CADASIL with Cysteine-Sparing Notch-3 Mutation

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DIAGNOSTIC STUDIES

- Cerebral angiography: 1.7 mm berry aneurysm left MCA at origin of anterior temporal, 1.5 mm berry aneurysm right posterior communicating artery origin
- Laboratory investigations for coagulopathies, leukodystrophies, vasculitides, demyelinating diseases, other causes of vascular dementia unrevealing
- Genetic testing for CADASIL "negative," but with missense mutation in Notch3 (A1020P)

TABLE ONE: NEUROPSYCHOLOGICAL FINDINGS

<table>
<thead>
<tr>
<th>IMPAIRMENTS</th>
<th>WCS learning efficiency</th>
<th>Trails B</th>
</tr>
</thead>
<tbody>
<tr>
<td>D-KEFS concept formation verbal response</td>
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TABLE TWO: COMMON FEATURES OF CADASIL

<table>
<thead>
<tr>
<th>Feature</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Recurrent ischemic episodes (TIA, Stroke)</td>
<td>28%</td>
</tr>
<tr>
<td>Dementia (90% gait disturbance; 86% urinary incontinence; 52% pseudobulbar palsy)</td>
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<tr>
<td>Cognitive deficits</td>
<td>48%</td>
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<tr>
<td>Migraine (87% with aura)</td>
<td>38%</td>
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<tr>
<td>Psychiatric disturbance</td>
<td>30%</td>
</tr>
</tbody>
</table>

FIGURE ONE: MRI OF PATIENT vs KNOWN CADASIL

COGNITIVE STATUS

Attention
- Digit Span = 5 F/ 4 B
- Serial 7's: 100–79 [could not proceed]
- Auditory Vigilance: 2/35 errors of omission
- Trails B: slow

Recall
- 5 objects: 1 trial to register; 2/5 spontaneous recall at 5 min; 3/5 with category cue, 5/5 from list
- Needed daughter’s assistance to relate history in sequence

Language
- Running speech WNL
- Naming, repetition, auditory comprehension, oral reading intact
- Verbal fluency: 25 “T”words in 1 minute

Praxis
- Axial, gestural, tool-use praxis intact

Visual-Spatial
- Clock Drawing: Self-corrected hand placement
- Copy of cube: intact

Frontal-Executive
- Go/no-go: 3/12 errors of commission
- Luria 3-step: required verbal cues
- Proverbs & similarities: WNL

WAIS III VIQ 118 PIQ 111 FSIQ 116

Donepezil 10 mg/day
Sertraline 50 mg/day
Tizanidine 4 mg TID (back pain)
Tramadol 50 mg TID (back pain)
Fexofenadine 60 mg BID
Nortriptyline 50 mg/day

Mildly positive Romberg

MRI FLAIR IMAGES: Left: Multiple isolated and confluent foci of T2 hyperintensities, with temporal sparing. Right: Other patient from our clinic with known CADASIL involving temporal lobes

CONCLUSION

Our case appears similar in both phenotype and mutation to that of 2 recently reported German kindreds.

The similarity of this case to the CADASIL phenotype (Table Two) argues that various NOTCH 3 mutations, even if cysteine-sparing, can result in the abnormal protein folding suspected in this syndrome.

Standard gene testing may need to be supplemented by review of recent literature to ascertain correct diagnoses.

REFERENCES