Hyaline protoplasmic astrocytopathy

Hyaline protoplasmic astrocytopathy (HPA) describes a rare histologic finding of eosinophilic, hyaline cytoplasmic inclusions in astrocytes, predominantly in the cerebral cortex. It has mainly been observed in children and adults with a history of developmental delay and epilepsy, frequently with focal cortical dysplasia (FCD), but the nature and significance of these inclusions are unclear.

Magaki et al. review the clinical and pathologic features of HPA and characterize the inclusions and brain tissue in which they are seen in surgical resection specimens from five patients with intractable epilepsy and HPA compared to five patients with intractable epilepsy without HPA using immunohistochemistry for filamin A, previously shown to label these inclusions, and a variety of astrocytic markers including aldehyde dehydrogenase 1 family member L1 (ALDH1L1), SRY-Box Transcription Factor 9 (SOX9), and glutamate transporter 1/excitatory amino acid transporter 2 (GLT-1/EAAT2) proteins. The inclusions were positive for ALDH1L1 with increased ALDH1L1 expression in areas of gliosis. SOX9 was also positive in the inclusions, although to a lesser intensity than the astrocyte nuclei. Filamin A labeled the inclusions but also labeled reactive astrocytes in a subset of patients. The immunoreactivity of the inclusions for various astrocytic markers and filamin A as well as the positivity of filamin A in reactive astrocytes raise the possibility that these astrocytic inclusions may be the result of an uncommon reactive or degenerative phenomenon [1)]

Approximately 42 cases of HPA have been reported, including 2 cases presented by Alzoubi et al., consisting of 23 female and 19 male patients. Patient ages ranged from 3 to 39 years. All patients had early-onset seizures (3-20 months of age), ranging from partial to generalized, that were refractory despite treatment with antiepileptic drugs. Postoperative follow-up intervals ranged from 2 to 93 months, and the clinical outcome was graded according to the Engel classification, showing variable results.

Clinicians should consider hyaline protoplasmic astrocytopathy in the differential diagnosis in patients with drug-resistant epilepsy, especially when they are associated with developmental delay and brain malformations. Increasing awareness of this entity among pathologists may promote a better understanding of this condition as well as better diagnosis and treatment for these patients [2)]

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Magaki S, Haeri M, Szymanski LJ, Chen Z, Diaz R, Williams CK, Chang JW, Ao Y, Newell KL, Khanlou N, Yong WH, Fallah A, Salamon N, Daniel T, Cotter J, Hawes D, Sofroniew M, Vinters HV. Hyaline protoplasmic astrocytopathy in epilepsy. Neuropathology. 2023 May 17. doi: 10.1111/neup.12909. Epub ahead of print. PMID: 37198977.

2)
Alzoubi H, Nobile G, d'Amati A, Nobili L, Giacomini T, Tortora D, Gaggero G, Gianno F, Giangaspero F, Antonelli M, Consales A. Hyaline Protoplasmic Astrocytopathy in the Setting of Epilepsy. Am J Clin Pathol. 2023 Feb 1;159(2):120-128. doi: 10.1093/ajcp/aqac145. PMID: 36495294.