Recognizing and Managing CADASIL

What is CADASIL?

Cerebral **A**utosomal **D**ominant **A**rteriopathy with **S**ubcortical **I**nfarcts and **L**eukoencephalopathy (CADASIL) is a **genetic small vessel disease** caused by mutations in the **NOTCH3** gene.

It is the most common monogenetic cause of stroke and vascular cognitive decline.

Typical Clinical Features

CADASIL has a heterogeneous presentation, age of onset, disease severity and clinical course. The age at onset is typically between 20-50 years. Most will develop symptoms by age 65 years.

- **Migraine with aura** (onset~30s)
- **Recurrent subcortical ischemic strokes** (onset~40s-50s)
- **Mood disturbances or psychiatric symptoms**
- **Cognitive decline** (onsest~50s)
- **Gait disturbance and urinary incontinence** (late stages)
- **Less commonly: Seizures, intracerebral hemorrhage, CADASIL coma**

Treatment Considerations

- No approved disease-modifying therapies currently exist.
- ✓ **Aspirin** monotherapy for secondary stroke prevention is considered safe.
- ⚠ **Avoid anticoagulation** unless a clear unrelated indication (e.g., A-fib).
- ⚠ **Thrombolysis** may be appropriate.
  - Risk-benefit discussion with physicians at the time of stroke
  - Caution if history of cerebral microbleeds
- ✓ Treat hypertension, dyslipidemia, tobacco use, and diabetes per standard guidelines.
- ✓ Migraines, for prevention and abortive treatment, follow guidelines for the general population.
- ✓ Manage mood and psychiatric disorders as in the general population.
- ✓ Contraception and pregnancy should be managed as in the general population.
- ⚠ Use MRI (or CT if MRI not available) to detect characteristic white matter changes.

Genetic Testing & Diagnosis

- Diagnosis confirmed with genetic testing for **mutations in NOTCH3**.
- Brain MRI typically shows **T2 hyperintensities**—some unique areas include the anterior temporal lobes and external capsule.

Guidelines & Resources

- **American Heart Association Scientific Statement (2023)**: Management of Inherited CNS Small Vessel Diseases. DOI: 10.1161/STR.0000000000000444
- **European Academy of Neurology Consensus Recommendations (2020)**: Monogenic Cerebral Small Vessel Diseases. DOI: 10.1111/ene.14183

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