2017 AANP Diagnostic Slide Session – Case #10

Andrew Guajardo, M.D.
The Johns Hopkins Hospital

Disclosures

- No relevant financial disclosures.

Clinical History

- 14 yo M with a h/o MDS s/p bone marrow transplant
- Significant family history for carcinoma and lymphoma
- Developmental delay
- Immunocompromised w/ recurrent infections
- GVHD

Radiology

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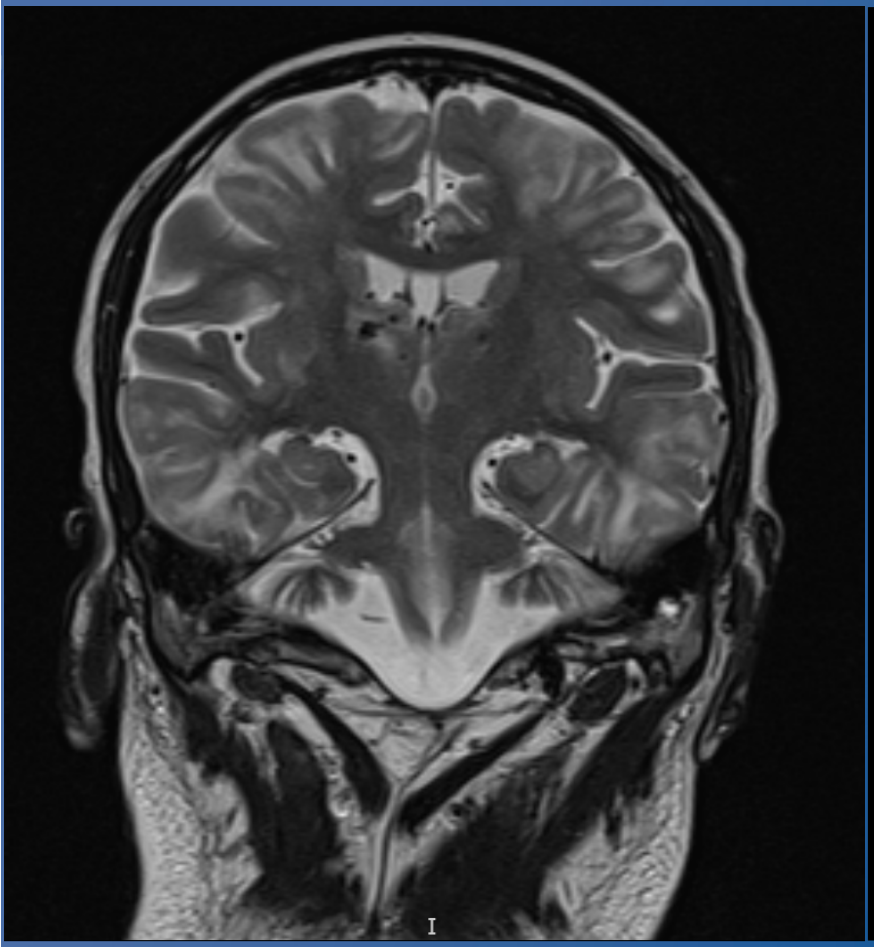
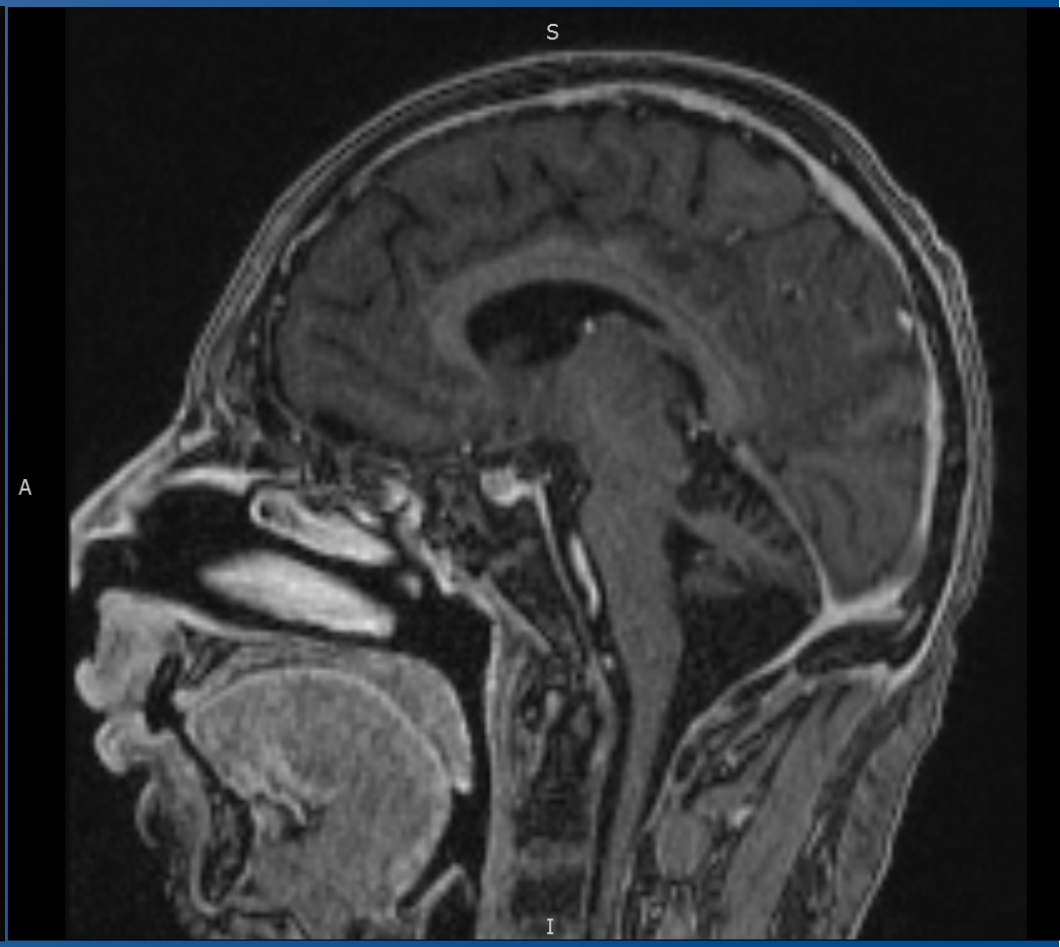
T2 Coronal MRI



T2 Sagittal MRI



Gross & Microscopic

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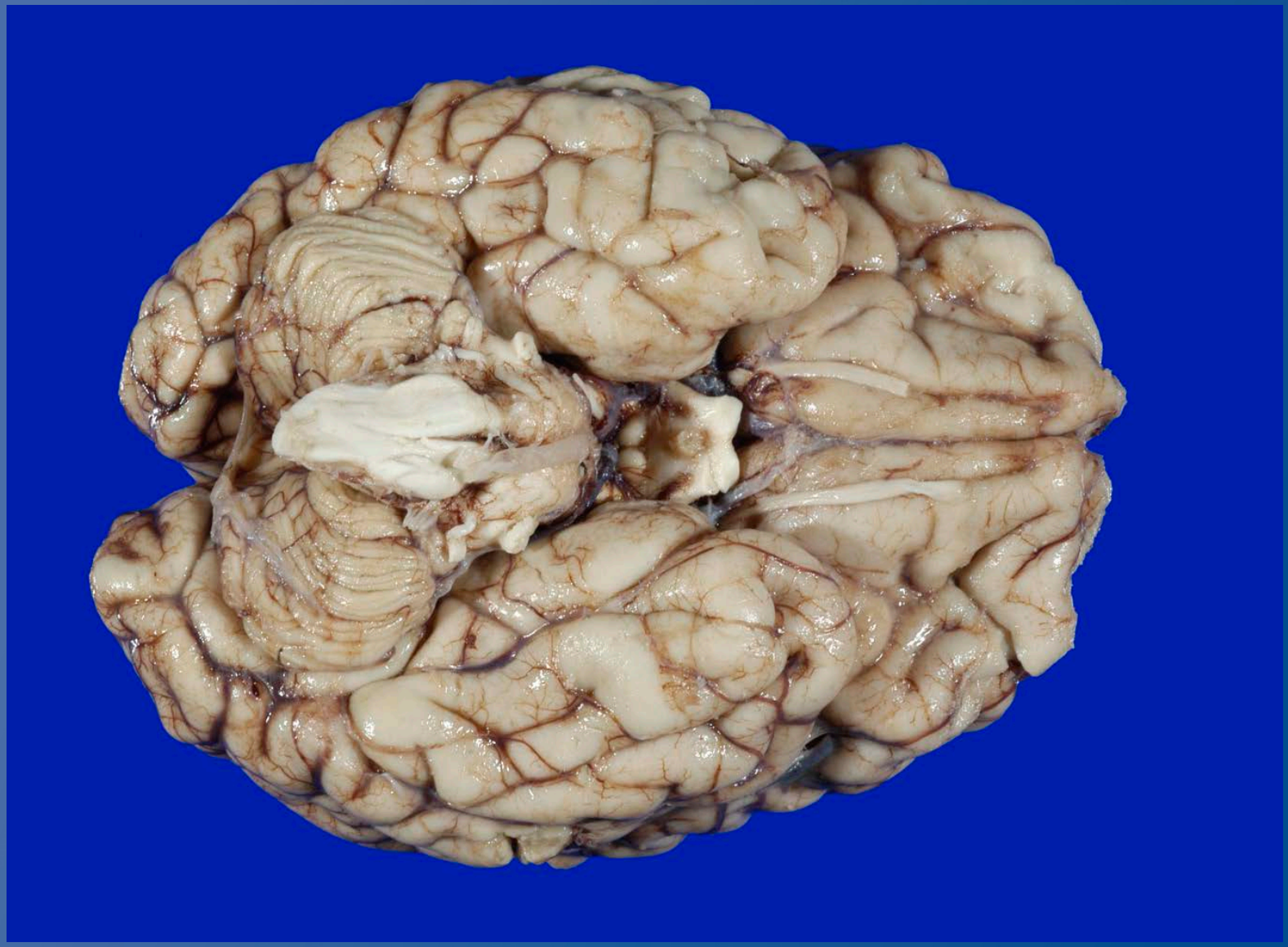

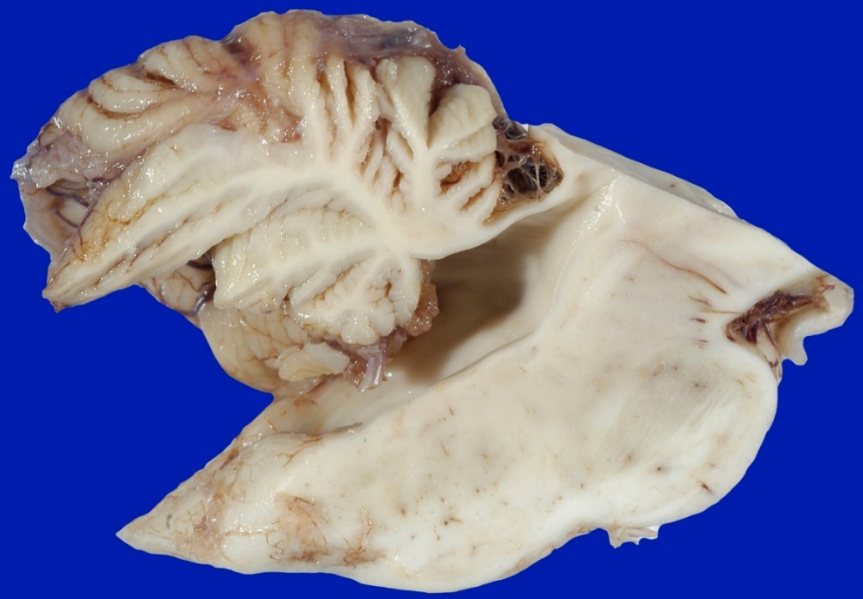


CM
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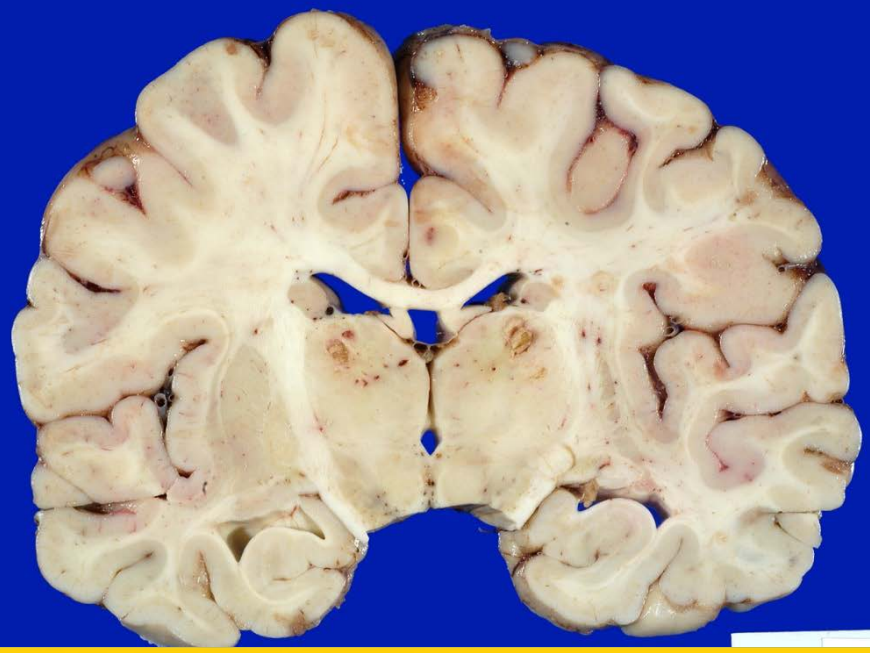

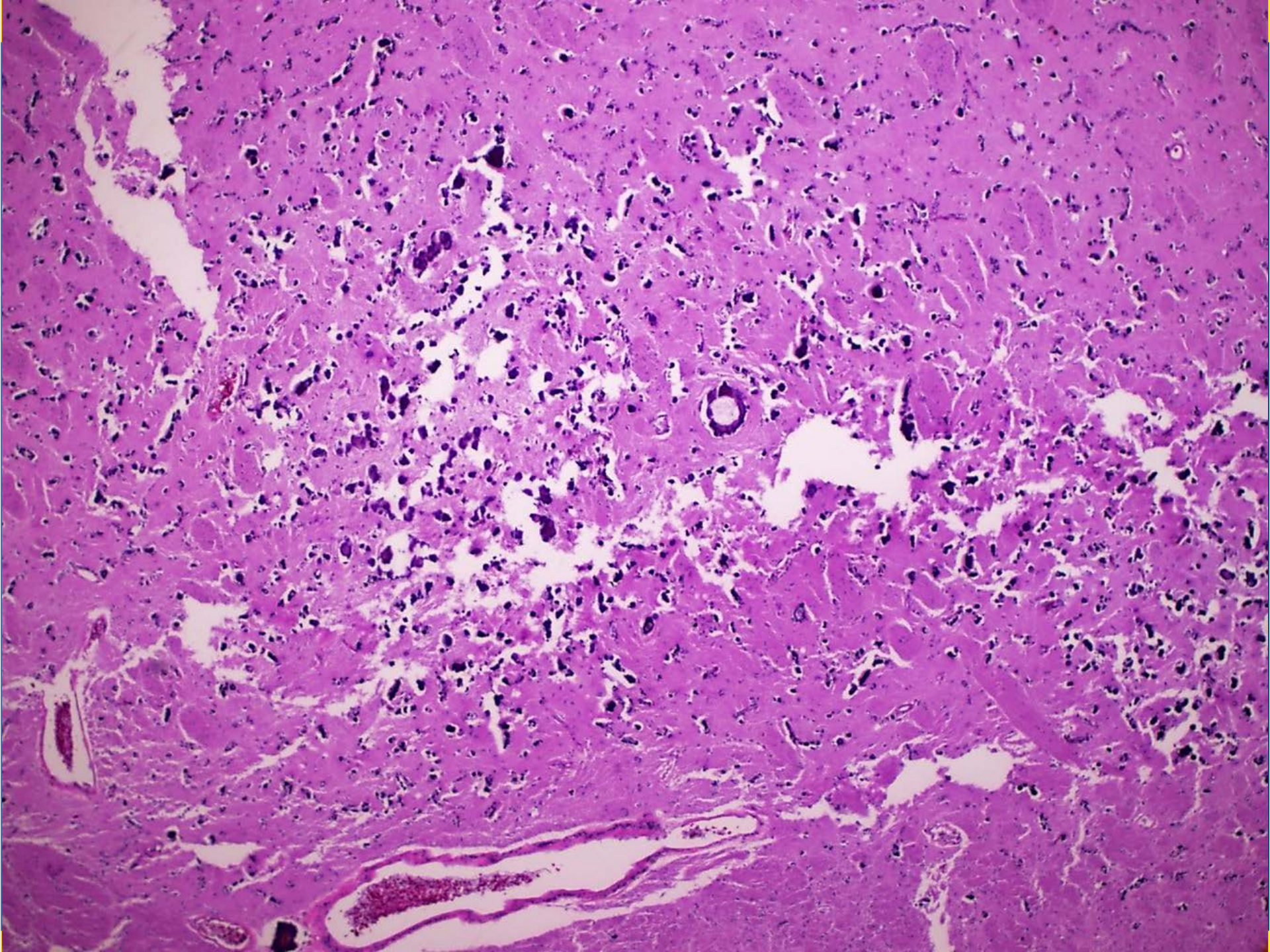

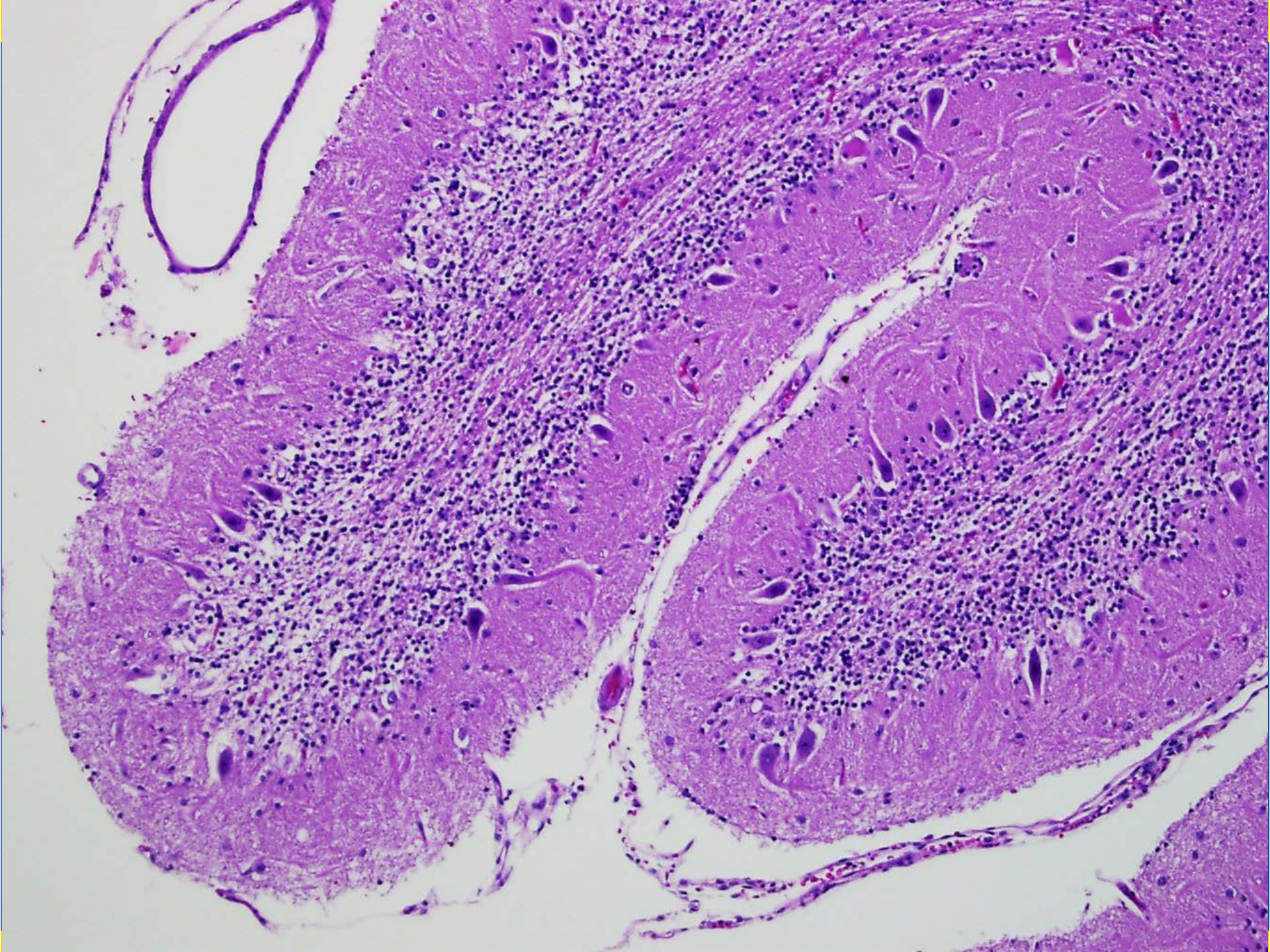

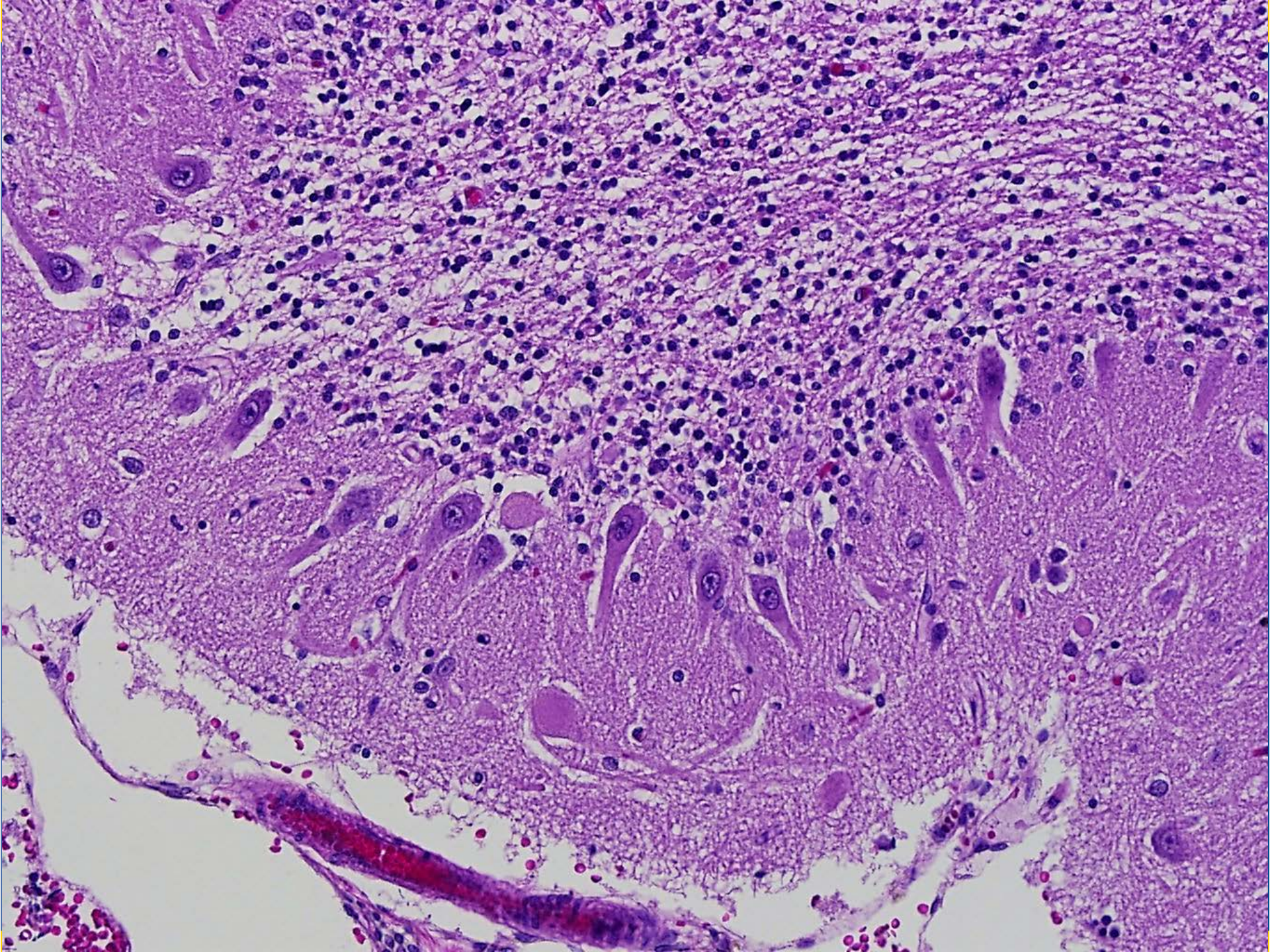

Differential Diagnosis & Discussion

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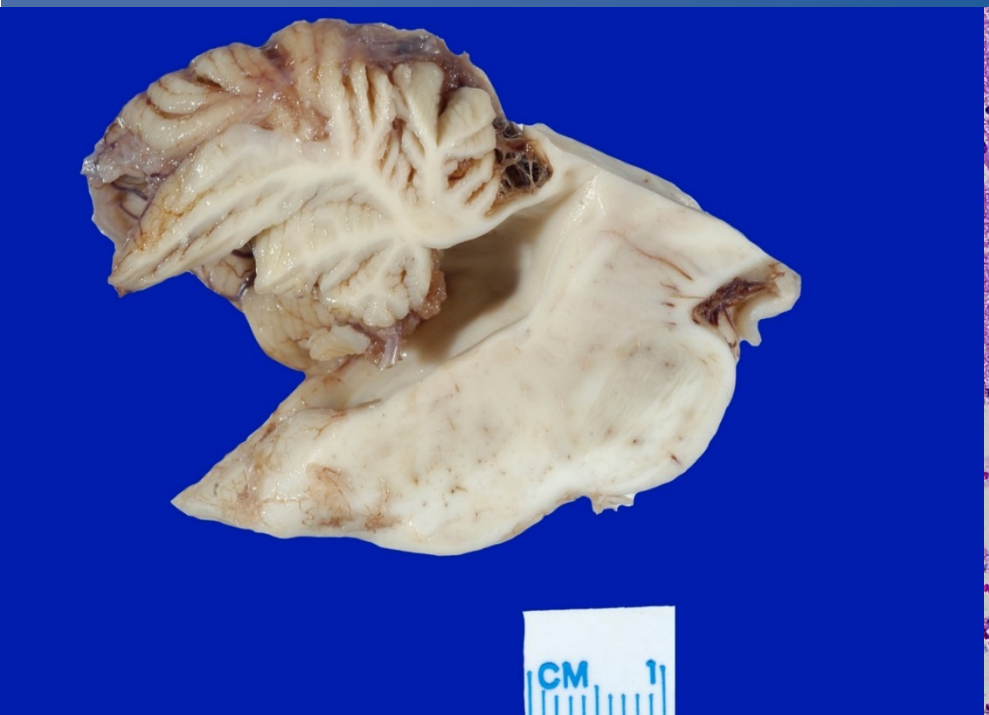

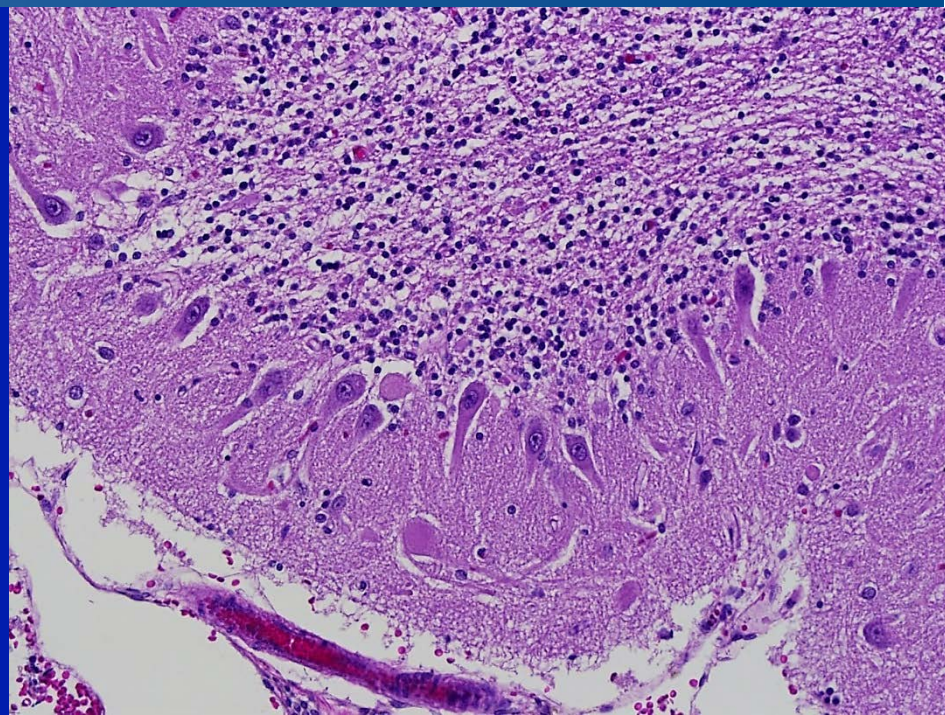

Additional Autopsy Findings

- Full autopsy performed
  - Reticulated hyperpigmentation of the skin, absent nail beds, alopecia, testicular atrophy
  - Organizing and interstitial fibrosis, lung
  - L ventricular papillary muscle infarct
  - Mineralization, neocortex, basal ganglia, thalami, and leptomeningeal vessels
- Genetic Testing
  - Significantly shortened telomere lengths in blood

?

Dyskeratosis Congenita

Hoyeraal-Hreidarsson Variant

Discussion

- charact
- Revesz
  calcifications

(Bakar et al., 2015)

Dyskeratosis Congenita - Telomeres

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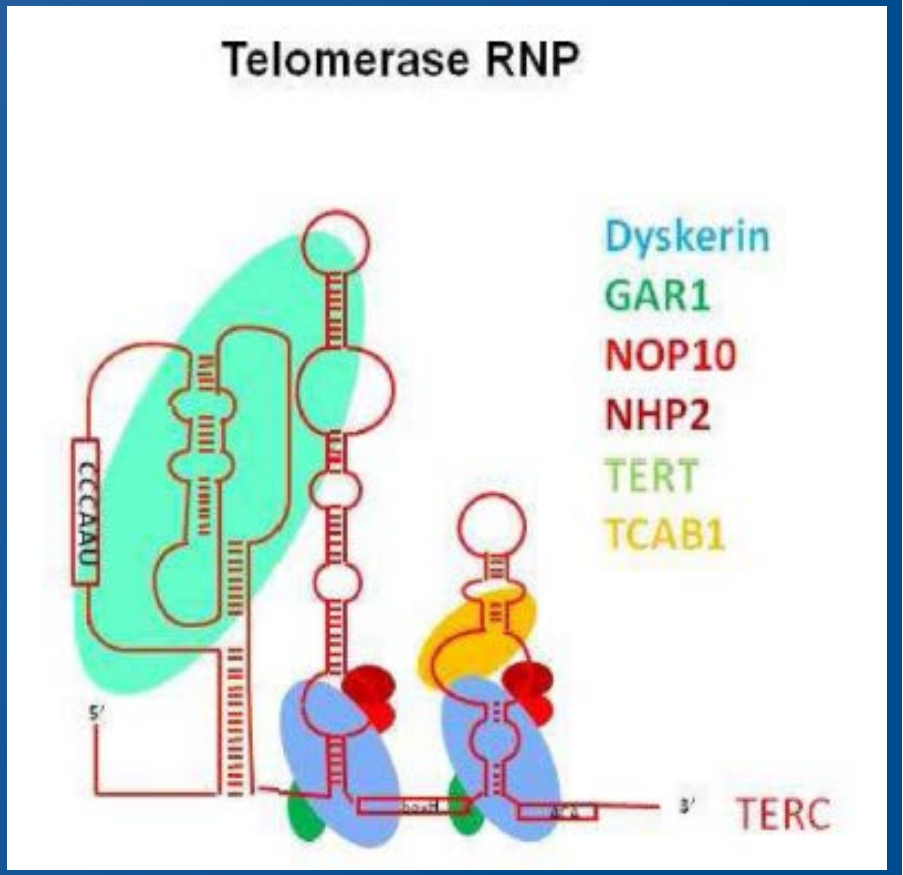
- Normally increased telomere activity is observed in tissues with rapid turnover (eg. mucosa, nails, skin, hematopoietic stem cells)
- All known causative mutations affect function of telomerase activity/assembly, or in telomere integrity
- Maintenance of telomeres generally a neoplastic feature
  - Shortened telomeres may result in p53 involved cell arrest
  - Rarely, additional mutations result in chromosome instability
  - Cycles of chromosomal fusion/breakage -> tumorigenesis

Published in final edited form as:
Cancer Genet. 2011 December ; 204(12): 635–645. doi:10.1016/j.cancergen.2011.11.002.

The genetics of dyskeratosis congenita

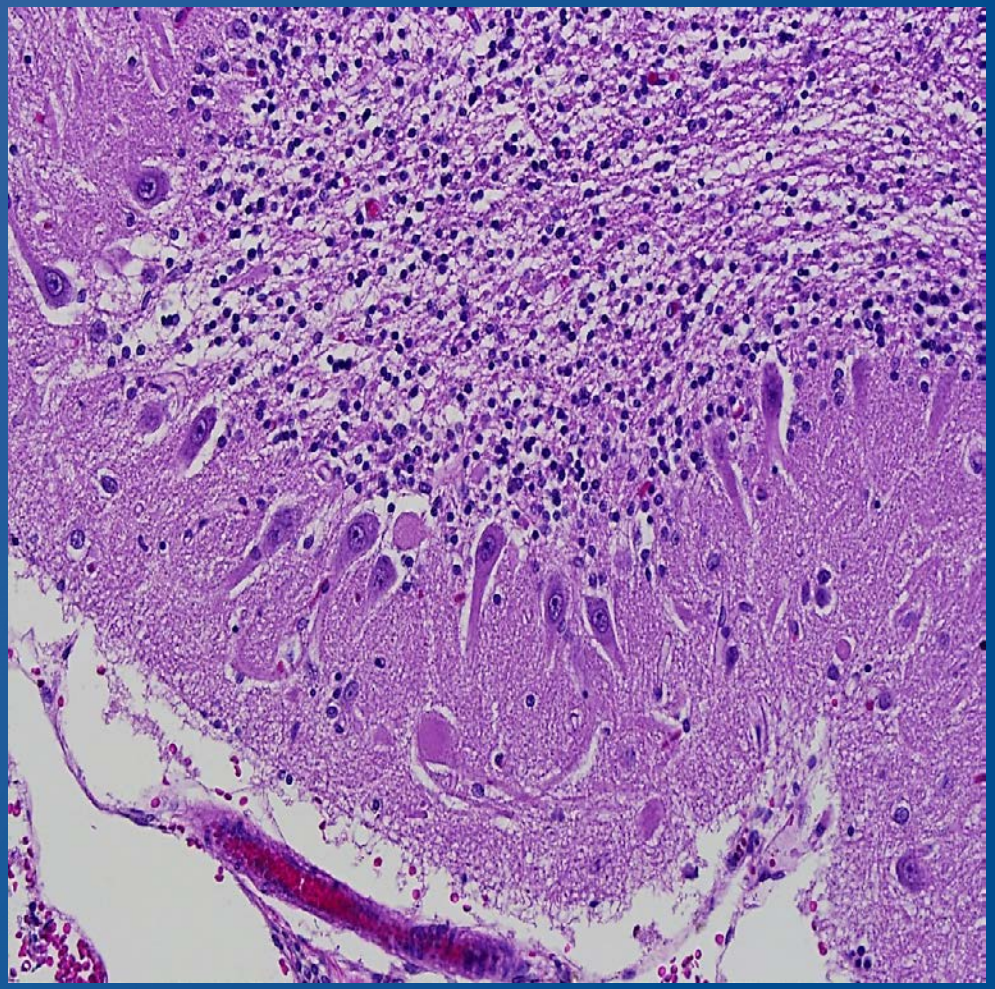
Philip J Mason[a,*] and Monica Bessler[a,b]
[a]Division of Hematology, Department of Pediatrics, Children's Hospital of Philadelphia, University of Pennsylvania
[b]Department Internal Medicine, University of Pennsylvania

- Most commonly due to X-linked recessive mutations in *DKC1* gene resulting in single amino-acid substitution of dyskerin
  - Less common autosomal dominant and recessive forms
- Our patient found to have telomere lengths <1st percentile, but no specific identifiable mutation
- Variable age of onset



Key Points - Pathology

- DC is a clinical, radiological, pathological, and genetic diagnosis
- Cerebellar hypoplasia characteristic of HH
  - Hypoplasia of the granular layer *without* loss of Purkinje cells
    - Different from Ataxia-Telangiectasia and Myelocerebellar disorder
  - Additional NP findings
    - Reported cerebral calcifications, delayed myelination, hypoplasia of corpus callosum



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