

High Resolution MRI of Xanthogranuloma of Choroid Plexus Induced by Hypercholesterolemia

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Introduction: Symptomatic intracranial xanthogranulomas mostly arise in the third ventricle, the choroid plexus of the lateral ventricle and the dura mater, showing hydrocephalus and neurological deficits due to mass effect ⁽¹⁾. Pathological findings of central nervous system xanthogranulomas are not rare (1.6-7%) ⁽²⁾. Although case reports have shown that such lesions are occasionally associated with hyperlipidemia, arteriosclerosis, diabetes mellitus, familial hyperproteinemia, juvenile xanthogranuloma, colloid cysts, or histiocytosis X⁽³⁾, the pathogenesis of this disease is still a matter of debate. Attempting to clarify the etiology of this disease, we fed rabbits a diet rich in cholesterol for an extended period of time. *In vivo* high-resolution MRI and histological studies were performed on brains of these rabbits.

Methods: New Zealand white rabbits were fed 0.125-0.25% cholesterol-enriched diets and maintained hypercholesterolemia for 28 months. *In vivo* high-resolution brain MRI of these rabbits were performed on a 3T scanner interfaced with an insertable gradient coil using 3D FIESTA sequence (100x100x200 μm^3 ; TR/TE, 12/6ms; FA, 20°; BW, 21kHz; phase cycling number/recon, 8/sum-of-squares). Following imaging, brains were dissected after a transcardial perfusion rinse. Hematoxylin and eosin (H&E) staining, Bielschowsky's silver staining, Oil Red O staining for lipids, Ram11 immunohistochemistry for macrophage cells and CD31 immunostaining for endothelial cells were performed on the 10 μm fresh frozen sections or 5 μm paraffin sections of fixed tissues.

Results: *In vivo* high-resolution MRI revealed that 5 of 6 cholesterol fed rabbits developed mass lesions in the choroid plexus. FIESTA images show these masses as tumorous swellings of the choroid plexus with focal areas of hypointensity. The lesions were mainly asymmetrically confined to the choroid plexus of lateral ventricle and ventral fornix in the roof of the third ventricle accompanied by hydrocephalus and remarkable enlargement of the ventricular system (Figure 1). Further histological studies showed that the lesions consisted of characteristic foamy macrophages (histiocytes) and capillary vasculature interspersed among prominent crystalline cholesterol clefts and lipid globules, which is consistent with the histopathology of a xanthogranuloma (Figure 2). Foam cells in and around the xanthogranuloma were positive for macrophage-specific markers. In some cases, the lesions invaded adjacent structures of the brain parenchyma, especially the fornix, hippocampus, and dorsal diencephalon.

Conclusion: *In vivo* high-resolution brain MRI reveals sizable xanthogranulomatous choroid plexus present in the hypercholesterolemic rabbits, which was further confirmed by histological and immunohistochemical examination of these brains. This work supports the view that hyperlipidemia/ hypercholesterolemia are predisposing factors for the formation of xanthogranuloma of the choroid plexus. Ongoing studies will probe this relationship further as well as investigating the connection to other neurodegenerative disorders such as Alzheimer's disease.

References:

1. Kepes JJ. "Xanthomatous" lesions of the central nervous system: Definition, classification, and some recent observations. In Zimmerman HM: Progress in Neuropathology, Vol. 4, New York: Raven Press, 1979; Vol 4, pp 179-213
2. Pear BL. Xanthogranuloma of the choroids plexus. Am J Roentgen, 1984, 143(2), 401-2.
3. Muenchau A, Laars R. Xanthogranuloma and xanthoma of the choroid plexus: Evidence for different etiology and pathogenesis. Clin Neuropathol 1997; 16:72

Figure 1

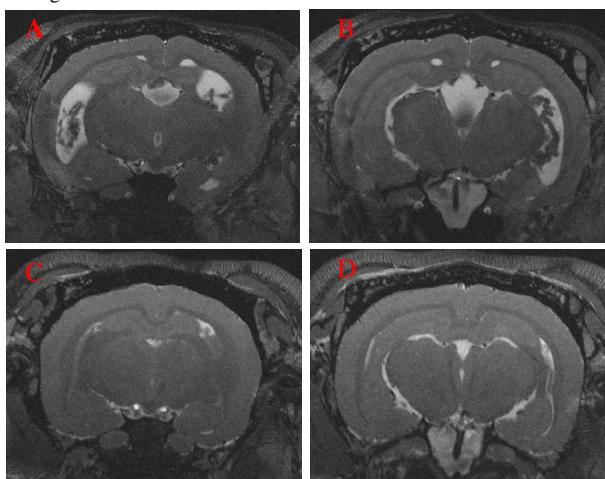


Figure 2

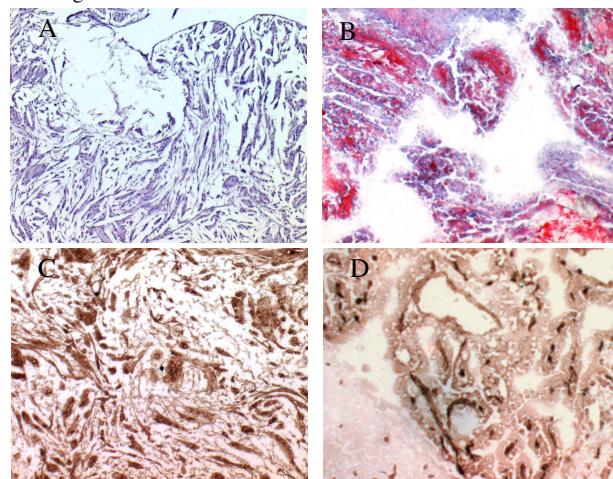


Figure 1. *In vivo* high-resolution MRI reveals mass lesions in the choroid plexus in cholesterol (CH) diet rabbit (A, B) compared with normal diet control (C, D). The lesion appears as a tumorous swelling of choroid plexus, mainly confined to the lateral ventricle with focal areas of hypointensity. Hydrocephalus and remarkable enlargement of lateral ventricles and third ventricle were seen.

Figure 2. Xanthogranuloma of the choroid plexus in cholesterol fed rabbit brain. A. H&E staining shows foamy histiocytes are surrounded by needlelike cholesterol clefts interspersed among foam cells. B. Oil-Red-O-stained section showing numerous red-stained lipid droplets among the cholesterol clefts and foam cells. C. Foamy cells stain positively with the Ram11, a marker for macrophages. D. CD31 immunostaining shows vasculature scattered among cholesterol clefts and foamy cells.