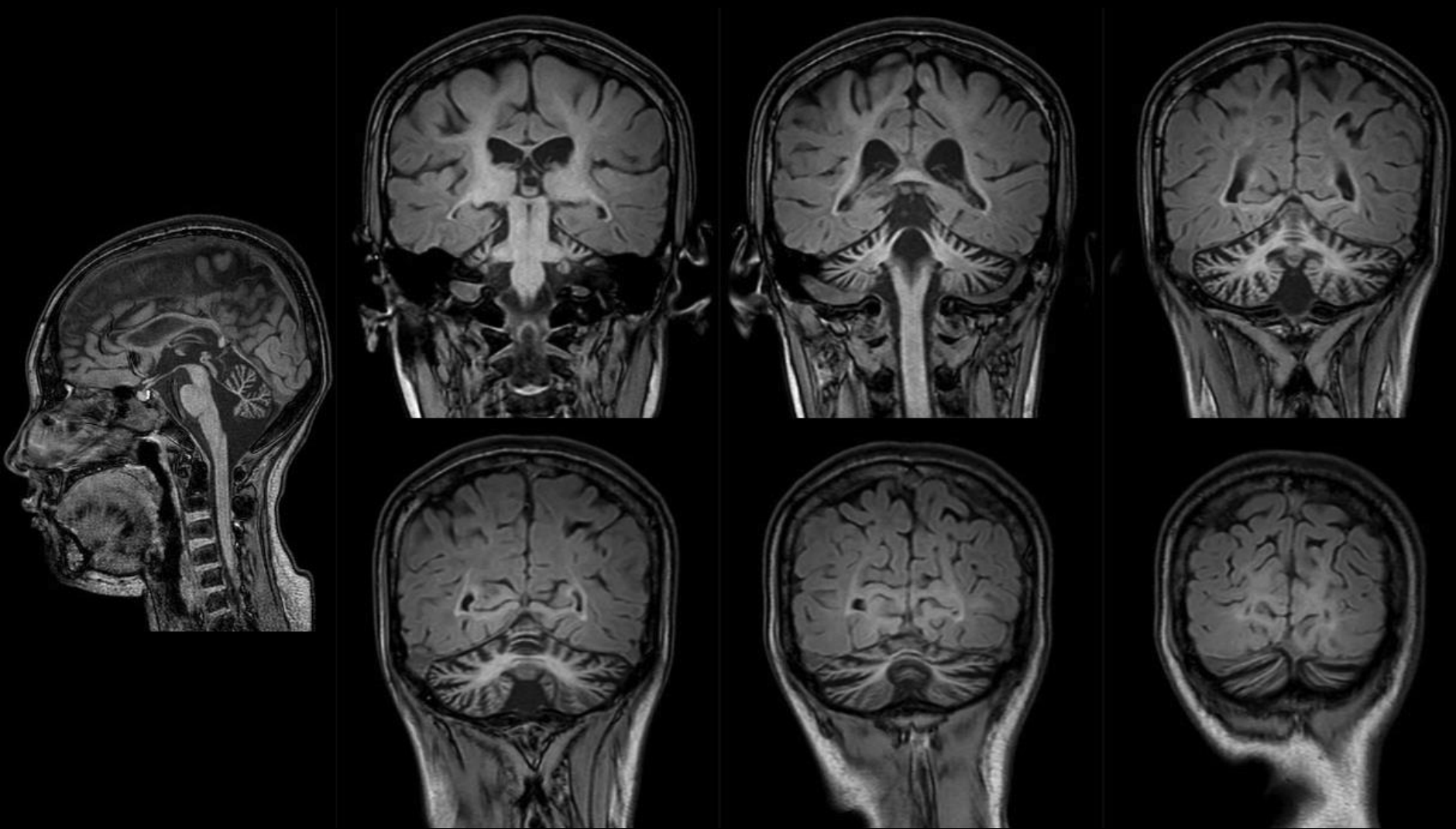
T2W axial 15year-old



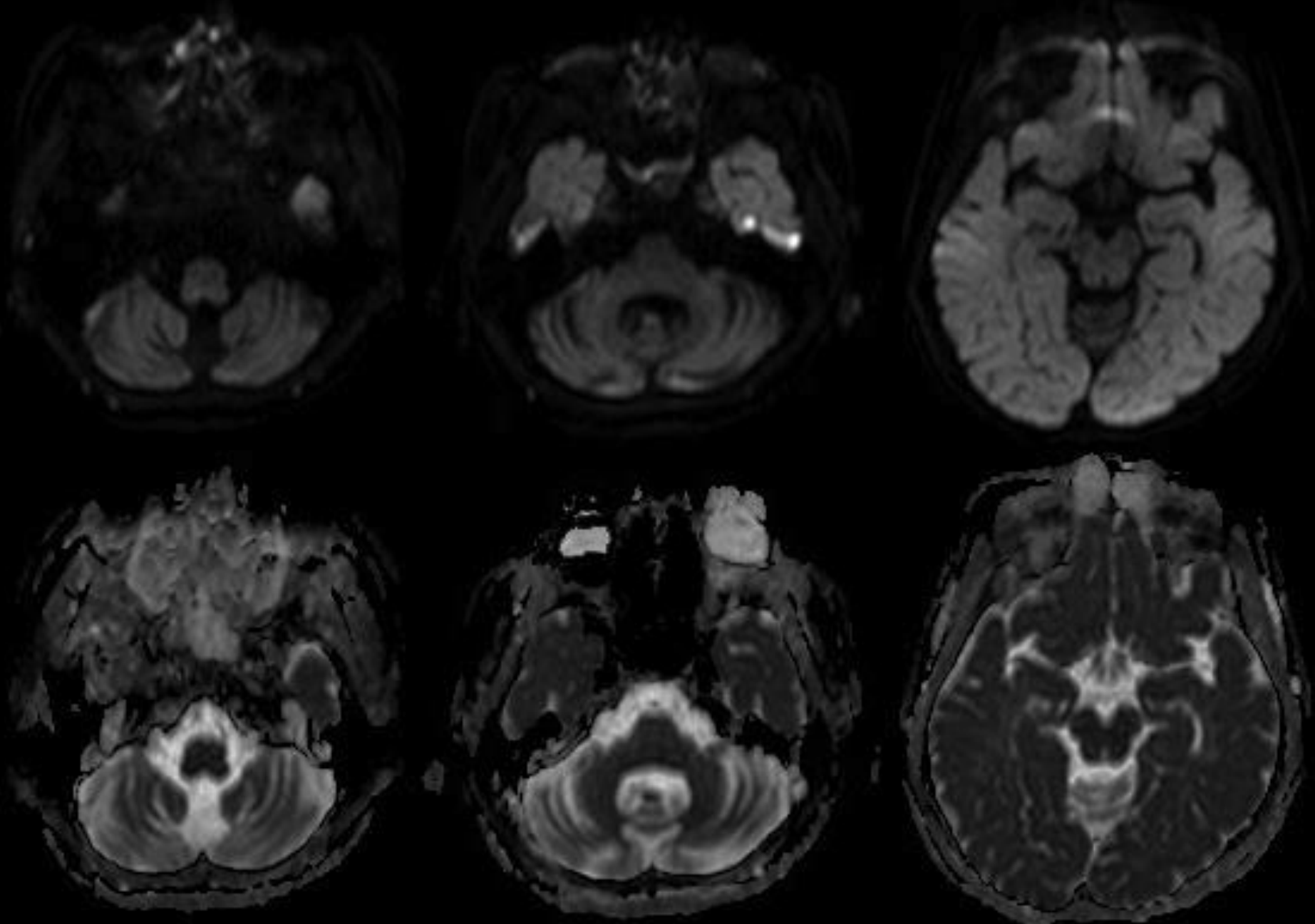
FLAIR image axial 15year-old



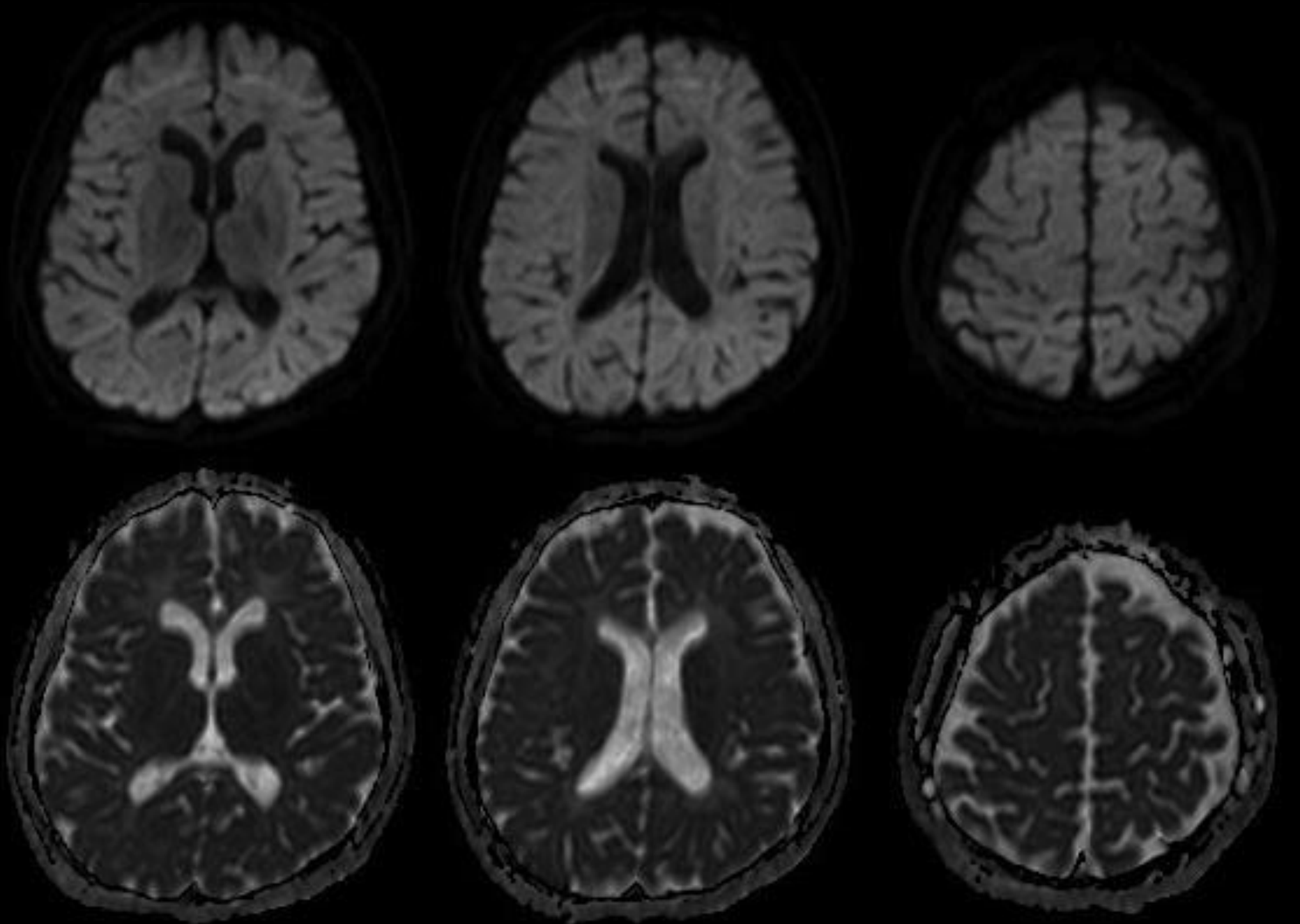
T1WI sagittal / coronal 15year-old



DWI / ADCmap 15 year-old



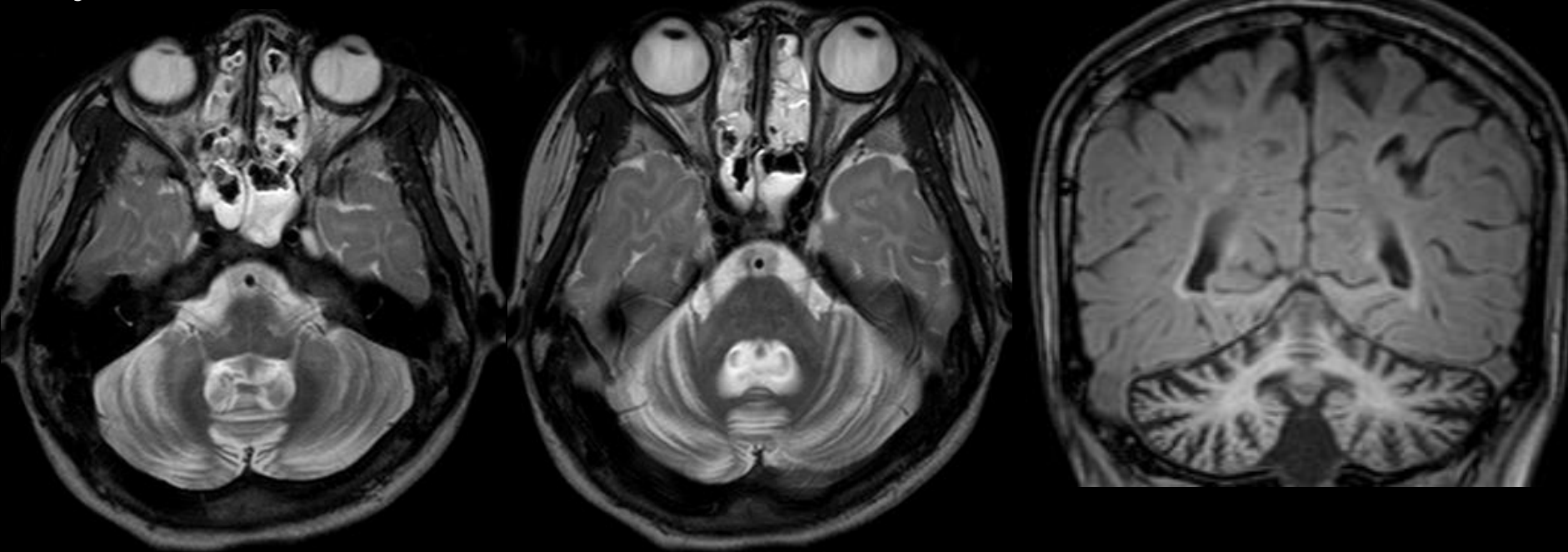
DWI / ADCmap 15 year-old



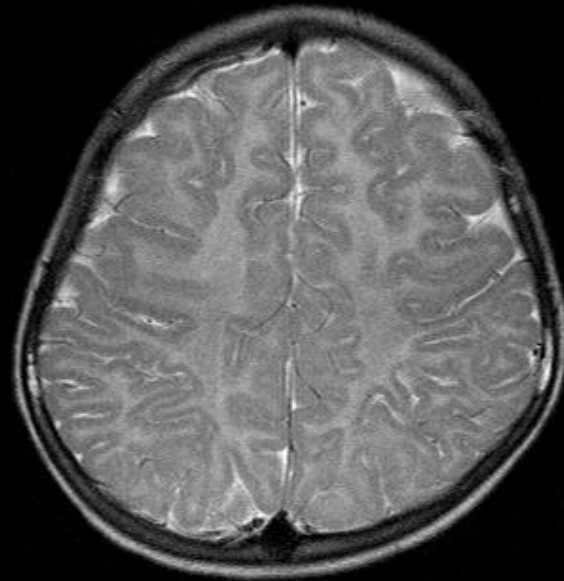
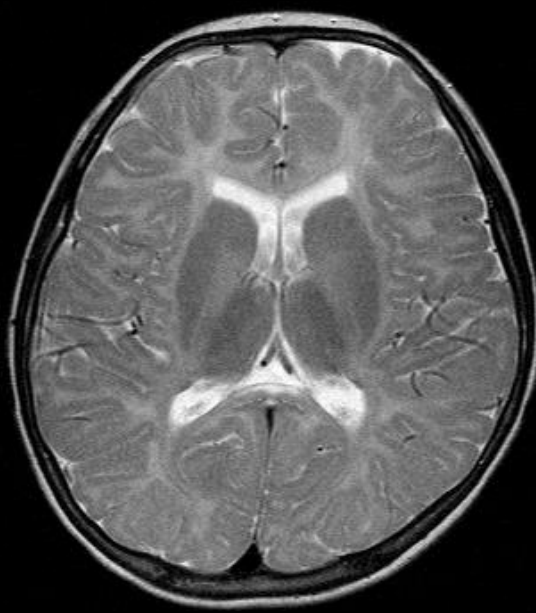
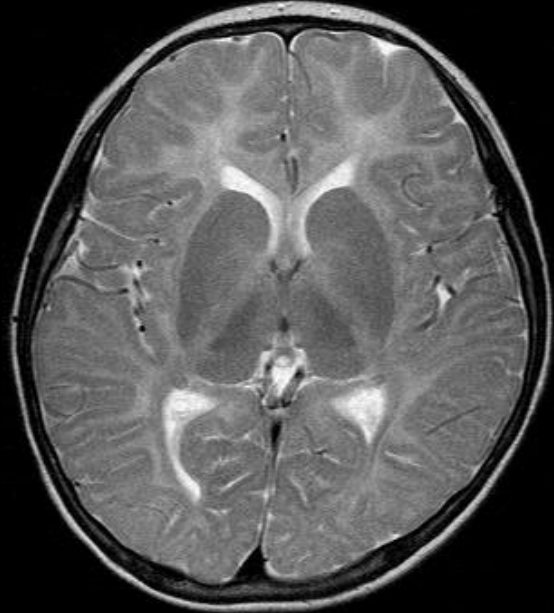
5year-old T2WI axial / coronal



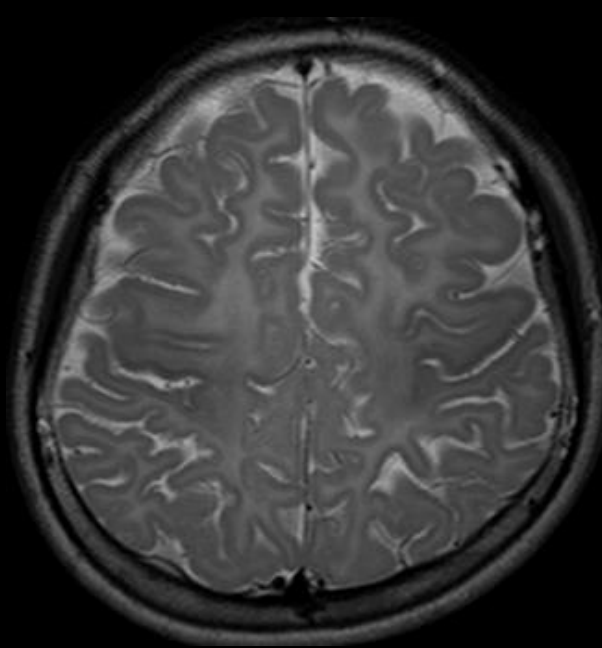
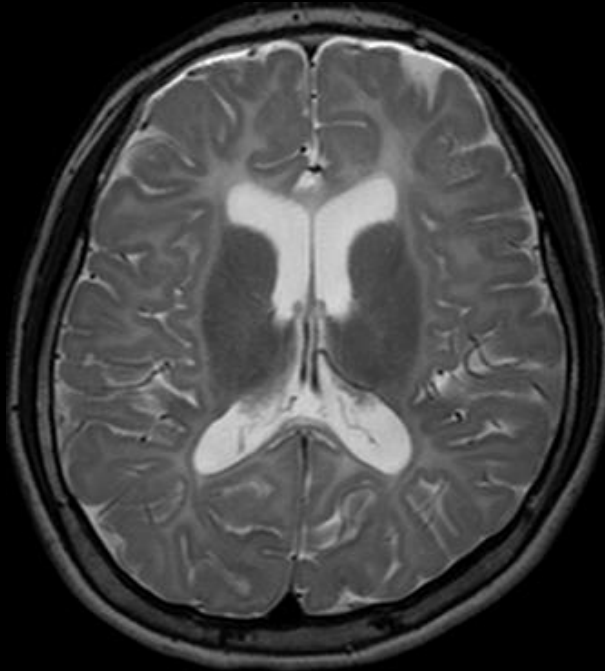
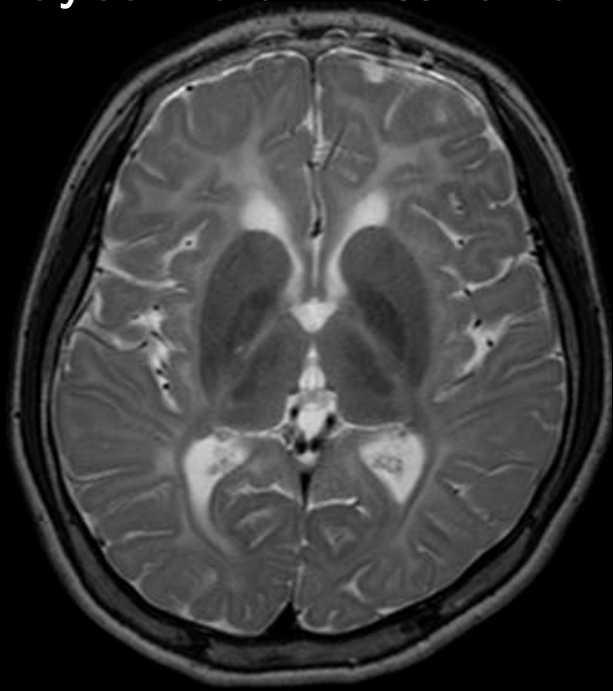
15year-old T2WI axial, T1WI coronal



5year-old T2WI axial



15year-old T2WI axial



5year-old T2WI sagittal



15year-old T1WI sagittal





# Diagnosis

One of Pol III-Related Leukodystrophies

Hypomyelination

with cerebellar atrophy

and hypoplasia of the corpus callosum

( HCAHC )

# 画像所見のまとめ

- ・大脳半球のびまん性の低髄鞘化
- ・病初期からの小脳萎縮と軽度進行
- ・脳梁の高度な菲薄化
- ・10年間で軽度の大脳萎縮
- ・視床外側部、内包後脚錐体路、視放線、  
歯状核の T2WI 低信号

# 低髄鞘化様所見からの鑑別

	低髄鞘化様	小脳萎縮	脳梁菲薄化	その他の画像的特徴	臨床的特徴
HH	+	-	+/-		歯牙異常
HCC	+	-	+/-		末梢神経障害
GM1 gangliosidosis	+	-/+(type2)		type1視床・基底核 T1WI高信号/T2WI低信号 type3尾状核・被核萎縮, T2WI高信号	cherry-red spot
GM2 gangliosidosis	+	-/+	+/-	視床のCT高吸収	cherry-red spot
Salla病	+	+/-	+	脳幹萎縮	重篤な精神運動発達遅滞
18q- syndrome	+		+/-,小さめ		顔面異形、低身長
PMD	+	+,初期は乏しい	+		水平 or 回旋性眼振
PMLD	+	+,初期は乏しい	+	橋 T2WI高信号	水平 or 回旋性眼振
Cockayne syndrome	+	+	+/-	基底核・歯状核の石灰化	光過敏、網膜色素変性症
Trichothiodystrophy	+	+	+	基底核の石灰化	魚鱗癬、爪・髪 of 異常
Fucosidosis	+	+	+	淡蒼球T1WI高信号/T2WI低信号	特異顔貌・骨格
H-ABC	+	+	+	基底核の萎縮	
Pol III-Related Leukodystrophy	+	+	+		

HH : hypomyelination and hypodontia

HCC : hypomyelination and congenital cataract

PMD : Pelizaeus-Merzbacher disease

PMLD : Pelizaeus-Merzbacher-like disease

H-ABC : hypomyelination with atrophy of thasal ganglia and cerebellum

# Pol III – Related Leukodystrophy

	低髓鞘化	小腦萎縮	腦梁菲薄化	性腺機能異常	齒牙異常
4H syndrome	+	+	+	+	+
ADDH	+	+	+	+	+
TACH	+	+	+	+	+
LO	+	+	+	-	+
HCAHC	+	+	+	-	-

4H syndrome : hypomyelination with hypogonadotropic hypogonadism and hypodontia

ADDH : Ataxia, delayed dentition, and hypomyelination

TACH : Tremor-ataxia with central hypomyelination

LO : Leukodystrophy with oligodontia

HCAHC : Hypomyelination with cerebellar atrophy and hypoplasia of the corpus callosum

# HCAHC : 提唱の由来

- ・臨床 : 小脳失調症状・精神発達遅滞  
緩徐に進行するマイルドな経過  
白内障、歯数・萌出異常、性腺機能異常なし
- ・画像 : 大脳のびまん性低髄鞘化、小脳萎縮、  
脳梁菲薄化



類似する 3 症例 (当院 2、他院 1) の検討から  
Sasaki M. et al. Diffuse cerebral hypomyelination  
with cerebellar atrophy and hypoplasia of the corpus  
callosum. Brain & Development 2009; 31:582–587.

により提唱された、比較的新しい疾患概念

# HCAHC : 臨床的特徴

- ・常染色体劣性遺伝
- ・初期運動発達は正常～軽度遅延
- ・処女歩行～2歳頃より不安定歩行を発現
- ・運動機能不全 (spasticity、cerebellar ataxia, and/or tremor)
- ・軽度～中等度の精神発達遅滞
- ・**緩徐に進行するマイルドな臨床経過**
- ・白内障、歯牙数・萌出異常、性腺機能異常なし

# HCAHC : 画像的特徴

- 大脳半球の低髄鞘化
- 病初期からの小脳萎縮
- 脳梁の高度な菲薄化
- 基底核の萎縮なし
- 橋の軽度萎縮・軽度のびまん性大脳萎縮を認める場合あり
- 視床前方外側・淡蒼球・視放線・歯状核の T2WI 低信号を認める場合あり

# HCAHC : 関連遺伝子と疾患概念

1) RNA Polymerase IIIのサブユニットA・B (POLR3A・POLR3B) をコードする *POLR3A*・*POLR3B* 遺伝子の変異  
: 本症例では *POLR3A*変異

2) RNA Polymerase III (Pol III)

: 神経系の発達を修飾する RNAs の転写に関する酵素  
→ 白質・髄鞘の発達と維持に与る tRNAs が機能不全  
→ 低髄鞘化が推定

3) *Pol III* – Related Luekodystrophy spectrum

Bernard G. et al. GeneReviews[Internet]. University of Washington, Seattle; Augst2, 2012.

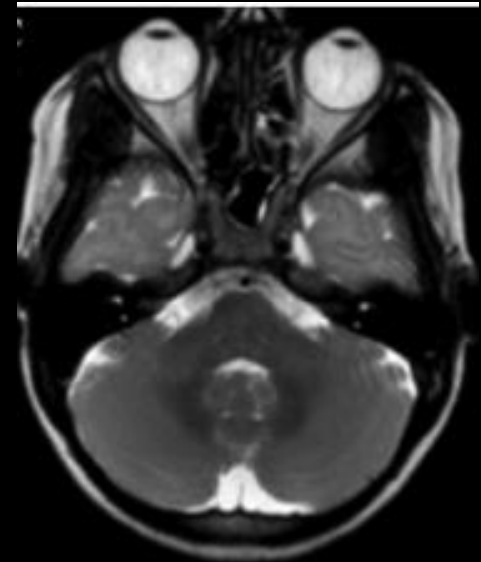
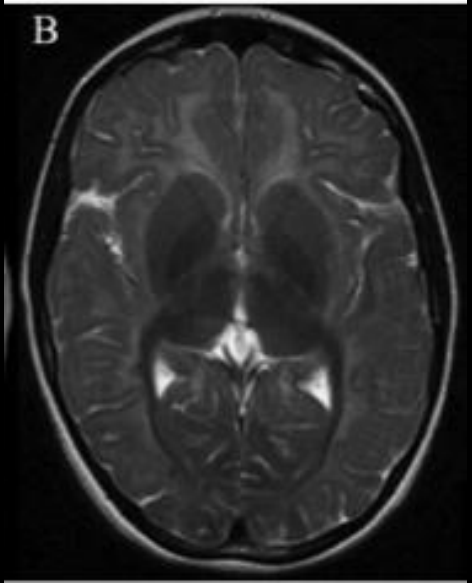
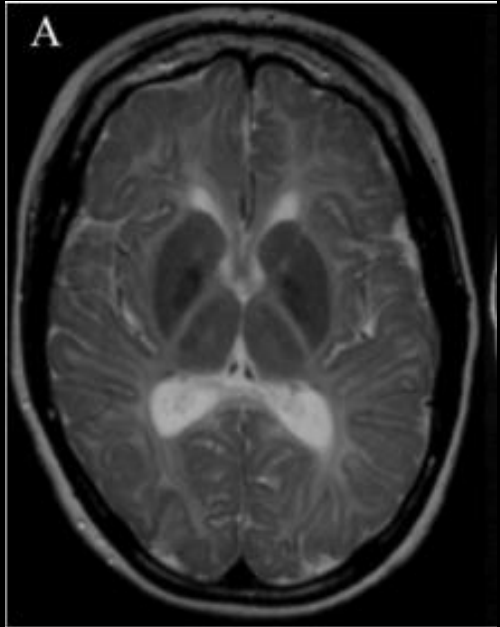
Tetreault M. et al. The American Journal of Human Genetics. 2011; 89: 652–655.

Dumay–Odelot G. et al. Cell Cycle 2010; 9: 3687–3699.

# Pol III-Related Leukodystrophy 13症例の 画像所見の検討 (4H syndrome, TACH)

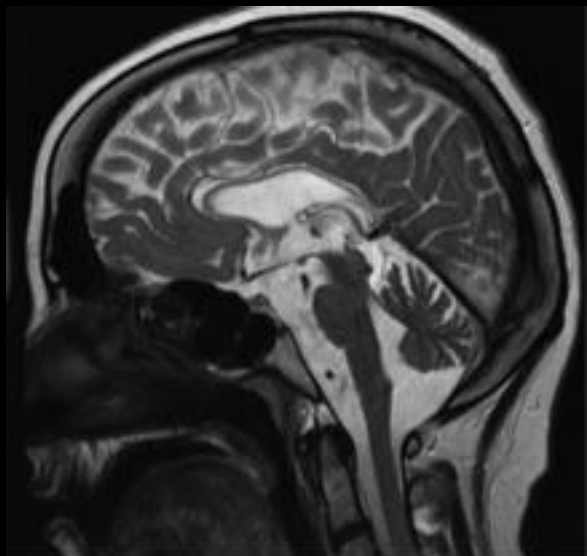
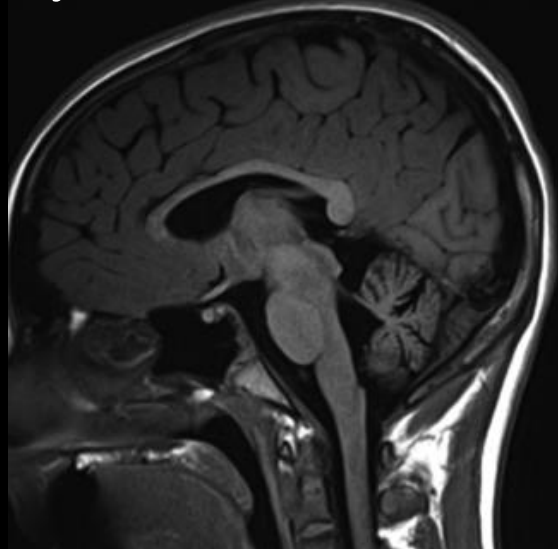
- ・ 大脳半球のびまん性低髄鞘化 (100%)
- ・ 小脳萎縮 (92%)
- ・ 脳梁菲薄化についての記載はない
- ・ 視床 and/or 淡蒼球に T2WI 低信号域 (100%)  
(視床前方外側に多い)
- ・ 視放線の T2WI 低信号 (92%)
- ・ 歯状核の T2WI 低信号 (69%)
- ・ 内包後脚錐体路の T2WI 低信号 (38%)

22 year-old male, *POLR3A*    17 year-old male, *POLR3B*    11 year-old male, *POLR3A*



17 year-old male, *POLR3B*

8 year-old male, *POLR3A*



# Take home point

- HCAHC

  - 臨床的特徴

    - : 小脳症状、軽度精神発達遅滞 など  
緩徐進行性でマイルドな臨床経過

  - 画像的特徴

    - : びまん性低髄鞘化、小脳萎縮、脳梁菲薄化

- *POLR3A*、*POLR3B* 変異

- Pol III-Related Leukodystrophy spectrum

# Reference

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