NHPRC Consortium Nonhuman Primate Research Center Consortium
Primate Pathology Image Database

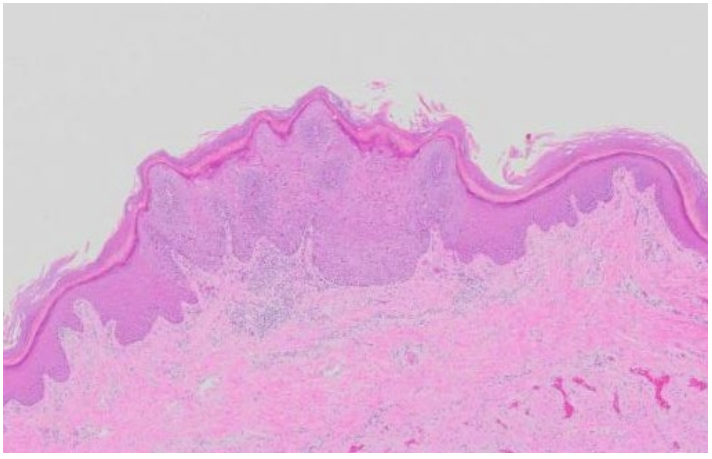
April 2020

Dear PPID Users,

Greetings to all. Hope this finds you all well and adapting to whatever Covid-19 related circumstances you find yourselves in. As the Covid-19 pandemic was accelerating globally in March, I let the newsletter take a short hiatus. Now we are back, grateful for the infrastructure that allows us to share this material with you all virtually. Covid 19 may be global but so are you all; PPID has users from Europe, Asia, Australia, New Zealand, and North America.

So this message is one of a series of brief monthly communications regarding the Primate Pathology Image Database (PPID), a product of the Nonhuman Primate Research Center Consortium. The newsletters are intended to provide updates on the PPID, highlight specific content, and solicit occasional input from users. **If you know of anyone who would like to gain access to the PPID, send them our way!**

The case for April 2020 is a juvenile male baboon (*Papio* sp.) Image ID 31954. There are both gross images and whole slide scans for this case in the database. I chose it, in part, because in these currently tumultuous and uncertain times, I wanted to use a very straightforward case.



You can access the PPID through https://info.nhprc.org/. Please follow the links on the homepage to access the Primate Pathology Image database and its supporting documentation, including this newsletter archive. The Primate Pathology Image Database is within the dropdown menu for applications. If you have any problems accessing the PPID please contact support@nhprc.org for help.

Answers for February cases are in the attached pdf.
Feel free to share any Covid 19 stories. I'd love to hear how everyone is doing.
Wishing you all the very best.

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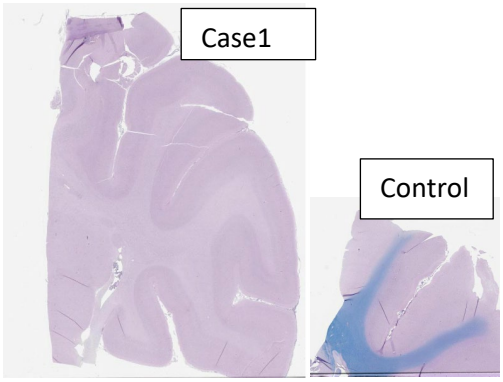
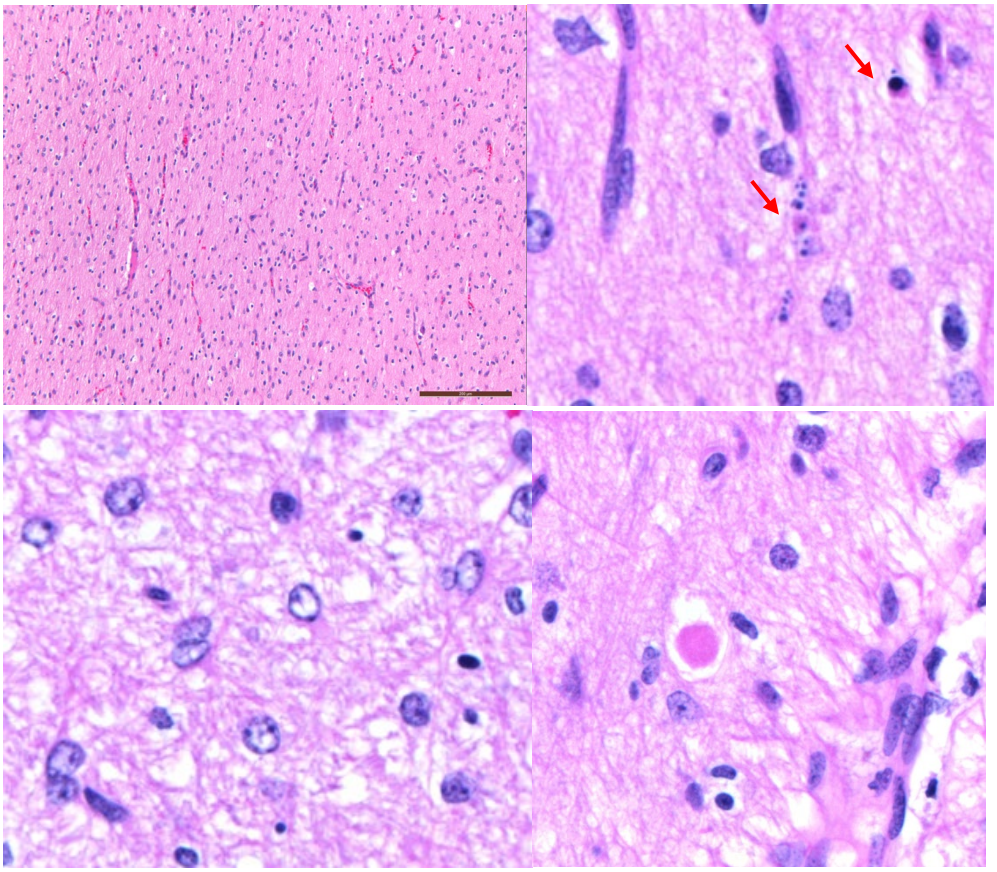
For February 2020, there were two cases united by the common theme of leukodystrophy. The images below are from Luxol fast blue/PAS stained sections.

Case 1 Image 65892, 54 day old male rhesus macaque. On the same slide is a section of cerebrum from an age matched control.



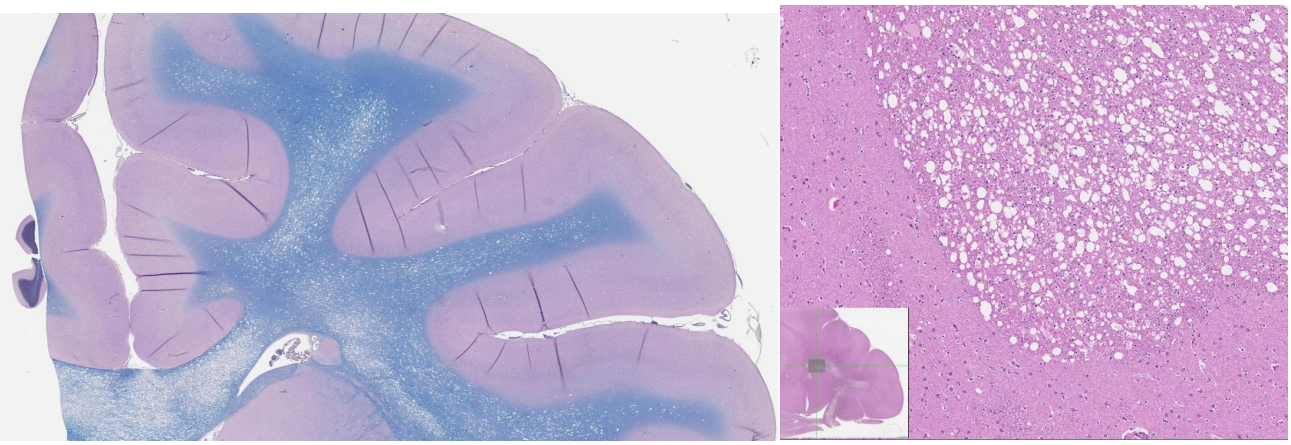
Case 1 presented with neurologic signs consisting of profound intention tremors which worsened with excitement, intermittent vertical and horizontal nystagmus with jerk phase to right, pupillary light reflexes and consensuals intact but mildly decreased, and apparently normal mentation with mostly normal but some abnormal vocalizations during examination.

Histologically, there was diffuse white matter gliosis with increased number of necrotic/apoptotic glia, numerous reactive astrocytes, and rare spheroids.

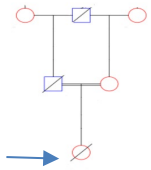


The results of the Luxol fast blue stain allowed us to narrow down the likely genetic defect responsible for the lesion. As the age matched control shows, a 54 day old macaque infant should have some degree of myelin development. This animal had none. Hypomyelination in humans is seen with Pelizaeus-Merzbacher disease caused by defects in *PLP1. PLP1* encodes for proteolipid protein, a major component of myelin. The gene is found on the X chromosome so, for the most part, males are affected. This male animal was hemizygous for the mutated gene.

Case 2. Image 65891, 1 year, 330 day old female rhesus macaque.



The second case presented with neurologic signs consisting of persistent mild tremor of hands, short seizure-like activity, episodic severe hand and arm tremors, and generalized seizures. The Luxol fast blue stain highlights the degree of white matter vacuolation which is most severe centrally. In this case, the list of potential genetic white matter disorders was more extensive and initial focus was on inborn errors of metabolism resulting in myelin vacuolation such as 'maple sugar urine' disease. It was entirely the genetics group, specifically Sam Peterson, who identified a defect in *CLCN-2,* which codes for ClC2, a chloride ion channel protein. Defects in this gene are the cause of CLCN-2 Related Leukoencephalopathy in humans. It is an extremely rare condition first described in 2013 with only 16 reported cases to date. ClC-2 is a ubiquitous protein; expression in the brain is primarily in astrocytes, neurons. The protein is involved in ion and water homeostasis. Defective ClC-2 results in intramyelinic edema. The disease has an autosomal pattern of inheritance. Interestingly, this animal was the product of a half sib mating.



February 2020's cases represented diseases in rhesus macaques for which the genetic basis has been determined through collaboration with Drs. Betsy Ferguson and Sam Peterson at the Oregon National Primate Research Center using the **Macaque Genotype and Phenotype Resource (mGAP)**. mGAP provides access to genotype data collected on a large, pedigreed, rhesus macaque colony housed at the Oregon National Primate Research Center (ONPRC) as well as animals from each of the National Primate Research Centers. It provides researchers with the tools to explore naturally occurring genetic variation in macaques. The database of DNA variants is curated and heavily annotated, and can either be viewed through its genome browser or downloaded for external use. mGAP is found at https://mgap.ohsu.edu/. Like the PPID, access is through a registered user mechanism. To request an account, please use the 'Request Access' link at the bottom of the page. mGAP is an NIH funded project, supported by R24OD021324. As with the PPID, feel free to share information about mGAP with colleagues who might be interested.

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