Case 2024-5

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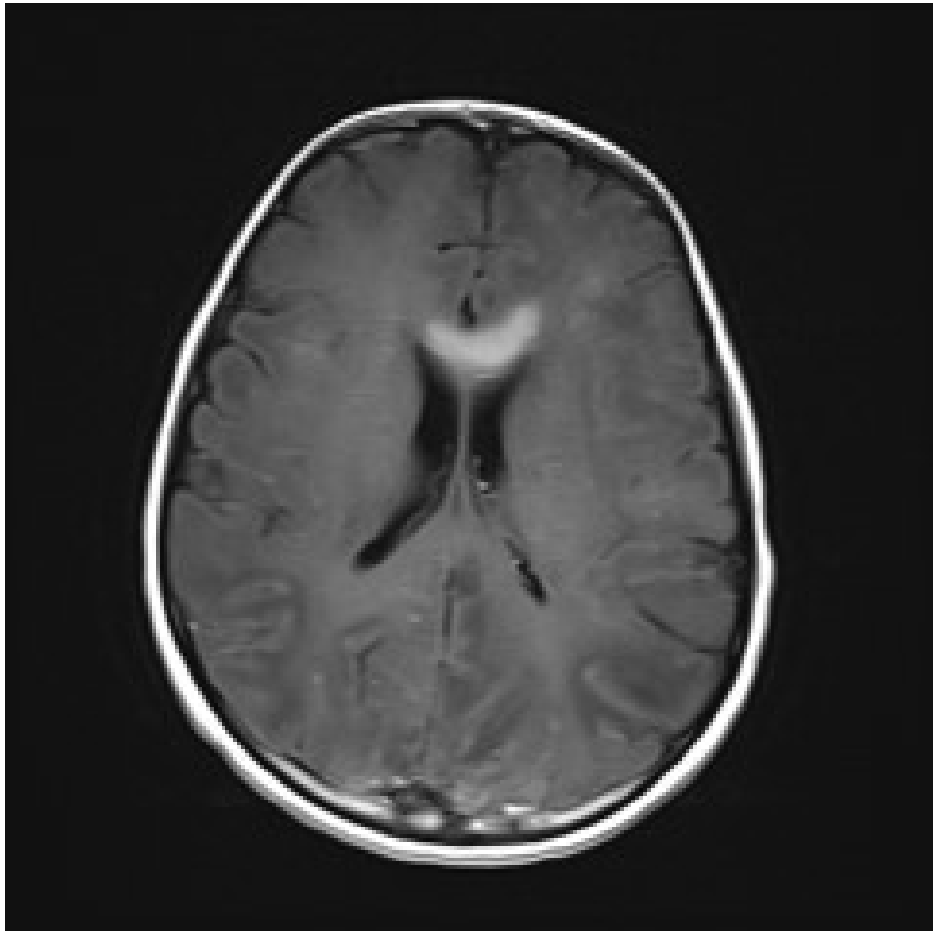
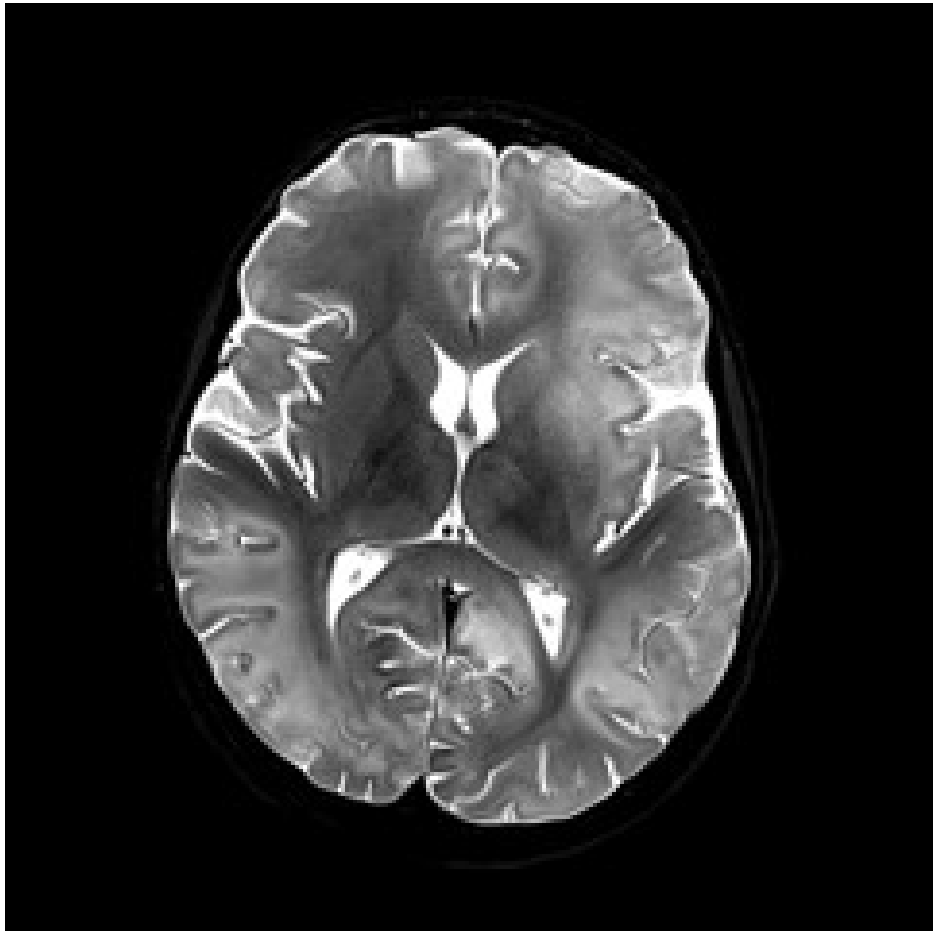
LIFE CHANGING MEDICINE

Clinical History

- A young male child in his first decade, adopted from India approximately three years prior to presentation
- Presented with altered mental status, seizures, and progressive symptoms including hypertonia, ataxia, myoclonus, and autonomic storming
- Imaging showed progressive T2/FLAIR abnormalities in the bilateral cerebral hemispheres



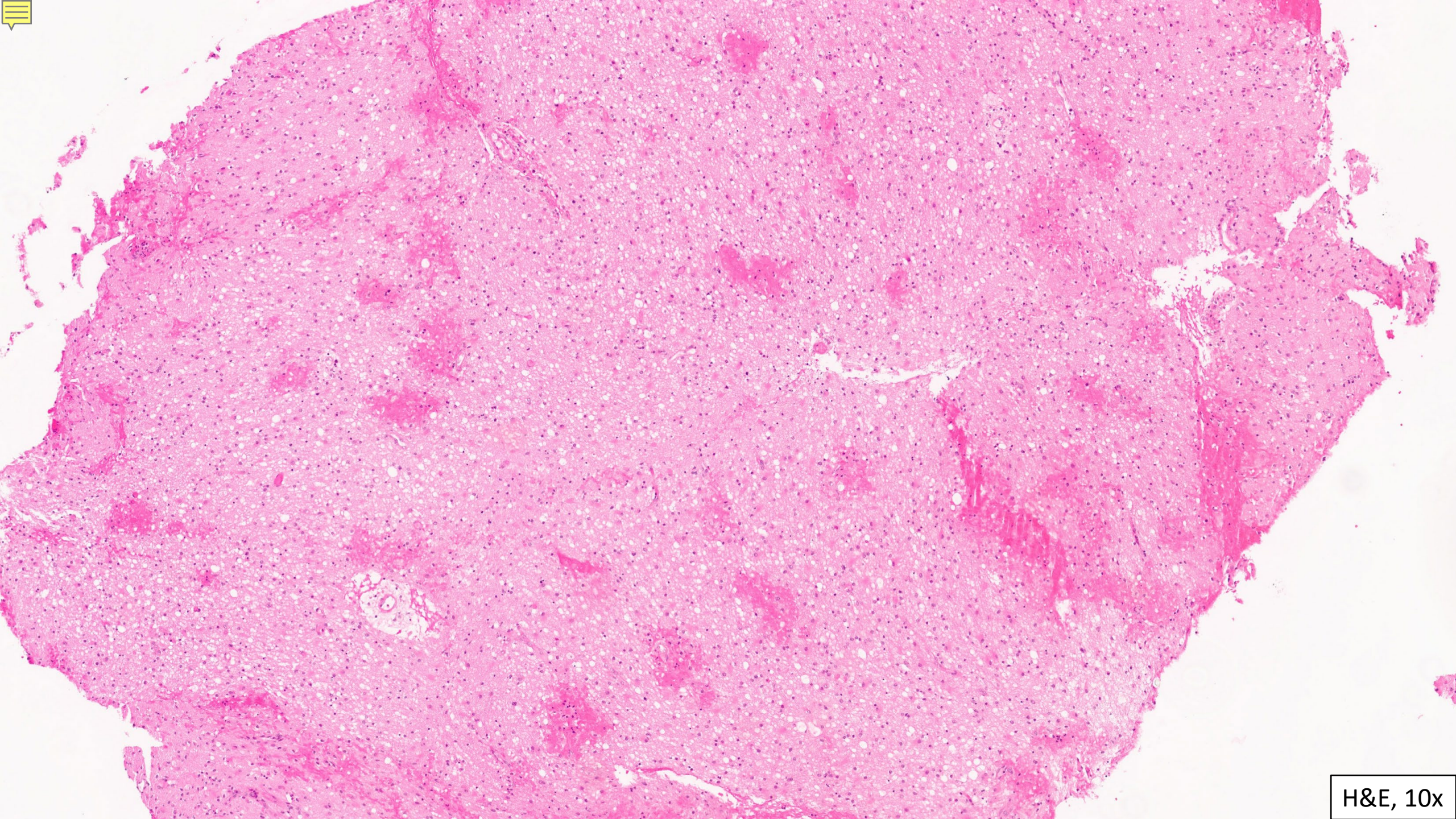
T1

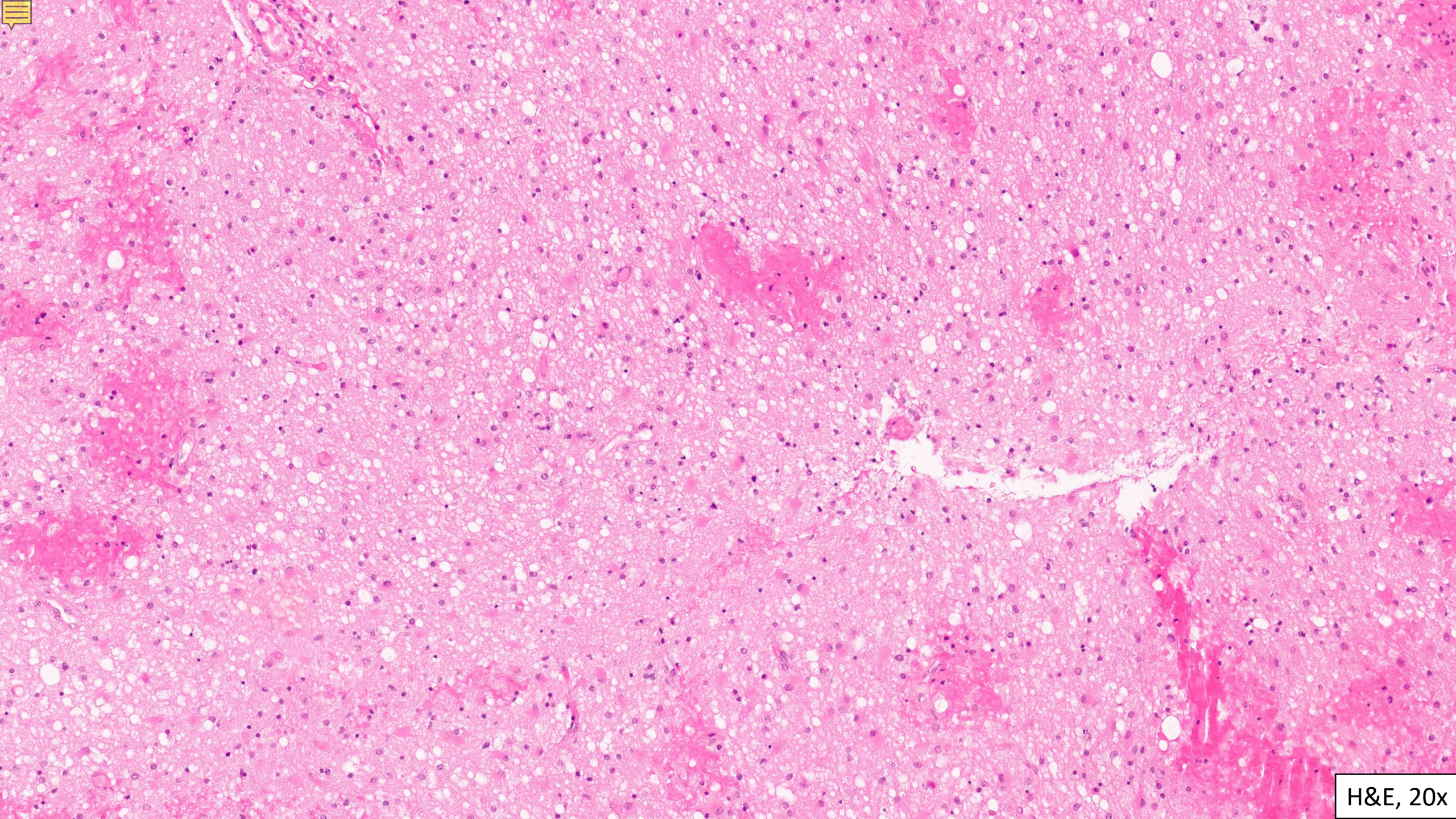


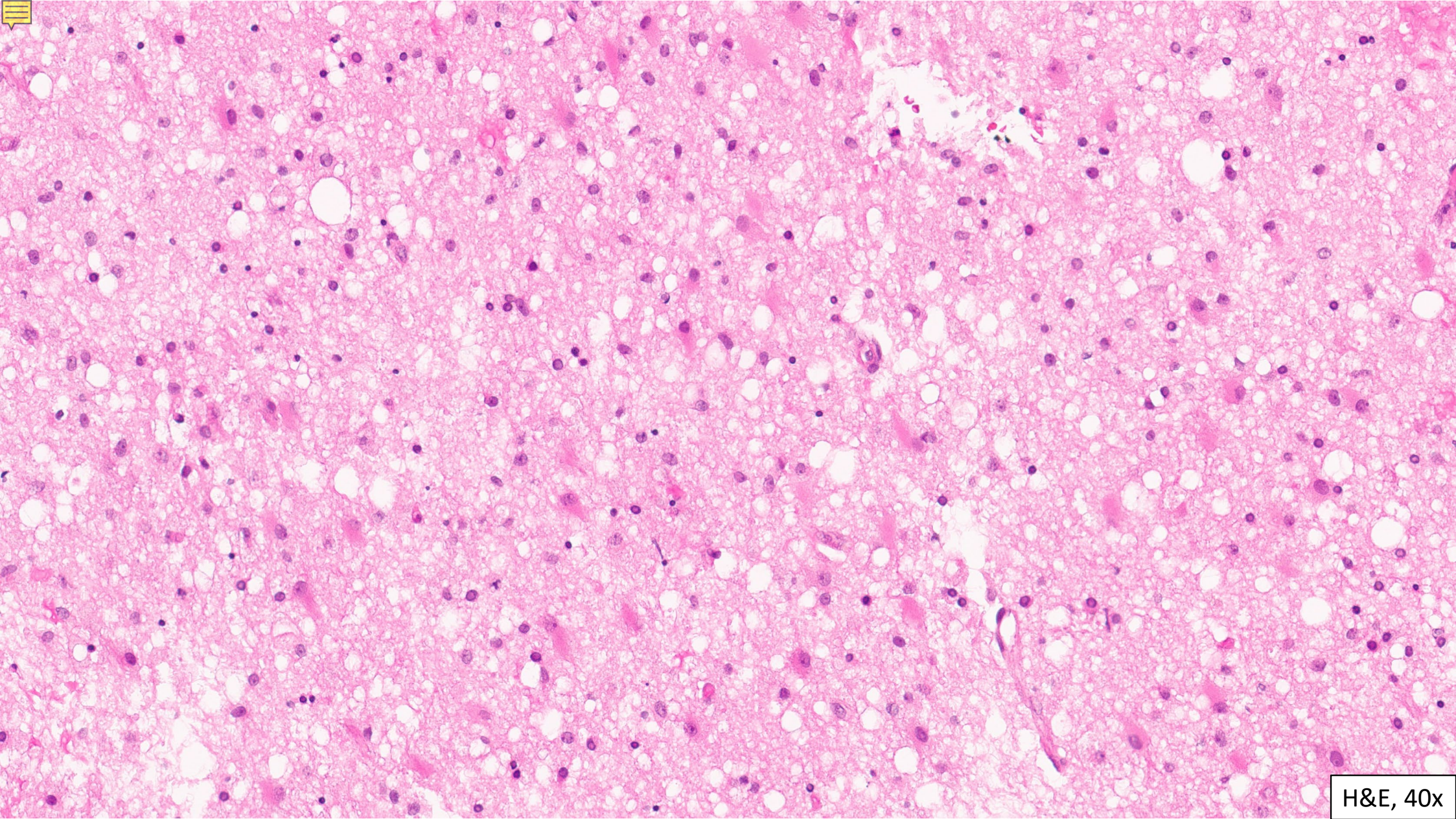
T2

Clinical History

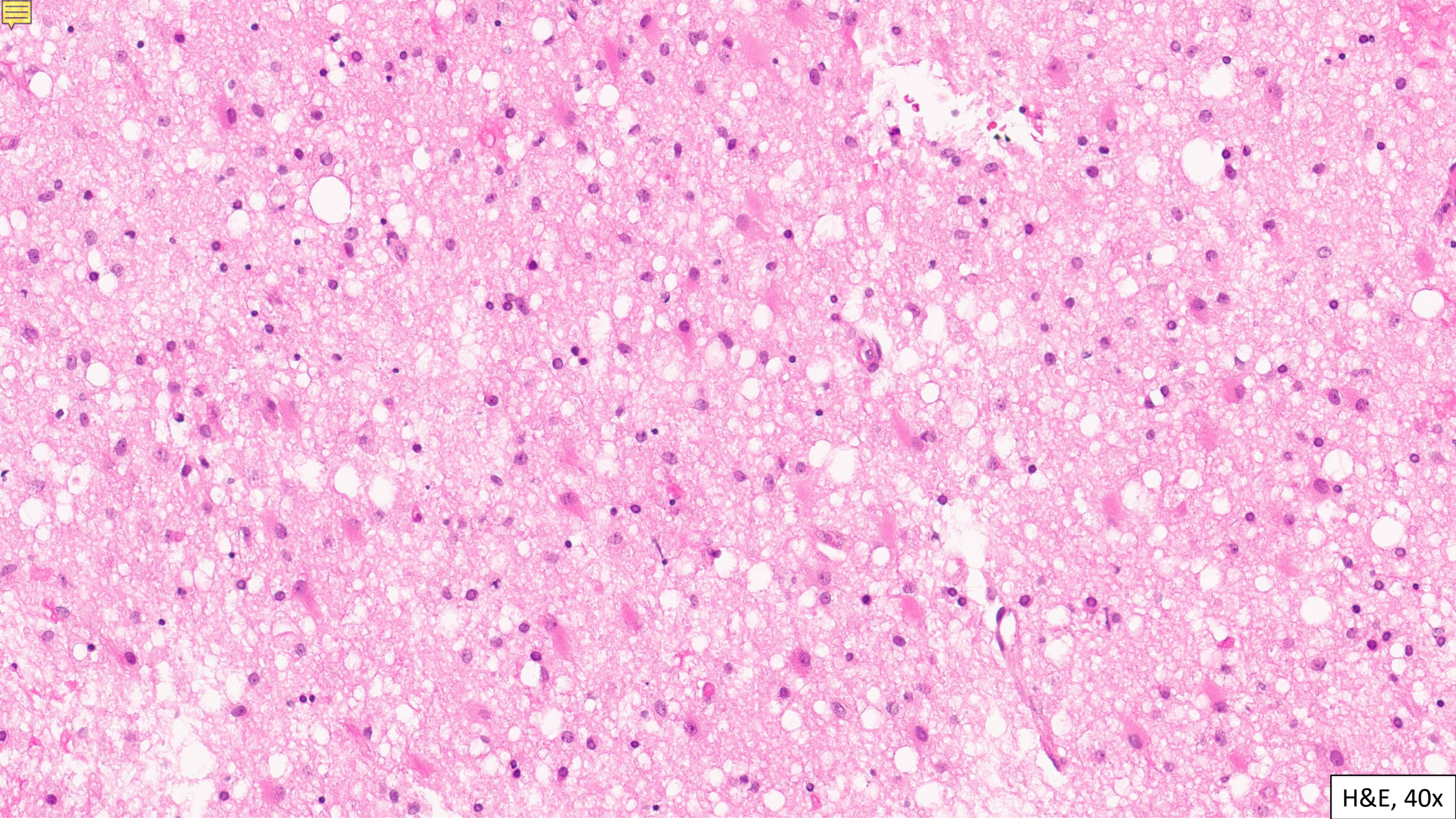
- Clinical differential diagnosis included infectious encephalitis, autoimmune encephalitis, vasculitis, and mitochondrial disease
- Extensive infectious workup was essentially negative
- Multiple lines of therapy failed (IVIG, PLEX, Rituximab)
- Brain biopsy was performed and reviewed at CDC:
  - Negative antigen testing for Measles, Eastern equine encephalitis virus, West Nile virus, and La Crosse encephalitis virus

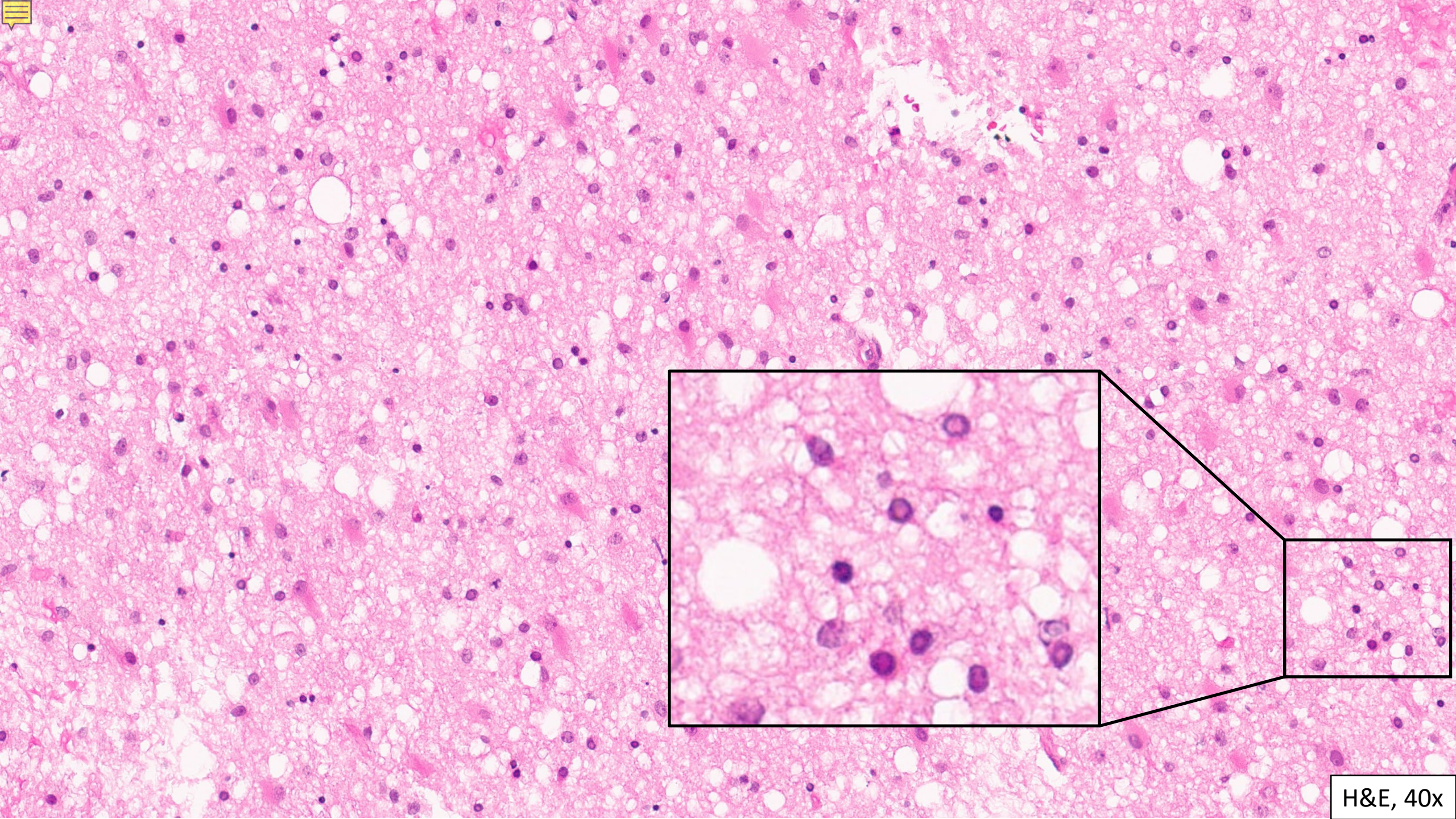

H&E, 10x


H&E, 20x


H&E, 40x

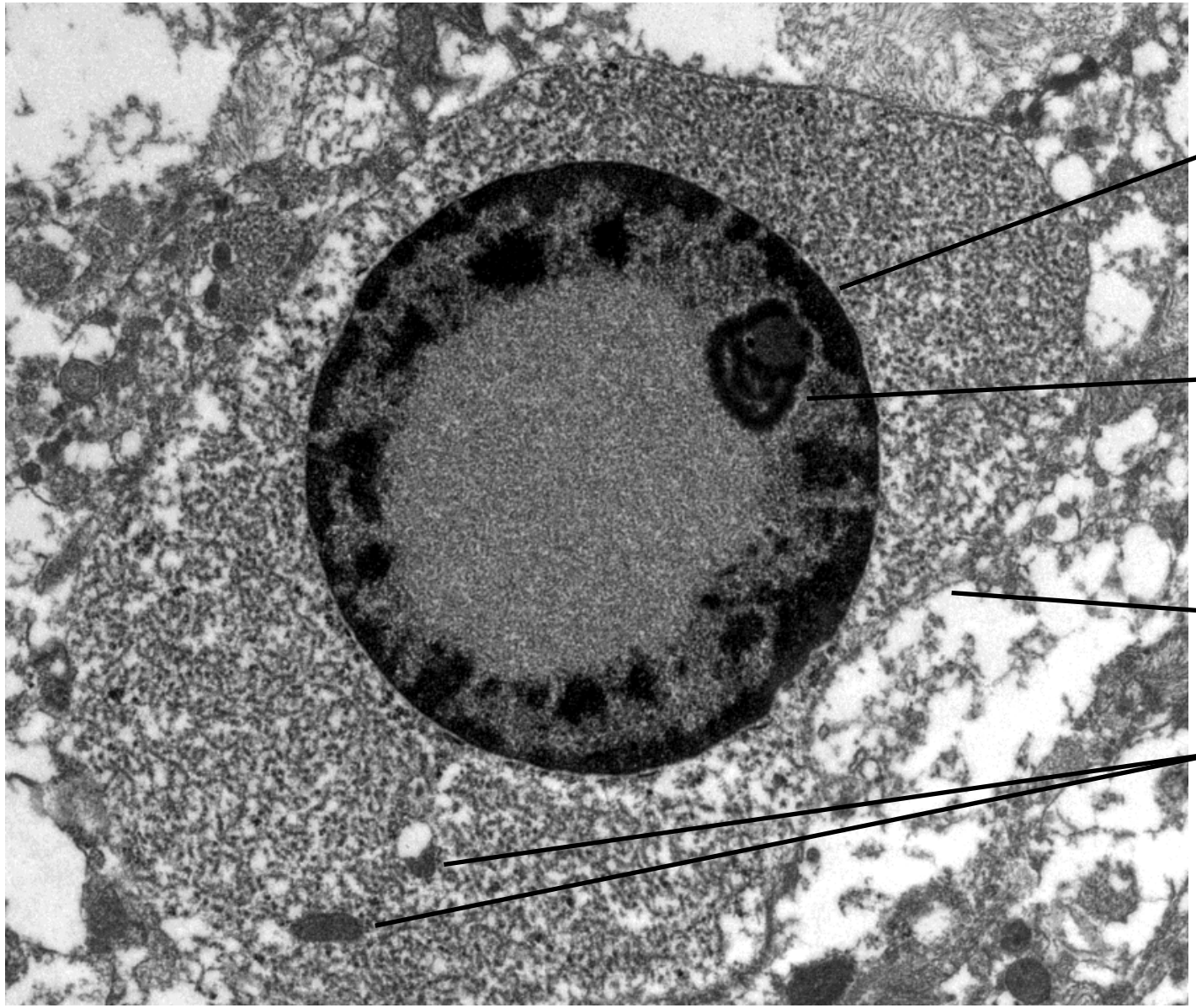
Differential diagnosis and workup?


H&E, 40x

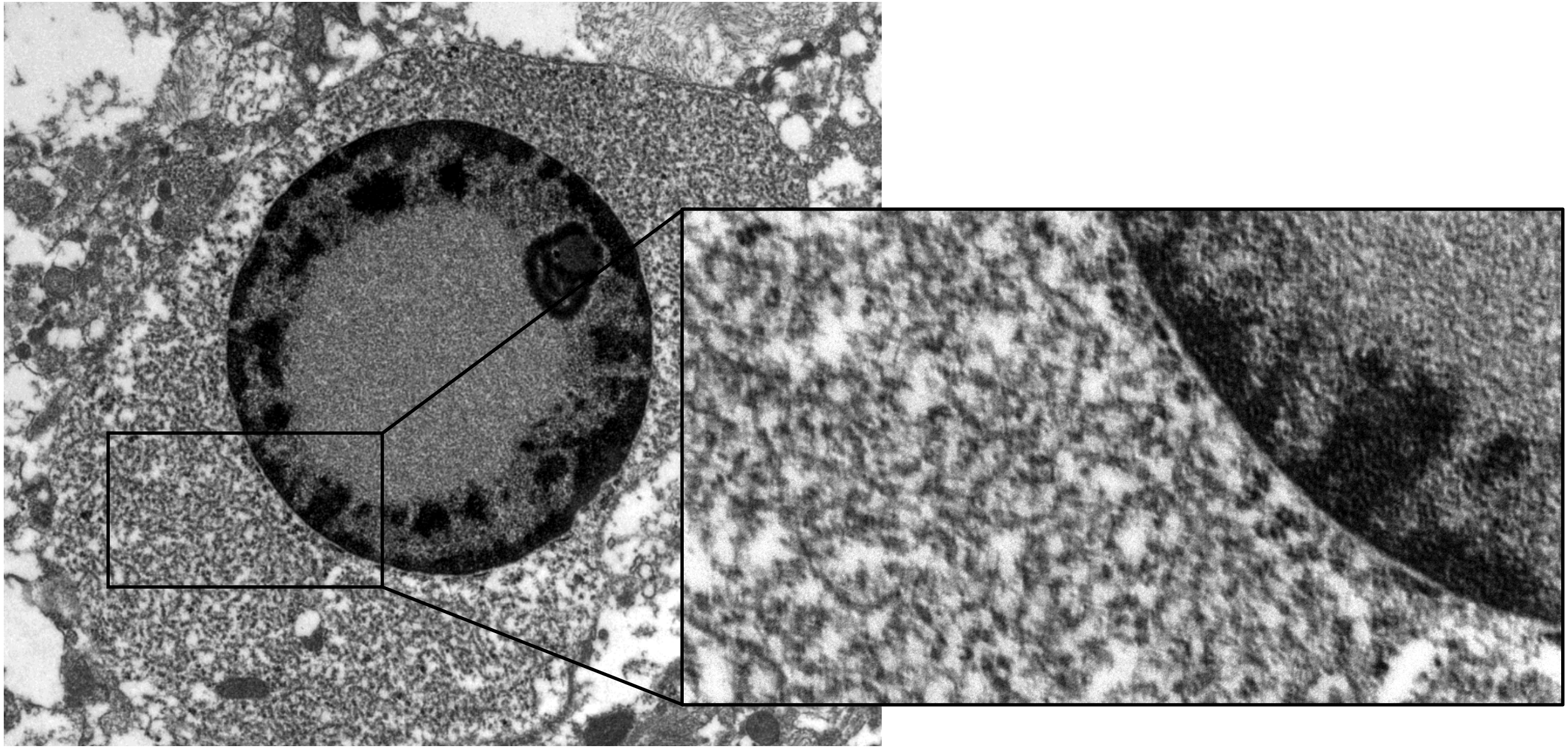


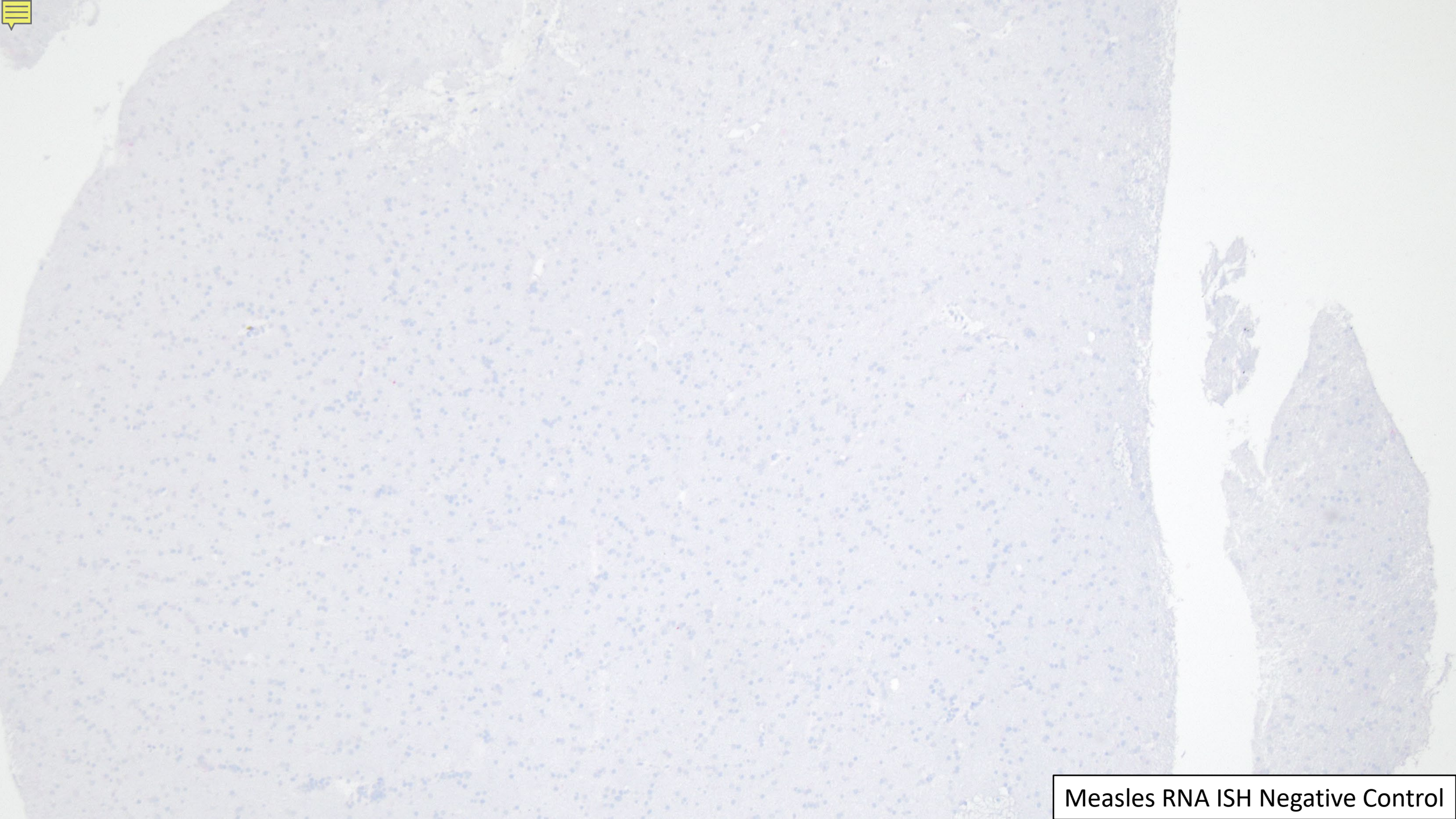
H&E, 40x

Electron Microscopy

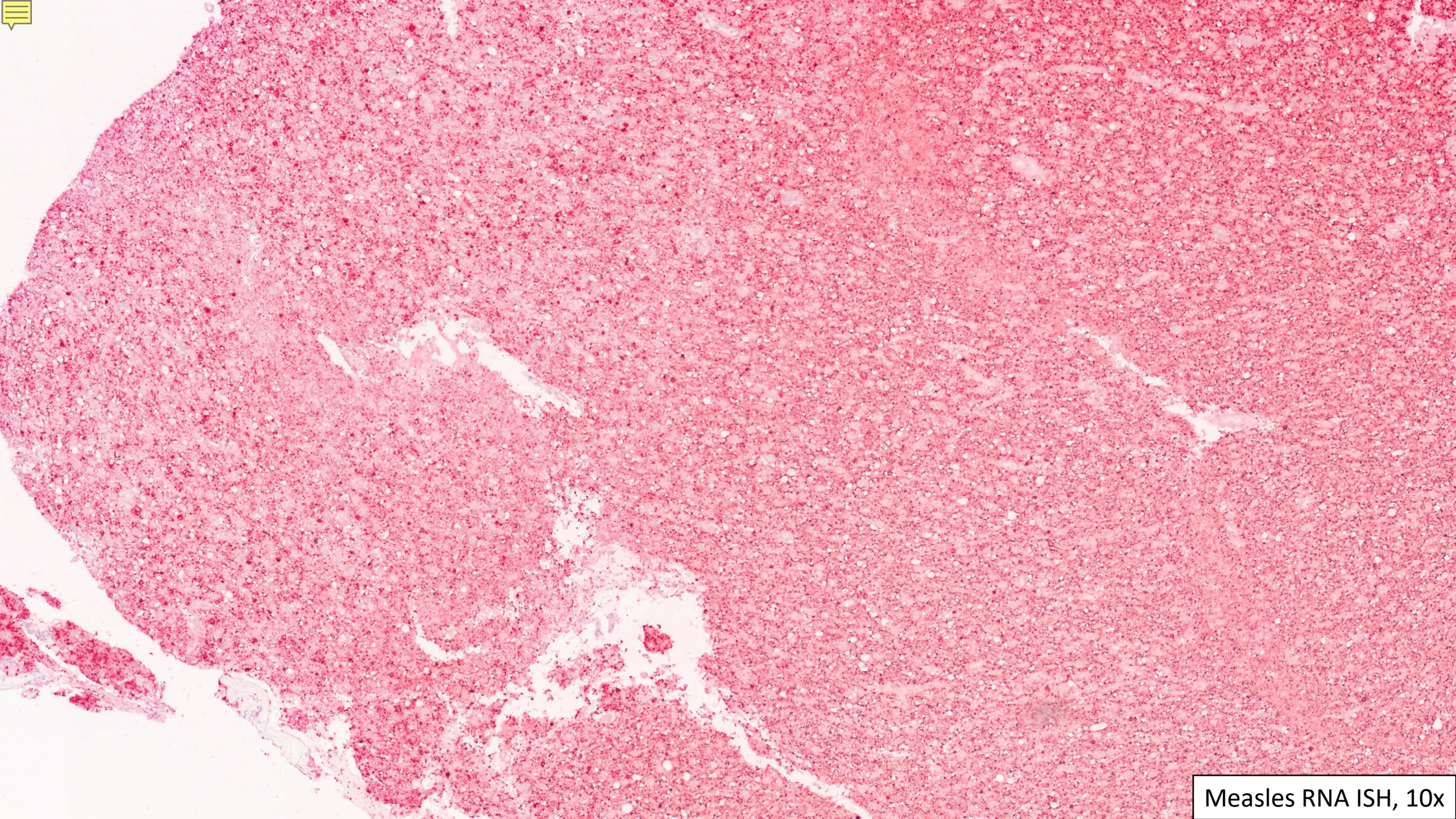


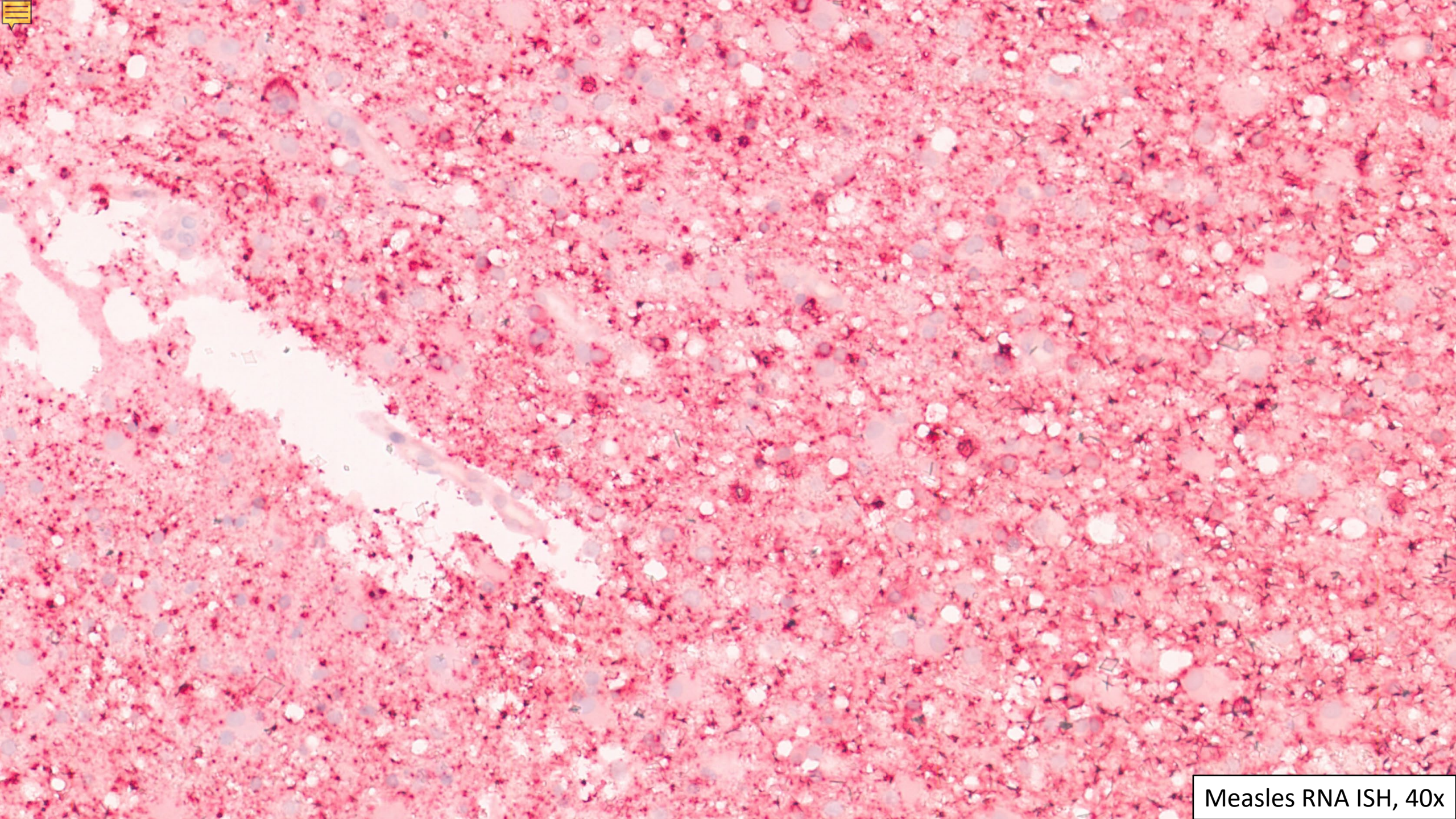
Electron Microscopy





Measles RNA ISH Negative Control


Measles RNA ISH, 10x


Measles RNA ISH, 40x

Final Diagnosis

Brain, Right Frontal, Biopsy:

Subacute Sclerosing Panencephalitis

Discussion Points

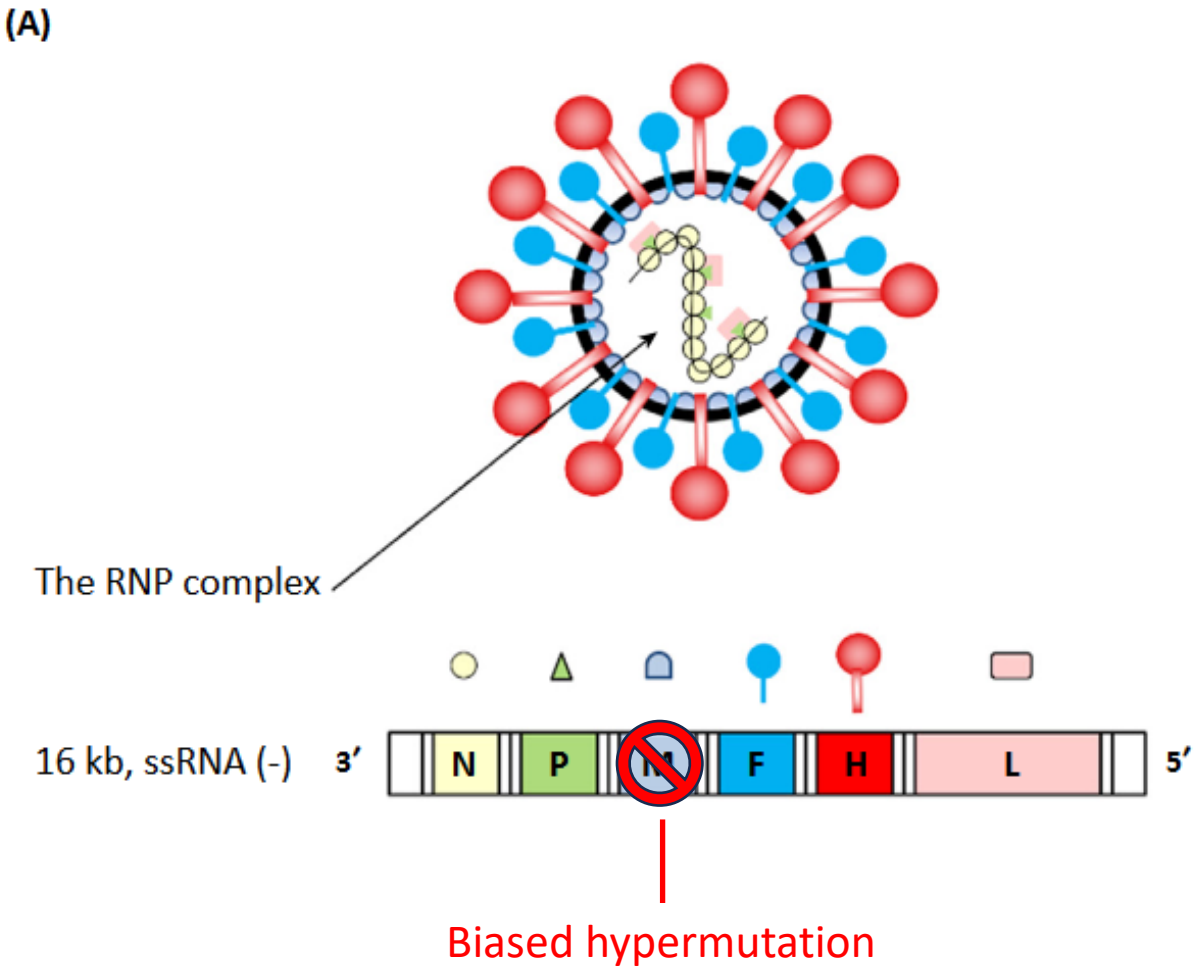
- SSPE is a progressive subacute encephalitis usually presenting years after initial infection by measles
- Likely first described by Dawson in 1933-34
- First associated with measles virus by Bouteille in 1965
- Some features overlap with measles inclusion body encephalitis (MIBE)
- MIBE occurs primarily in immunocompromised individuals and has an accelerated course
- Both SSPE and MIBE are progressive, incurable diseases with high mortality

Differential Diagnosis: SSPE vs MIBE

- MIBE occurs weeks to months after infection, not years
  - Our patient had no recent infection and likely was exposed in the years prior to adoption
- MIBE is primarily associated with immunosuppression
  - Our patient had no known baseline immunosuppression
- MIBE often has abundant inclusions (as seen in this case), normally sparser in SSPE
  - Possibly related to therapeutic immunosuppression in this case

Pathogenesis of SSPE

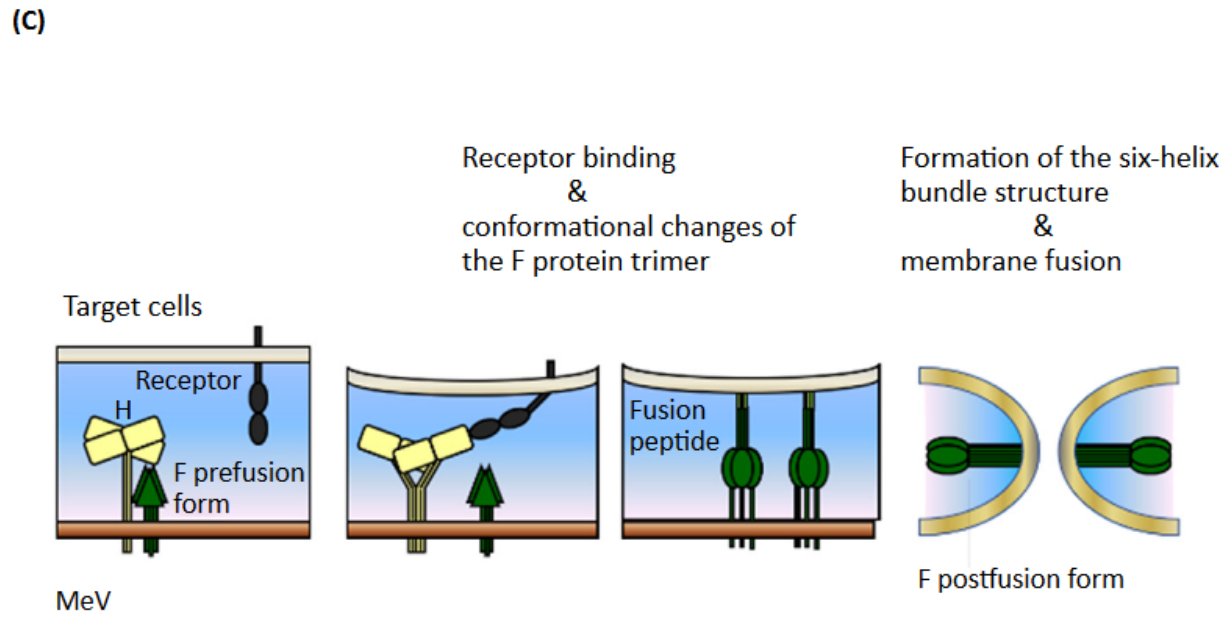
- SSPE is hypothesized to be caused by a mutated form of the measles virus
  - Virus enters brain during acute infection, but is not cleared
  - Over time CNS RNA editing (e.g. ADAR1) selectively hypermutates the matrix gene preventing its translation and reducing viral release
  - This explains the negative measles antigen (M protein) testing on IHC and viral escape from immune detection



Watanabe et al., 2019

Pathogenesis of SSPE

- SSPE is hypothesized to be caused by a mutated form of the measles virus
  - Measles fusion protein production persists, allowing for intercellular fusion events and massive direct cell-to-cell spread of viral nucleic acid
- Application of RNAscope technology to SSPE
  - The strong diffuse expression of viral RNA demonstrates the spread of the disease far beyond what is appreciated on H&E and EM



Watanabe et al., 2019

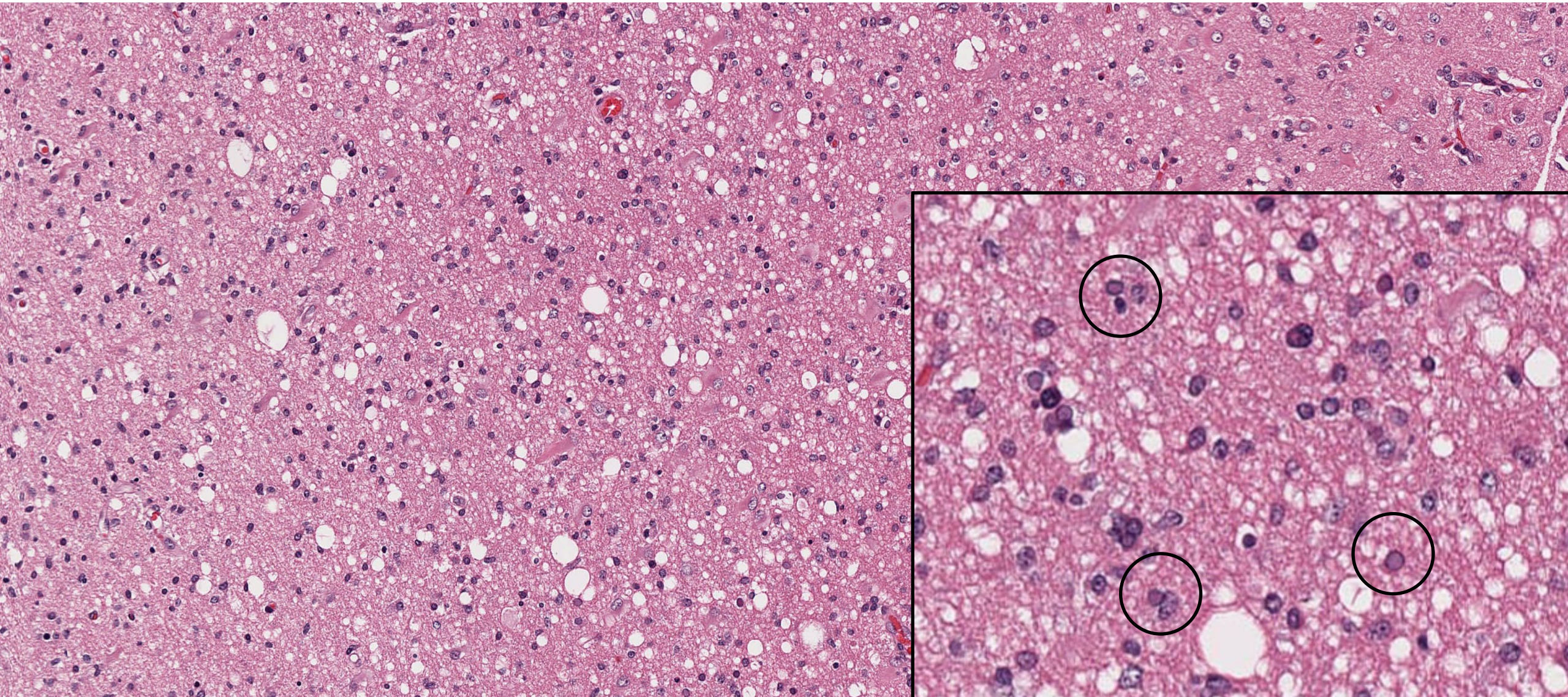
Patient Follow-Up

- The patient passed away about five months after presentation
- No autopsy was performed

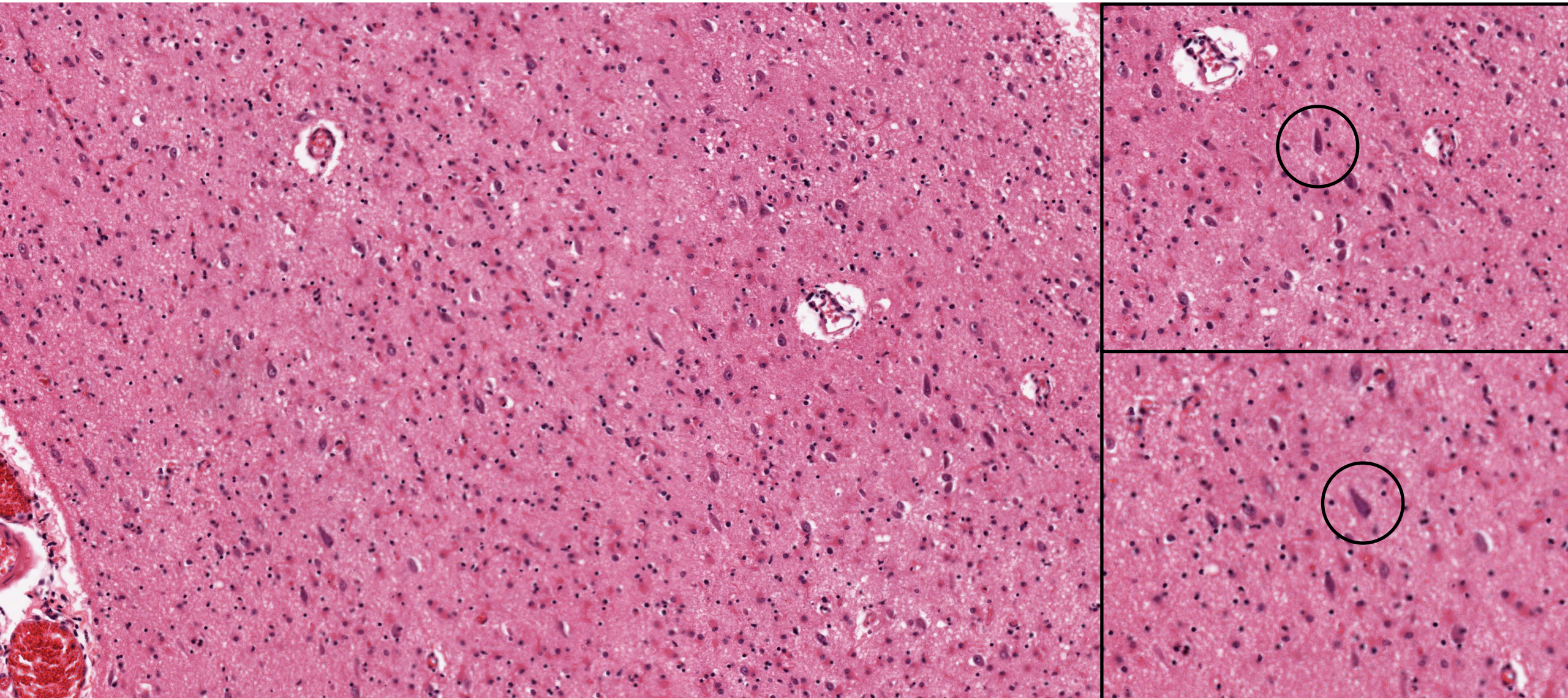
Take-Home Points

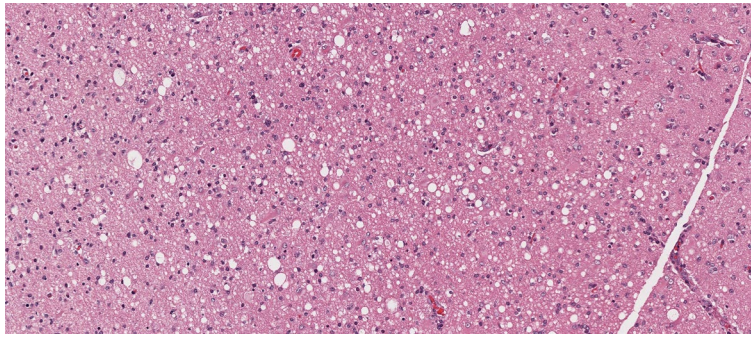
- Measles virus infection and SSPE/MIBE are currently rare but decreasing vaccination rates could mean an increase in cases
- Negative measles virus IHC does not necessarily indicate absence of the virus
- RNA ISH can be employed to resolve difficult cases

SSPE, 2003 DSS



SSPE, 1983 DSS

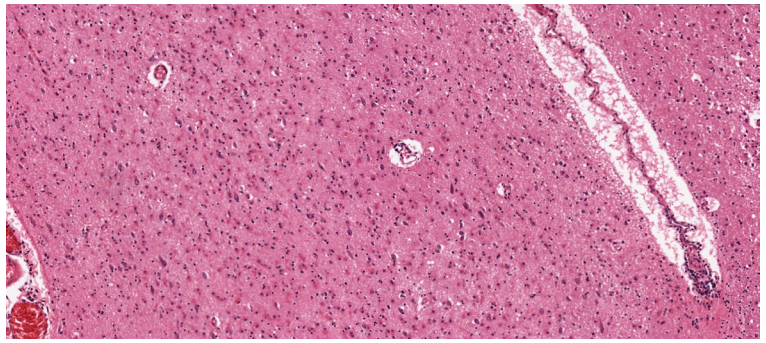




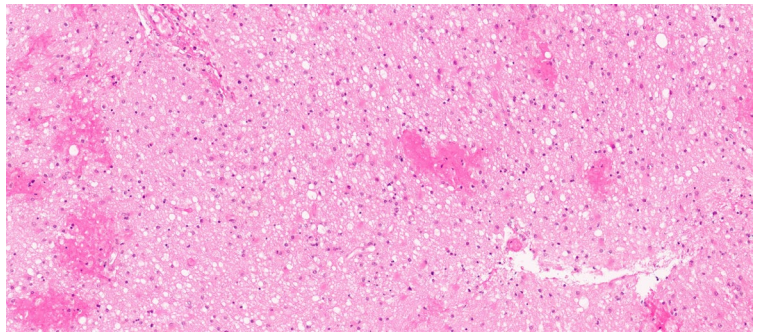
2003 DSS

2044 DSS??

1983 DSS



2024 DSS



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