NATURAL HISTORY OF THE DANON DISEASE PHENOTYPE IN A LARGE AFFECTED POPULATION

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Background: Danon disease (OMIM#300257) is a rare X-linked dominant disorder originally described in boys affected with cardiomyopathy, skeletal myopathy, and intellectual dysfunction. Affected females develop cardiac conduction disease and cardiomyopathy later in life. To date, the majority of reports have focused on the severe nature of the cardiomyopathy in single families or small case series.

Methods: We developed a Danon disease registry and a patient-information website (www.danondisease.org) under an IRB protocol in order to identify multiple families affected by Danon disease. Family members are evaluated in person or interviewed by telephone. Reported medical data and family history data are collected and reviewed and we ask about cardiac and non-cardiac signs and symptoms of Danon disease.

Results: To date, 40 families with confirmed or suspected Danon disease have been collected, with the largest pedigree having 14 affected individuals. The average age of first symptom is 8.2 years and 24.4 years for males and females, respectively. The average age of diagnosis is 11.1 years and 33.7 years for males and females, respectively. Cardiomyopathy in boys is predominantly hypertrophic (75%), but dilated disease does occur (8%); in females 46% and 15% have hypertrophic or dilated cardiomyopathy, respectively. Cardiac conduction abnormalities occur in 75% of males and 61.5% of females. Muscle weakness is reported in 82% of males and, somewhat surprisingly, in 62% of females, suggesting that myopathy in females has been under-recognized previously. Extra-cardiac problems include: retinal pigmentary changes (52%), mild cognitive disability (100% males; 38% females), and abdominal complaints (~25%; including pain, diarrhea/constipation).

Conclusions: Based on data from the largest cohort reported to date, Danon disease presents with broad phenotype. Both males and females develop a phenotype with females being diagnosed approximately 2 decades after males. We also noted prevalent skeletal myopathy complaints and mild cognitive concerns in females that have not been reported previously.