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HYPOTHALAMITIS,
A CASE OF UNKNOWN ETIOLOGY

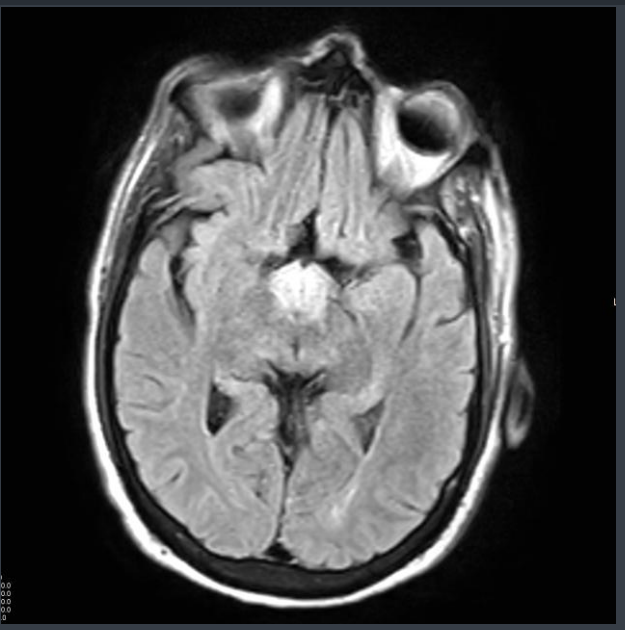
CLINICAL PRESENTATION

A 64-year-old male with a history of chronic lymphocytic leukemia complicated by splenomegaly and currently being treated with zanubrutinib (initiated 8/2024 and held briefly 9/2024 for a hernia repair complicated by post-operative hemorrhagic shock), presented with waxing and waning encephalopathy following a sinus infection treated with azithromycin. Presenting symptoms included episodes of agitation, confusion, and significant sleep disturbances.

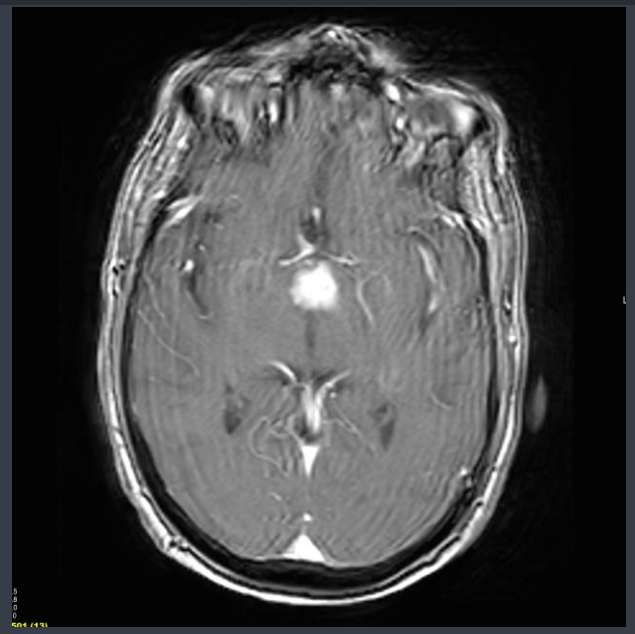
INITIAL IMAGING

Initial Non-contrast CT Head 5/8/25 without significant findings.

INITIAL IMAGING

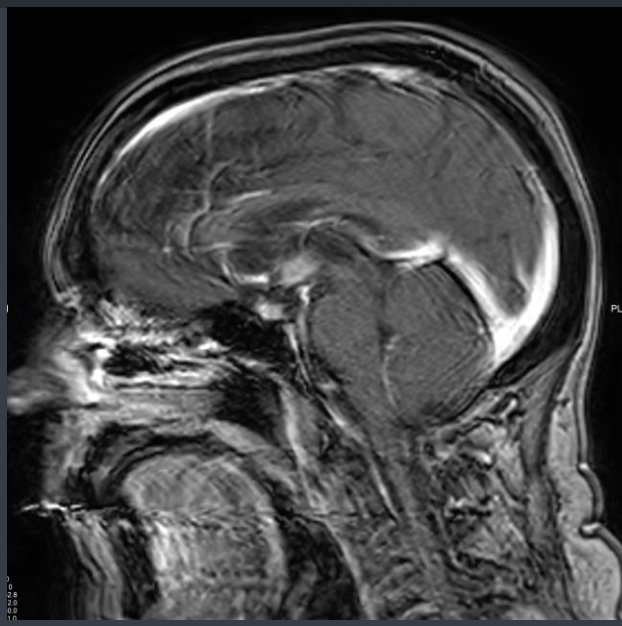


Axial T2 FLAIR



Axial Post Contrast

Coronal Post Contrast



Sagittal Post Contrast

Initial MRI Brain with contrast 5/8/25 demonstrating a FLAIR hyperintense enhancing lesion of the bilateral hypothalamus.

MANAGEMENT

- Laboratory and clinical evaluations suggested endocrine and neurological dysfunction consistent with hypothalamic involvement.
- Lumbar puncture was recommended by neurology with CSF studies largely unremarkable.
- IL-2 Receptor was positive raising concern for sarcoidosis with possible neurological involvement and outpatient biopsy of a known lung nodule was planned.
- The patient's zanubrutinib therapy was suspended and IV corticosteroid therapy with prednisone as well as IVIG was initiated.

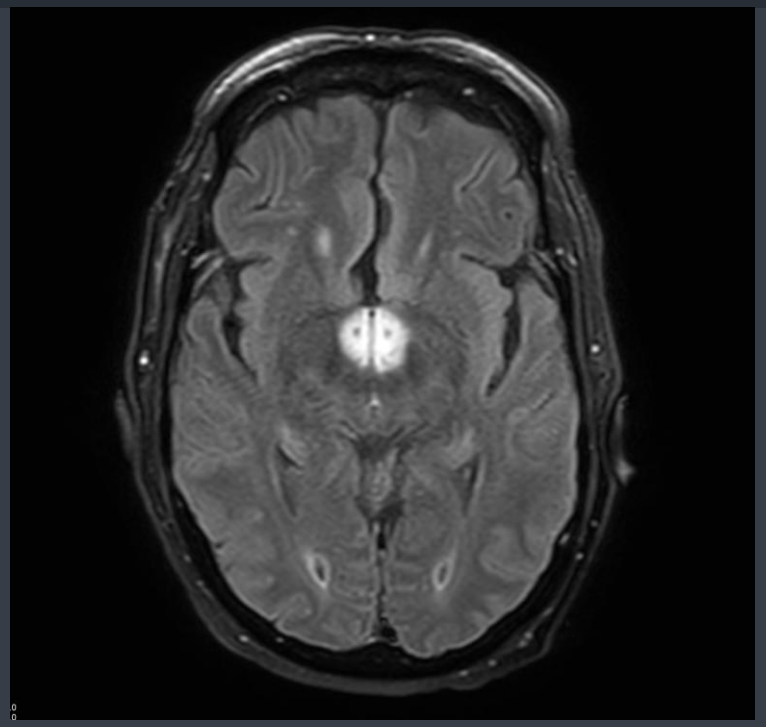
Fluoroscopic guided lumbar puncture at L3-L4 thecal space.

OUTCOME

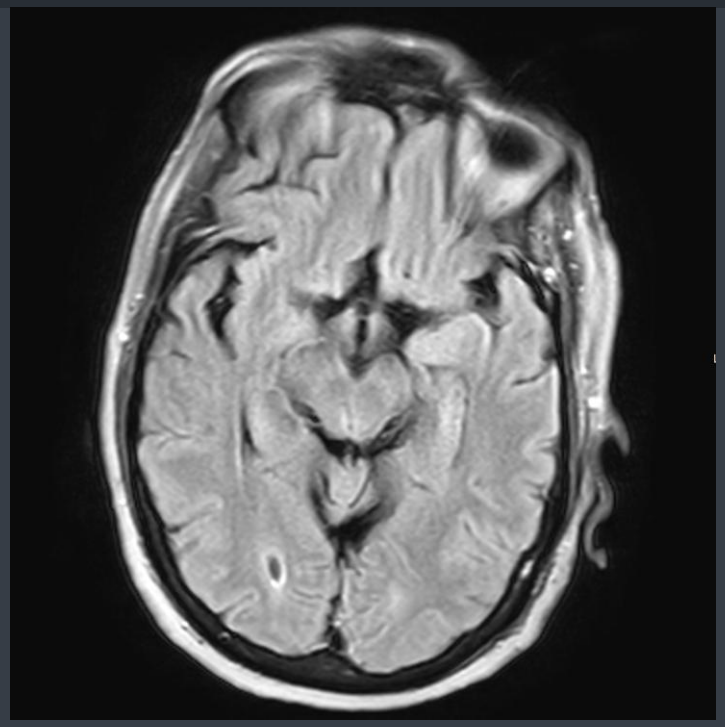
- After a prolonged hospital course, the patient showed clinical improvement with no further episodes of encephalopathy or agitation and was discharged home.
- Outpatient bronchoscopy performed with interval resolution of lung nodule and no biopsies taken; no confirmatory sarcoid studies completed.
- Patient's zanubrutinib was restarted after bronchoscopy.
- Corticosteroid therapy tapered and concluded 8/8/2025.
- Patient re-presented to the ED for a similar clinical picture 8/13/25 with worsening of imaging findings. He deferred inpatient admission and was restarted on high dose steroids.
- Continued outpatient follow-up with sleep medicine, endocrinology, hematology/oncology, and neurology alongside repeat MRI brain scheduled for 10/31/25.

FOLLOW UP IMAGING

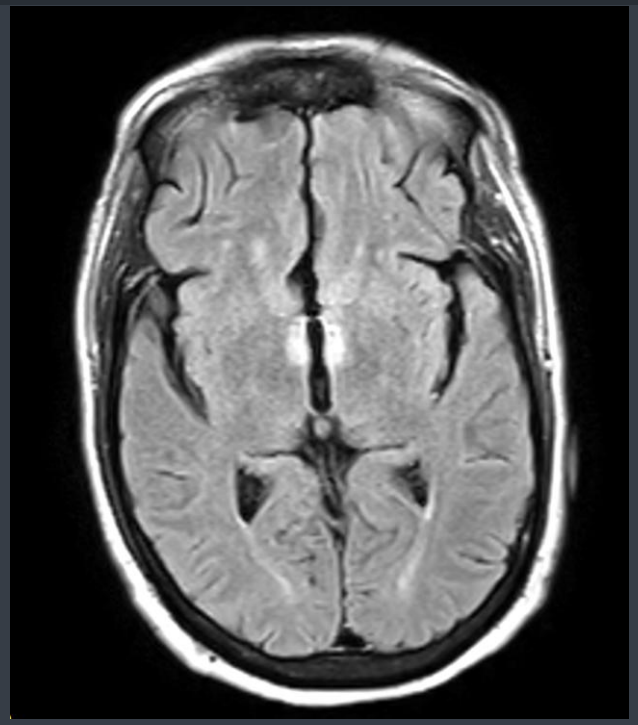
Axial T2 FLAIR 5/16/25



Axial T2 FLAIR 7/10/25



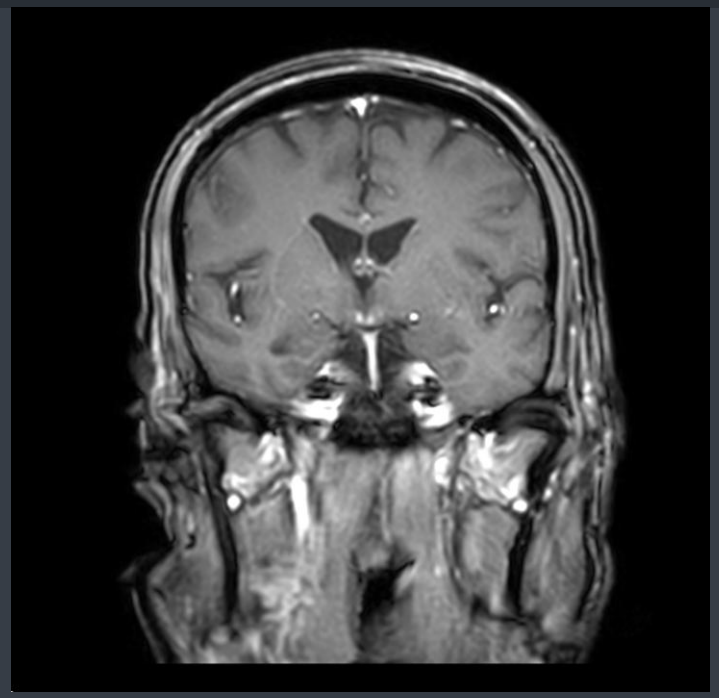
Axial T2 FLAIR 7/10/25



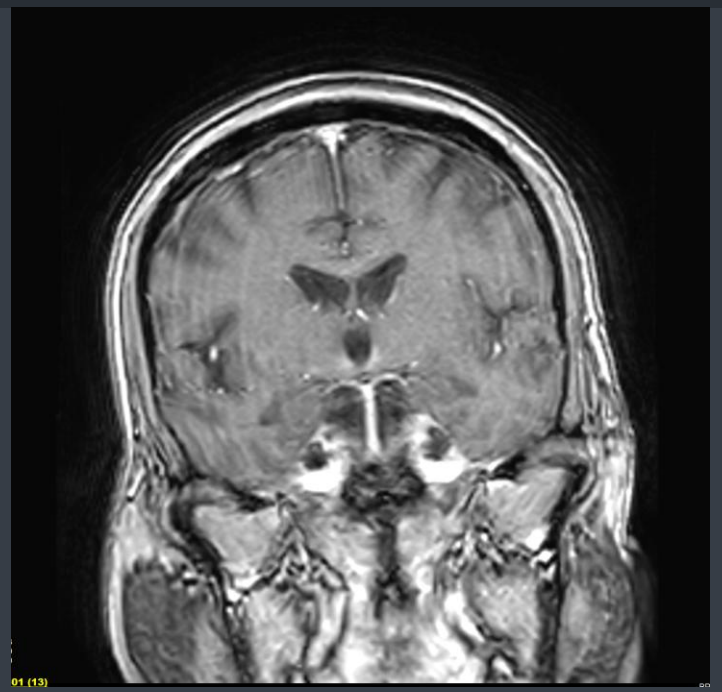
Initial follow up MRI Brain with contrast 5/16/25 (left) demonstrating persistent FLAIR hyperintensity of the hypothalamus. Secondary follow up 7/10/25 (middle) with minimal residual FLAIR hyperintensity. Repeat ED presentation 8/13/25 (left) with progressive FLAIR hyperintensity.

FOLLOW UP IMAGING

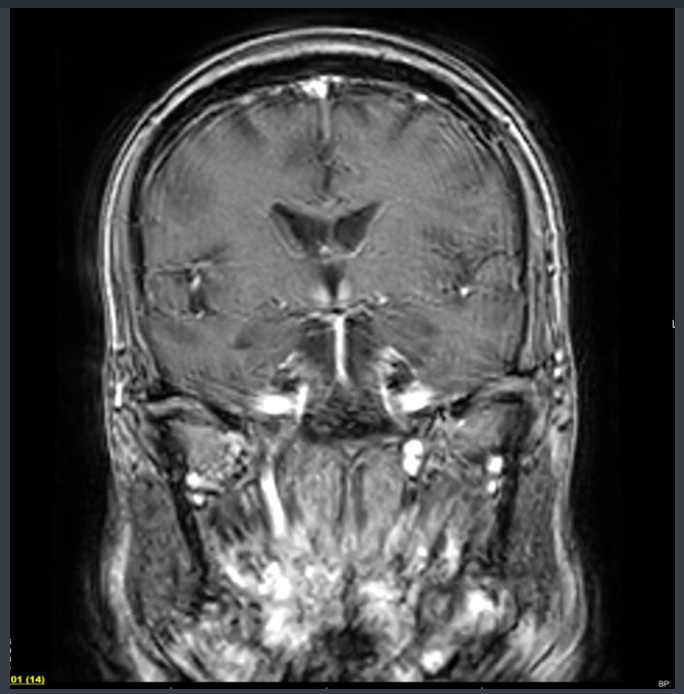
Coronal T1 post contrast 5/16/25



Coronal T1 post contrast 7/10/25



Coronal T1 post contrast 7/10/25



Initial follow up MRI Brain with contrast 5/16/25 (left) demonstrating persistent though improved contrast enhancement of the hypothalamus bilaterally. Secondary follow up 7/10/25 (middle) with minimal residual enhancement. Repeat ED presentation 8/13/25 (left) with progressive worsening of enhancement.

TAKE HOME POINTS

- Autoimmune hypothalamitis should be considered in patients presenting with hypothalamic symptoms following infection or targeted immunotherapy.
- Our patient represents a case of relapsing and remitting clinical symptoms with imaging correlation that follows closely with steroid treatment timeline.
- Though there is limited data on BTK inhibitors such as zanubrutinib, given the immunomodulatory effects of this class of therapy, further investigation should be directed at assessing possible links. To date there have been no reported CNS adverse effects of this drug including hypothalamitis.

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