KD Diagnosis and DNA Testing

Introduction: Kennedy's Disease or Spinal and Bulbar Muscular Atrophy (SBMA) is a rare neuromuscular disease caused by mutation in the androgen receptor (AR) gene on the X-chromosome. In men, the disease slowly progresses over decades resulting in loss of skeletal and bulbar muscles with weakness, fasciculations, cramps and difficulties in speech and swallowing. Initial symptoms often include fatigue, muscle cramping, fasciculation, tremor, and muscle weakness. However, in some SBMA patients, difficulty with swallowing (dysphagia) and speech (dysarthria) are observed first. Symptom onset is most common in in men in their 30s and 40s, but can vary from teens to 70s. Disease progression is generally slow, occurring over decades. Some female carriers experience SBMA symptoms, but with less severity than male patients [1].

SBMA patients are often misdiagnosed with amyotrophic lateral sclerosis (ALS). SBMA should be suspected over ALS when: (1) there is a family history suggestive of X-linked inheritance; (2) a male with gynecomastia, which may present at an early age or partial androgen insensitivity (erectile dysfunction, decreased libido, infertility and testicular atrophy); (3) slow progression of symptoms compared to ALS; (4) sensory neuropathy; and (5) absence of upper motor neuron findings on exam [1].

DNA Testing: SBMA diagnosis is confirmed by molecular genetic testing for the CAG trinucleotide expansion in the AR gene on the X-chromosome. Molecular gene testing is 100% sensitive and specific, and readily available in clinical reference laboratories. Symptoms of SBMA are observed in men and some carrier women with 38 or more CAG repeats. If SBMA is suspected, your primary care physician (PCP), OB/GYN, genetic professional, or neurologist can collect a blood/cheek swab sample for DNA testing.

In the US, the Genetic Information Nondiscrimination Act (GINA- 2008) and the Affordable Care act (2010) protect the privacy of individual's genetic information and protect them from health insurance and employment discrimination. It is illegal to discriminate based on genetic status. Genetic testing is a highly personal decision that depends on an individual's health status (presence of symptoms), age, genetic risk status, and personal and/or religious beliefs.

To inquire whether your health insurance covers the genetic testing, call your insurance provider and ask them whether they cover CPT code 81204. We have identified several laboratories in the US that perform the genetic test for SBMA. The genetic testing cost without insurance (out-of-pocket) is $250 to $500.

- GeneDx: AR Repeat Analysis Test (Test Code 820).
- Athena: Kennedy's Disease (SBMA) DNA Test (Test Code 117).
- Prevention Genetics: X-linked Spinal and Bulbar Muscular Atrophy (Kennedy Disease) via the AR Gene CAG Repeat Expansion (Test Code 7501).
- Mayo Clinic Laboratories: Spinobulbar Muscular Atrophy (Kennedy Disease), (Test ID: SBULB).
- In the UK genetic tests van be organized through the NHS following a referral by your GP to a consultant neurologist.

Neurologists and other physicians commonly run a panel of genetic tests to screen for over 200 genetic neuromuscular disorders (muscular dystrophies (MD), inherited myopathies, mitochondrial disorders, congenital myasthenic syndromes, Limb-Girdle MD, Duchenne MD, Becker BMD, Spinal Muscular Atrophy, etc.). However, these standard gene panels may NOT cover SBMA. If SBMA is suspected, your doctor needs to request a separate test that determines the number of CAG repeats in the AR gene, as described above.

If you need financial assistance paying for the DNA test, KDA may be able to help. Please use our Contact Us form with "DNA Test" in the subject line, and we will send you an application form to be completed by your physician and yourself.

Next Steps: If you are diagnosed with SBMA, we encourage you to connect with others that are impacted by this rare disease including:

- Join the Kennedy's Disease Association or Kennedy's Disease UK
- Connect with others on Facebook through
  - KDA and KD-UK
  - Kennedy's Disease Patient group
  - Kennedy's Disease Downunder
  - Kennedy's Disease Raising Awareness
  - Kennedy's Disease Support & Awareness - Canada
  - SBMA JAPAN
  - SBMA Russia
- Attend a KDA or KD-UK conference in-person or online.
- Participate in a ZOOM chat group for SBMA men and carriers.
- Register with CoRDS (Coordination of Rare Diseases at Sanford), a nonprofit, international patient registry for all rare diseases. CoRDS compiles information on rare diseases, connects researchers with patients, and will notify you of emerging clinical trials. The registry is free.

References:

1. Pradat, P.F., Bernard, E., Corcia, P., Couratier, P., Jublanc, C., Querin, G., Morélot Panzini, C., Salachas, F., Vial, C., Wahbi, K. and Bede, P., 2020. The French national protocol for Kennedy's disease (SBMA):consensus diagnostic and management recommendations. *Orphanet J. Rare Diseases*, 15(1), pp.1-21.

Kennedy's Disease Association
www.kennedysdisease.org

Kennedy's Disease UK
www.kd-uk.com