Venous collagenosis: a pathological correlate of white matter hyperintensities
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BACKGROUND
• White matter hyperintensities (WMH) are biomarkers for cerebral small vessel disease, which has a prominent role in stroke, dementia and aging.1,2
• Pathological correlates of WMH include myelin loss, activated microglia and arteriolar disease.3
• A few small studies describe collagenosis of the deep medullary veins as being involved WMH pathogenesis.3
• As periventricular WMH become larger and confluent, periventricular infarcts (PVIs) may form

Purpose:
➢ To use an image-pathology correlative study to explore a potential relationship between WMH and venous collagenosis

METHODS

Participants:

WMH Cohort
• Autopsy confirmed AD patients (n=22)
• Controls (n=18) without neurodegenerative phenomena at autopsy

PVI Cohort
• Subjects (n=6) were part of the Sunnybrook Dementia Study
• All had a pathologic diagnosis of AD
• 12 PVIs were identified on imaging

Tissue Pathology:

WMH Cohort
• Tissue blocks were obtained (Figure 1); 66 from the AD cases and 54 from Controls
• Blocks were embedded in paraffin, cut into 4 μm thick sections, and stained with H&E/LFB and Masson's trichrome

PVI Cohort
• MRIs were used to localize PVIs in formalin-fixed coronally sectioned archived cadaveric brain tissue; 30 blocks were created from 12 PVIs
• Tissue blocks were embedded in paraffin, cut into 5 μm sections, and stained with
  • H&E/LFB
  • Masson's trichrome
  • immunohistochemistry for GFAP, CD68 and neurofilament

Assessing Venous Collagenosis in the WMH and PVI cohort
• % stenosis of large veins (% lvs): [external diameter - internal diameter]/external diameter X 100 on trichrome
• Venous collagenosis severity in medium and small calibre veins (0-3) was assessed

RESULTS

WMH analysis on imaging:
• WMH severity was semi-qualitatively assessed using the Fazekas Scale on 3 levels (anterior, middle and posterior)

Vascular Pathology in the WMH cohort
• Venous collagenosis in both small and medium calibre veins was a common finding in both the AD and Control groups
• Average % lvs was 19.8% and was a frequent finding

WMH and Correlations
• WMH scores significantly correlated with:
  ➢ periventricular white matter pallor (rs(116)=0.252, p=0.006)
  ➢ collagenosis of small veins (rs(114)=0.268, p=0.004)
  ➢ collagenosis of medium veins (rs(114)=0.266, p=0.004)
  ➢ % lvs (rs(112)=0.377, p=0.000)
• % lvs is the strongest predictor of WMH (β=0.330, df=108, p=0.000)

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DISCUSSION
• Venous collagenosis is a frequent finding in individuals with WMH and may:
  ➢ increase vascular resistance leading to decreased perfusion of deep white matter
  ➢ lead to edema in the deep white matter by shunting blood from the internal cerebral veins to the transmedullary veins
  ➢ impair interstitial fluid drainage and facilitate the accumulation of certain toxins such as Beta-amyloid2
• Stenosis of both the small and large veins may be a possible mechanism underlying periventricular WMH with PVIs

CONCLUSION
• Venous collagenosis in periventricular veins of all calibre may underlie the pathogenesis of WMH and possibly lead to infarction
• Neuropathologists should attend to and document the presence of venous collagenosis in the standard neuropathological examination

REFERENCES