Hippocampal sclerosis, ILAE Type 3 (CA4 predominant neuronal loss)

Clinical history. A 10-year-old girl with left temporal lobe epilepsy since the age of one year, who previously underwent surgery for a dysembryoplastic neuroepithelial tumour (DNT) at another hospital.

Histopathology and immunohistochemistry. We received en bloc resected and formalin-fixed hippocampal tissue (1.5x1.5x0.6 cm). The specimen was dissected at 5-mm thickness along the coronar plane and embedded into paraffin. H&E staining revealed a tumour with moderate cellularity, infiltrating the entorhinal cortex and subiculum. The tumour was predominately composed of glial cells showing small round or ovoid nuclei and eosinophilic cytoplasm with ramifying processes. No mitotic figures were demonstrated. Within the glial tumour matrix, there were dysplastic ganglion cells. Small infiltrating clusters of tumour cells could be identified also in the hippocampus proper. There were decreased pyramidal cell densities in sectors CA1 and CA2, whereas CA3 and CA4 were almost depleted of pyramidal cells. Granule cell loss also could be identified in the dentate gyrus, which showed bi-laminated architecture in addition.

Immunohistochemistry for GFAP confirmed the astroglial component of the tumour, which showed only low proliferation (1% Ki67). MAP2 immunoreactivity led to identification of dysplastic ganglion cells, but no neoplastically transformed glial cell elements. CD34 immunoreactivity stained positive for the majority of tumour cells, as well as infiltrating tumour cell clusters within the hippocampus proper. NeuN immunoreactivity confirmed a slight decrease in neuronal cell density in CA1 and CA2, as well as subtotal pyramidal cell depletion in CA3 and CA4. No immunoreactivity for p53 or for mutation-specific IDH1 was demonstrated.

Comments. This case presented with dual pathology, i.e. hippocampal sclerosis and a CD34-immunoreactive ganglioglioma (WHO I°). The tumour was located outside the hippocampus proper, but already showed infiltrating cell clusters (perfectly visible using CD34 immunoreactivity). Although pyramidal cell densities are reduced in all segments of the hippocampus, they are most pronounced in CA3 and CA4. Neuronal cell depletion in CA3 and CA4 and granule cell dispersion were not interpreted to result from tumour infiltration, and this atypical pattern of hippocampal sclerosis was classified according to the ILAE system as HS Type 3 (Blumcke et al., 2013). Based on the clinical information, we expected to review a DNT, but could not identify any DNT-specific cellular architecture (i.e. specific glio-neuronal element or multinodular growth pattern).

Microscopic findings in HS ILAE Type 3

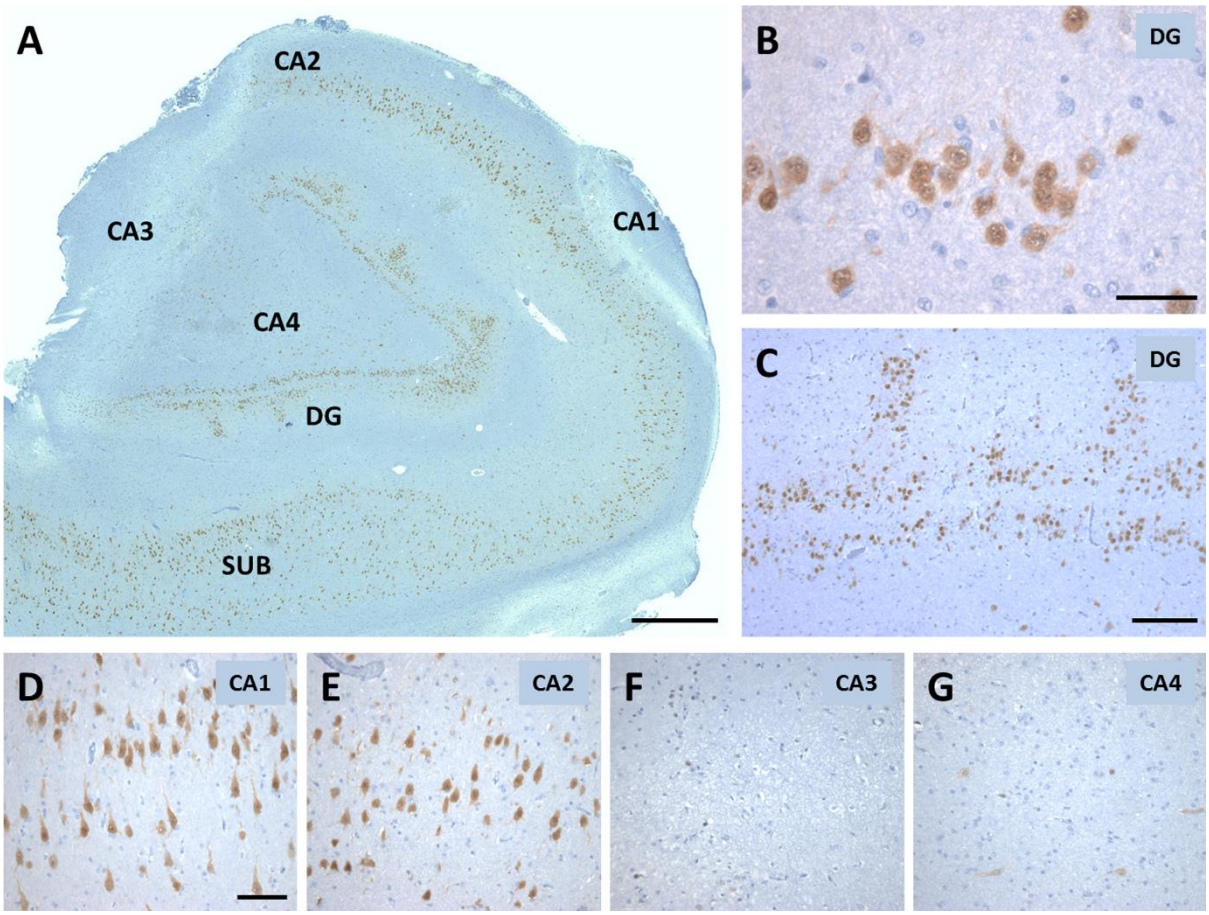

Figure 1. NeuN immunohistochemistry. (A) Slightly decreased pyramidal cell densities in sectors CA1 and CA2, whereas CA3 and CA4 are almost depleted of pyramidal cells. (B, C) The granule cell layer with severe cellular loss (B), as well as a bi-laminated architecture and heterotopic clusters in circumscribed areas (C). (D-G) Slight decrease in neuronal cell density in CA1 and CA2, as well as subtotal pyramidal cell depletion in CA3 and CA4. Scale bar in (A): 1000 µm. Scale bar in (B): 50 µm. Scale bar in (C): 200 µm. Scale bar in (D-G): 100 µm.