Brain – Intramyelinic Edema

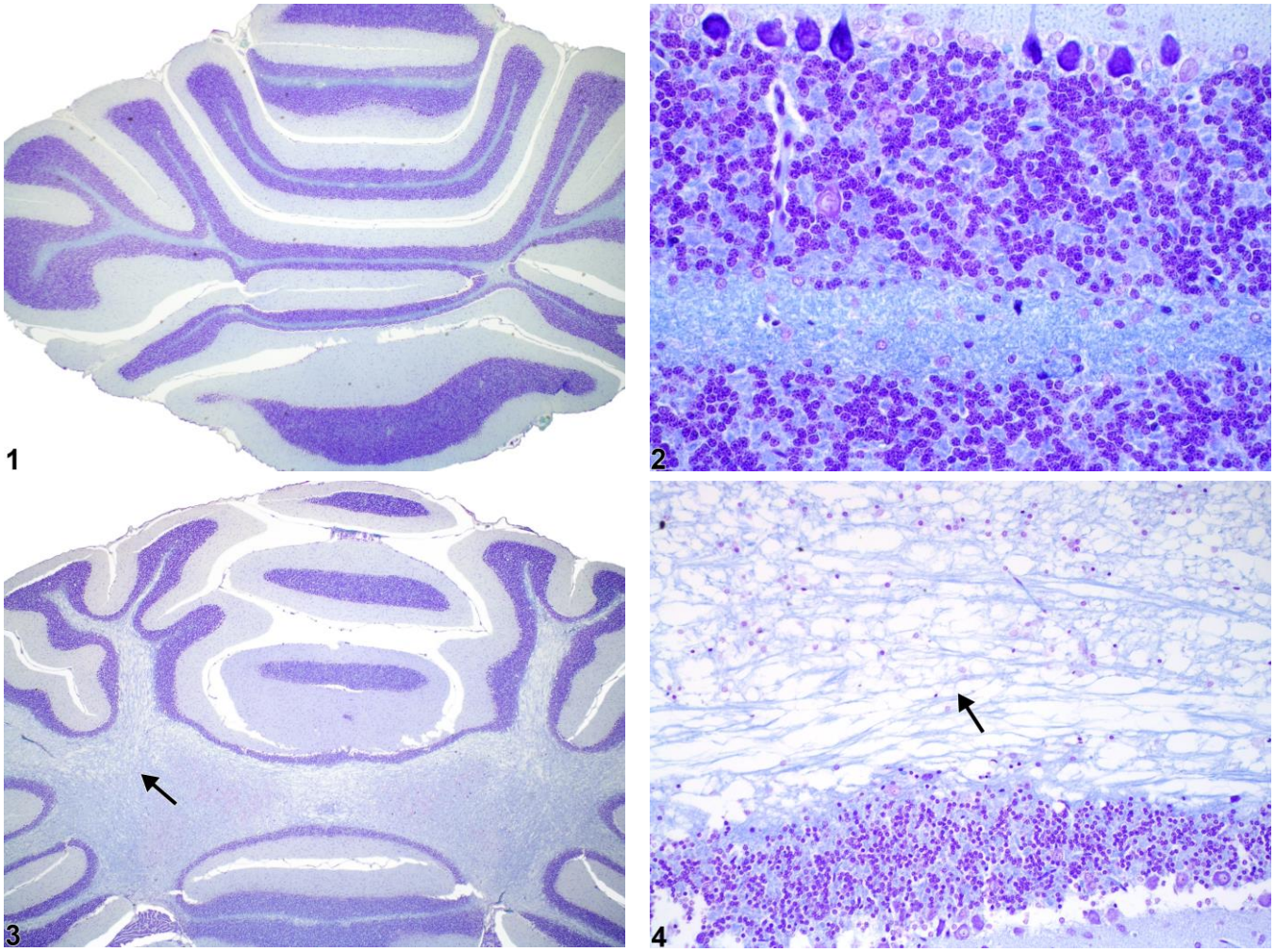

Figure Legend: Figure 1 Normal appearance of myelin in cerebellar white matter stained with Luxol fast blue and cresyl violet in a control rat. Luxol fast blue and cresyl violet stain. Image kindly provided by Dr. G. Krinke. **Figure 2** Normal appearance of myelin in cerebellar white matter stained with Luxol fast blue and cresyl violet in a control rat (higher magnification of Figure 1). Luxol fast blue and cresyl violet stain. Image kindly provided by Dr. G. Krinke.**Figure 3** Brain, cerebellum–morphologic features of toxin-induced intramyelinic edema in white matter (arrow) stained with Luxol fast blue and cresyl violet in a rat. Luxol fast blue and cresyl violet stain. Image kindly provided by Dr. G. Krinke. **Figure 4** Brain, cerebellum–morphologic features of toxin-induced intramyelinic edema in white matter (arrow) stained with Luxol fast blue and cresyl violet in a rat (higher magnification of Figure 3). Luxol fast blue and cresyl violet stain. Image kindly provided by Dr. G. Krinke.

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Comment: The presence of "sponginess" (Figure 4, arrow) of the white matter is always of concern to the neuropathologist since it is commonly an artifact of poor fixation and autolysis. Figure 1 and Figure 2 show the normal appearance of myelin in rat cerebellar white matter stained with Luxol fast blue and cresyl violet. Assessment of the tissue for indicators of poor fixation and autolysis is extremely important to determine genuine white matter lesions. Valid white matter lesions such as demyelination have some useful hallmarks of authenticity (see Spinal Cord - Demyelination), such as bilateral symmetry and the presence of swollen axons or macrophages in affected areas. Other white matter lesions such as intramyelinic edema are observed as severe spongiform change of white matter without any evidence of myelin breakdown or cellular reaction. Classically, intramyelinic edema is caused by lipophilic compounds that result in separation of myelin lamellae at the intraperiod line (confirmed by electron microscopy). In the CNS, this is due to the accumulation of fluid in the cytoplasm of oligodendroglial cells. Well-studied examples of this form of white matter lesion include exposure to hexachlorophene, as shown in Figure 3 and Figure 4. Chronic exposure to hexachlorophene also produces astrocytic hypertrophy and proliferation, as demonstrated by glial fibrillary acid protein immunohistochemical staining. Removal of hexachlorophene exposure has been shown to lead to a reversal of the clinical and microscopic spongiform effects in rats.

Recommendation: In NTP studies where intramyelinic edema cannot be differentiated from demyelination or axonopathy under light microscopy, the lesion should be diagnosed as white matter vacuolation. This should be followed by special evaluation by a neuropathologist. In the case of suspected intramyelinic edema, where axonopathy and inflammatory responses are generally absent, examination of only well-fixed material by electron microscopy may be confirmatory.

When present in NTP studies, the subsite should be noted and lesion severity graded.

References:

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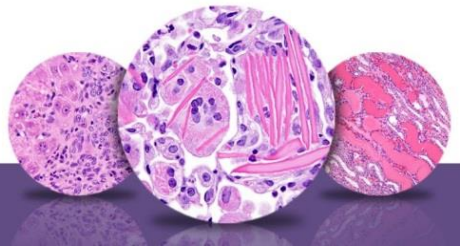

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References:

Tripier MF, Berard M, Toga M, Martin-Bouyer G, Le Breton R, Garat J. 1981. Experimental hexachlorophene encephalopathy in mice and baboons: Light and electron microscopic study. Acta Neuropathol Suppl 7:40-43.
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